UNIVERSITY OF WINCHESTER

Return To Physical Activity After High Tibial Osteotomy With And Without Graft Materials.

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Doctor of Philosophy

August 2020

This thesis has been completed as a requirement for a postgraduate research degree of the University of Winchester.

DECLARATIONS:

No portion of the work referred to in the Thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

I confirm that this thesis is entirely my own work.

I confirm that no work previously submitted for credit has been reused verbatim. Any previously submitted work has been revised, developed and recontextualised relevant to the thesis.

I confirm that pages 75-119 in the thesis have been published in advance of its submission and appropriately referenced in the text.

I confirm that no third party proof-reading or editing has been used in this thesis

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ABSTRACT

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High tibial osteotomy (HTO) is a form of knee surgery that treats painful osteoarthritis. It achieves this by correcting deformity in a malaligned tibia to adjust the weightbearing line through the joint. HTO preserves, rather than replaces, the knee and is therefore particularly relevant for physically active patients. Despite physical activity being a key surgical indication for HTO, previous research shows that most patients only return to physical activity at a level similar to their pre-operative status, and only a small proportion of patients improve any further. The aim of this thesis was to provide a greater understanding of the interaction between HTO and physical activity to improve outcomes after surgery; and to determine the factors that limit post-operative activity participation.

This thesis presents the findings of six original studies plus a systematic review of the literature. The use of graft materials during HTO – both the type of graft material and whether they are necessary at all – is an operative variable that was highlighted as having a potential influence on physical activity levels (Chapters 2 and 4). Biomechanical and clinical studies (Chapters 5 and 6) were conducted to test this. In addition to operative variables, it was clear that other unknown factors influenced the post-operative return to physical activity. Two qualitative studies (Chapters 7 and 8) were conducted in which patients and surgeons were interviewed to determine these factors. Pain and a number of psychosocial variables were commonly identified by patients as having a role in their physical activity behaviours. The surgeons reported that the management of patient expectations is prominent in the information they provide to patients prior to surgery. Areas of contention among surgeons were detected including timelines to achieve post-operative milestones and whether to advise limitations on certain types of physical activity. The final two studies (Chapters 9 and 10) focused on the interaction between return to physical activity, pain, and patient expectations.

Overall, this thesis found that more attention should be paid to improving physical activity outcomes after HTO, since being active is a key indication for the procedure. The use of allograft wedges during HTO is recommended for routine use where possible because they are clinically and biomechanically preferable to the alternatives, allowing patients to return to higher levels of physical activity after surgery. Physical pain is not necessarily a limiting factor for activity participation once recovered from surgery, although a certain residual level is likely. Addressing psychosocial factors and improving the accuracy of patient expectations is likely to result in additional positive activity outcomes after HTO. The implications for the findings presented, and recommendations for areas of future research, are discussed.

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LIST OF ABBREVIATIONS

ACL – Anterior cruciate ligament

ADL – Activities of daily living

APQ – Activity participation questionnaire

ANOVA – Analysis of variance

BMI – Body mass index

BW – Bodyweight

CI – Confidence interval

CONSORT – Consolidated standards of reporting trials

DFO – Distal femoral osteotomy

GP – General practitioner

HIV – Human immunodeficiency virus

HTO – High tibial osteotomy

HSS – Hospital for special surgery

KOOS – Knee injury and osteoarthritis outcome score

LSX – Lateral sensor x-axis

LSY – Lateral sensor y-axis

LSZ – Lateral sensor z-axis

MCID – Minimum clinically important difference

MeSH – Medical subject headings

MINORS – Methodological index for non-randomised studies

MSY – Medial sensor y-axis

MSZ – Medial sensor z-axis

OKS – Oxford knee score

PAR-Q – Physical activity readiness questionnaire

PEEK – Polyetheretherketone

PIS – Pain intensity scale

PRISMA – Preferred reporting items for systematic-reviews and meta-analyses

QoL – Quality of life

RCT – Randomised controlled trials

RPE – Rating of perceived exertion

SD – Standard deviation

TKA – Total knee arthroplasty

UCLA – University of California: Los Angeles

UKA – Unicompartmental knee arthroplasty

VAS – Visual analogue scale

VS – Vertical sensor

RESEARCH OUTPUTS

Outputs from chapters in this thesis

Publications

Belsey, J., Yasen, S.K., Jobson, S., Faulkner, J., and Wilson, A.J. (2020) Return to physical activity after high tibial osteotomy and unicompartmental knee arthroplasty. *American Journal of Sports Medicine*.

Belsey, J., Diffo Kaze, A., Jobson, S., Faulkner, J., Maas, S., Khakha, R., Wilson, A.J. and Pape, D. (2019) Graft materials provide greater static strength to medial opening wedge high tibial osteotomy than when no graft is included. *Journal of Experimental Orthopaedics,* 6, 13.

Belsey, J., Diffo Kaze, A., Jobson, S., Faulkner, J., Maas, S., Khakha, R., Pape, D. and Wilson, A.J. (2019) The biomechanical effects of allograft wedges used for large corrections during medial opening wedge high tibial osteotomy. *PLoS One,* 14(5), 14.

Podium presentations

“Fill the wedge – biomechanical implications”, presented at the 4th Luxembourg Osteotomy Congress, Nov 2018, Luxembourg.

“Does bone grafting increase the static strength of high tibial osteotomy?”, presented at the European College of Sport Science Congress, Jul 2018, Dublin, Ireland.

“Filling the gap”, presented at ESSKA, May 2018, Glasgow, Scotland. (co-author on presentation).

“The use of bone wedge allograft in high tibial osteotomy – a prospective follow-up study of pain and time to union”, The European Society of Sports Traumatology, Knee Surgery & Arthroscopy (ESSKA), May 2018, Glasgow, Scotland. (co-author on presentation).

“Static strength of HTO with and without graft materials: a biomechanical analysis”, presented at the British Association for Surgery of the Knee (BASK) conference, Mar 2018, Leicester, UK. (author of presentation).

Poster presentations

"Static strength of high tibial osteotomy with and without graft materials: a biomechanical study", e-poster at ESSKA conference, May 2018, Glasgow, Scotland.

"The biomechanical effects of allograft wedges used for large corrections during high tibial osteotomy", e-poster at ESSKA conference, May 2018, Glasgow, Scotland.

Outputs external to this thesis

Publications

Diffo Kaze, A., Maas, S., **Belsey, J.,** Hoffmann, A., Seil, R., van Heerwaarden, R. and Pape, D. (2019) Mechanical strength of a new plate compared to six previously tested opening wedge high tibial osteotomy implants. *Journal of Experimental Orthopaedics,* 6(1), 15.

Diffo Kaze, A., Maas, S., Kedziora, S., **Belsey, J.,** Haupert, A., Wolf, C., Hoffmann, A. and Pape, D. (2018) Numerical comparative study of five currently used implants for high tibial osteotomy: realistic loading including muscle forces versus simplified experimental loading. Journal of Experimental Orthopaedics, 5(28), 17.

Diffo Kaze, A., Maas, S., **Belsey, J**., Hoffmann, A. and Pape, D. (2017) Static and fatigue strength of a novel anatomically contoured implant compared to five current open-wedge high tibial osteotomy plates. *Journal of Experimental Orthopaedics,* 4(1), 39.

Poster presentations

"Minimally Invasive Surgery in Knee Osteotomy Achieves Equivalent Radiological Outcomes to Traditional Approaches", e-poster at: ESSKA conference, May 2018, Glasgow, Scotland; BASK conference, Mar 2018, Leicester, England; and BASK conference, Mar 2017, Liverpool, England.

CHAPTER 1 - INTRODUCTION

1.1 2000+ years of lower limb realignment

A knee osteotomy is a joint preserving surgical technique whereby the weightbearing line of an affected leg is altered by realigning either one of, or both, the tibia and femur (Lee and Byun, 2012; Lobenhoffer, 2017). It is mostly used to relieve the symptoms of painful osteoarthritis of the knee. Pain is the result of the weightbearing line passing disproportionately through one side of the knee – normally the medial side – causing accelerated degeneration of the meniscus and cartilage. An osteotomy can be performed to realign a bone, thereby shifting the weightbearing line away from the damaged compartment of the knee over to the healthier undamaged side (Lee and Byun, 2012; Lobenhoffer, 2017). This results in a reduction in pain and delays the need for a knee replacement, while allowing a return to physical activity (Laprade *et al.*, 2012; McNamara *et al.*, 2013).

The concept of correcting deformities in the lower limb dates back to the time of Hippocrates (Kos, Greece; 460-370 BC), who created a traction device that used external pressure to achieve limb realignment (Smith, Wilson and Thomas, 2013). By the 16th century, deformity correction had advanced: it was crudely achieved by breaking the affected bone and bracing it in the position of desired alignment until healing occurred (Smith, Wilson and Thomas, 2013). It was not until the 19th century that a more precise approach was attempted by employing a method of realigning the bone (*osteo*) by cutting (*tomy*), rather than breaking it. John Rhea Barton (Pennsylvania, USA; 1794-1871) is credited as the person who performed the first successful osteotomy in history (Di Matteo *et al.*, 2013; Smith, Wilson and Thomas, 2013). First performed in 1826 for severe ankylosis (stiffness and adhesion) of the hip of a 21 year old man, Barton performed the procedure in just 7 minutes (Barton, 1827). It was 9 years until Barton performed the first known knee osteotomy: this time in just 5 minutes, and without anaesthesia (Di Matteo *et al.*, 2013; Smith, Wilson and Thomas, 2013). Two years later, in 1837, Barton received a letter of thanks from his first knee osteotomy patient, who reported having returned to life as normal: able to practice medicine and ride horseback for miles at a time (Di Matteo *et al.*, 2013). Although what might be defined as "normal life" has undoubtedly changed since the 19th century, the goal of osteotomy as a means of allowing a return to normality remains relevant today.

Where John Rhea Barton pioneered the osteotomy technique, Scottish surgeon Sir William Macewen (Glasgow, UK; 1848-1924) cemented its place in orthopaedic practice by publishing the first book specifically concerning the topic of osteotomy surgery in 1880 (Macewen, 1880). Contained within the book were the results of 1,800 patients who successfully underwent osteotomies of the lower limbs with no subsequent major complications. Osteotomy surgery has regularly been performed ever since. However it lost popularity in the 1970's due to the advent of knee arthroplasty, which at the time boasted superior results and fewer complications (Smith, Wilson and Thomas, 2013). The concept of joint replacement (arthroplasty) rather than joint preservation (osteotomy) can be traced back to Anthony White (London, UK; 1782-1849), who performed the first joint replacement (in the hip) in 1822 (Trebse and Mihelic, 2012). The first knee arthroplasty was subsequently performed by Themistocles Glück (Berlin, Germany; 1853-1942) in 1890 (Trebse and Mihelic, 2012). However it was John Insall (1930-2000) who developed the surgical technique, which resulted in the positive outcomes that outshone osteotomy in the 1970's (Trebse and Mihelic, 2012; Smith, Wilson and Thomas, 2013).

Despite the success of arthroplasty, a small number of osteotomy proponents continued to develop operative techniques, rehabilitation protocols, and methods of assessing post-operative outcomes (Smith, Wilson and Thomas, 2013). Nowadays, knee osteotomy is preferred for young, physically active patients in whom a knee arthroplasty would be less favourable: high activity after knee replacements is associated with an increased risk of prosthesis failure and subsequent revision arthroplasty (Smith, Wilson and Thomas, 2013; Han *et al.*, 2017). Technological advances and developments in the procedures of knee osteotomy have led to positive outcomes and low rates of major complications in recent years (Chahla *et al.*, 2016; Woodacre *et al.*, 2016; Kunze *et al.*, 2019); however the number of osteotomies performed annually is in decline, whereas the incidence of knee arthroplasties is increasing (Wright *et al.*, 2005; Hunt *et al.*, 2014; Elson *et al.*, 2015; Kley, 2020). This is due to a number of factors including: industry pressure, the perception that osteotomies are difficult and high risk compared with arthroplasties, and a low number of centres of excellence and training initiatives for osteotomy surgery (Kley, 2020).

Osteotomies around the knee are an effective procedure that successfully reduce the symptoms of painful osteoarthritis and allow a return to physical activity after surgery (Brouwer *et al.*, 2014; Hoorntje *et al.*, 2017). Preserving the knee, and delaying joint replacement, is more relevant today than ever when considering the physical- and mental-health benefits of physical activity, and the prevalent trend in many countries of an ageing population with an increasing life expectancy. This thesis presents research that adds to the body of osteotomy literature, which can be used to promote the procedure as effective, safe, and current. This will help osteotomy to further assert itself as a discrete treatment that is appropriate for a specific type of patient, distinct from one who would benefit more from an arthroplasty.

1.2 Types of osteotomy about the knee

1.2.1 Distal femoral osteotomy

A distal femoral osteotomy (DFO) is one that is performed in the metaphysis of the distal femur, proximal to the epiphysis. A DFO is performed where there is valgus alignment due to a deformity in the femur that requires correction. This valgus deformity is either a result of congenital malalignment of the bone or as a consequence of lateral compartment osteoarthritis of the knee (Rosso and Margheritini, 2014). The two most commonly performed techniques are medial closing-wedge DFO and lateral opening-wedge DFO (Thein *et al.*, 2012).

In a medial closing-wedge DFO the distal femur is cut twice medio-laterally to within approximately 10 mm of the lateral cortex to allow the removal of a pyramidal wedge of bone. The resultant gap is then gradually closed – being careful to avoid a fracture of the intact lateral cortex, which acts as a hinge – and held in place using a fixation plate and screws (Figure 1.1). In a lateral closing-wedge DFO the distal femur is cut once latero-medially to within approximately 10 mm of the medial cortex. A gap is then prised open – once more taking care to avoid fracture of the contralateral hinge – and is similarly held in place using a fixation plate and screws. By laterally opening or medially closing the distal femur by a margin dependent on the amount of deformity (and therefore the amount of correction needed), the weightbearing line through the knee is shifted from the damaged lateral compartment over to the healthy medial compartment. This realignment relieves the pressures exerted through the lateral compartment of the knee that have been the cause of the painful osteoarthritis. Medial closing-wedge DFO heals more quickly and is recommended where smaller corrections are required, but lateral opening-wedge DFO is technically simpler to perform and results in a more precise correction (Thein *et al.*, 2012; Rosso and Margheritini, 2014).

DFO can also be performed for varus alignment where symptoms of medial compartment osteoarthritis require surgical intervention for relief (Hoorntje *et al.*, 2019). Normally, such symptoms would only be treated with a DFO if congenital malalignment of the femur is the cause. If no such deformity is present in the femur, and a patient displays varus alignment and medial osteoarthritis, an osteotomy in the proximal tibia is more commonly performed (Smith, Wilson and Thomas, 2013).

Figure 1.1: Post-op x-ray of a medial closing-wedge distal femoral osteotomy

(Figures 1.1 to 1.4 used gratefully with permission from Mr Sam Yasen, consultant orthopaedic surgeon at Basingstoke & North Hampshire Hospital)

1.2.2 High tibial osteotomy

A high tibial osteotomy (HTO) is performed in the proximal tibia, distal to the tibial head, normally to treat varus malalignment and medial compartmental knee osteoarthritis (Brinkman *et al.*, 2008). The two most common techniques are medial opening-wedge HTO and lateral closing-wedge HTO (Figure 1.2) (Amendola and Bonasia, 2010; Smith, Wilson and Thomas, 2013). The principal methods of these techniques are much the same as those outlined above for DFO, so will not be repeated here. Once the desired wedge is created, the weightbearing line is consequently shifted from the damaged medial compartment over to the healthy lateral compartment of the knee, relieving painful symptoms (Figure 1.3). In an opening-wedge osteotomy – tibial or femoral – the resultant gap can be left unfilled or a graft material can be inserted (Amendola and Bonasia, 2010). The implications of each surgical option are discussed in more detail throughout this thesis. In cases where patients have severe malalignment due to congenital deformities in both the femur and the tibia, an osteotomy can be performed in both bones – a double osteotomy – in order to achieve the desired alignment (Figure 1.4).

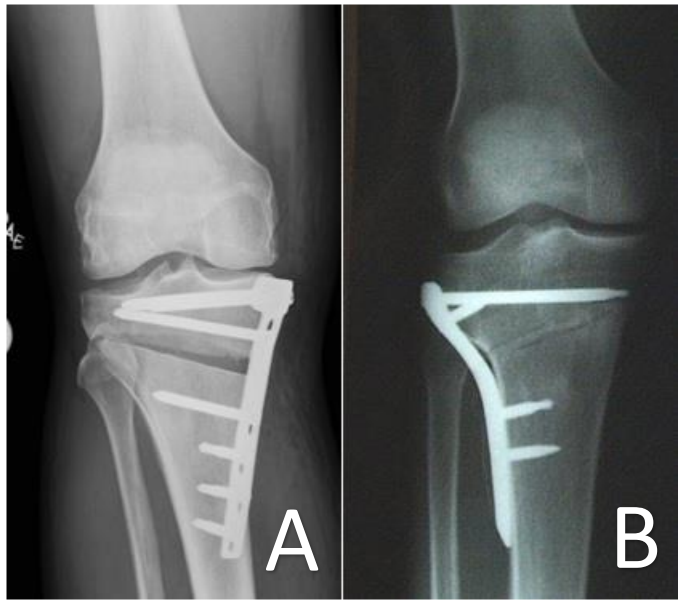

Figure 1.2: Medial opening-wedge HTO (A) and lateral closing-wedge HTO (B)

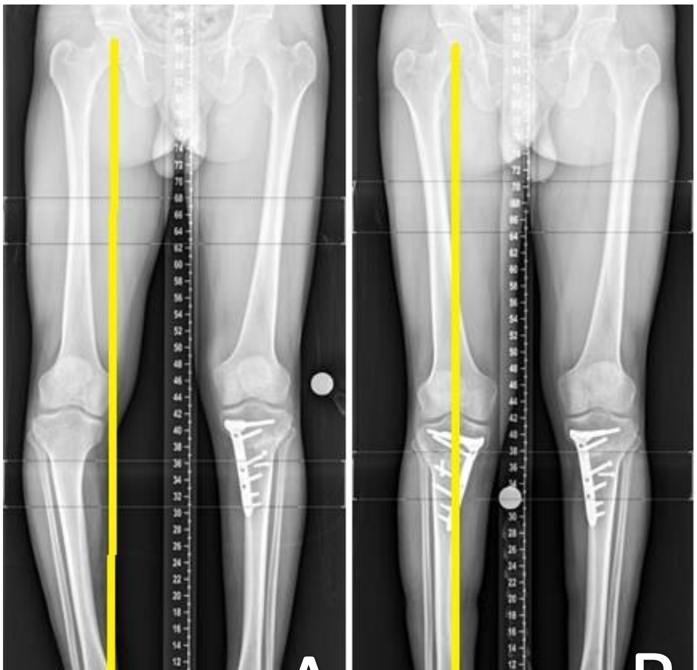

Figure 1.3: X-rays showing the (yellow) weightbearing line pre- (A) and post- (B) medial opening-wedge HTO

Figure 1.4: Double osteotomy for deformity correction in both the femur and the tibia

Lateral closing-wedge HTO was long considered the gold-standard but it requires a fibular osteotomy to be performed in order to access the proximal tibia, making it more technically demanding, plus corrections can only be made in the frontal plane (Brinkman *et al.*, 2008). Furthermore, in large corrections the resultant offset of the proximal tibia can be problematic for later conversion to total knee arthroplasty (Brinkman *et al.*, 2008). Medial opening-wedge HTO avoids the abovementioned issues associated with lateral closing-wedge HTO. It also allows for corrections to be made in the frontal and sagittal planes, and is technically simpler to perform. (Brinkman *et al.*, 2008; Amendola and Bonasia, 2010). Medial opening-wedge HTO has since become the most commonly performed osteotomy about the knee (Amis, 2013) and is the procedure around which this thesis is centred. The results of this thesis will therefore have the potential for greater impact in terms of the number of people they could affect compared to research based on less frequently performed techniques. Where the term "HTO" is used in this thesis, it refers specifically to medial opening-wedge high tibial osteotomy, unless otherwise stated.

1.3 Research aims and questions

A physically active patient is one of the key determinants that points towards osteotomy as a preferable treatment compared to arthroplasty (Shahcheraghi *et al.*, 2007; Bonasia *et al.*, 2014). However, a lack of research in this area means that the impact of HTO on post-operative activity levels is poorly understood. The primary aim of this thesis was to better understand the interaction between HTO and physical activity, with a view to improving outcomes after surgery; and to determine where any activity limitations may be post-operatively.

This thesis begins with a critical literature review to provide an overview of what is currently known about HTO, and to present areas of controversy or gaps in knowledge that may be relevant to post-operative physical activity (Chapter 2). After identifying areas for research in Chapter 2, the direction of the project is contextualised in the methodology (Chapter 3) where the philosophy that underpinned the approaches taken and the methods used is discussed. The relevance of physical activity as a surgical indication specifically for HTO (over arthroplasty) is evaluated in a systematic review presented in Chapter 4, which combines with the preceding two chapters to provide the overall justification for this project.

The remaining studies, which satisfy the primary aim of this thesis, are presented in chapters 5 to 10. The following graphic displays the research questions that are answered in each of these chapters:

Chapter 5

Does the use of graft materials in HTO result in an osteotomy construct that is biomechanically preferable to HTO where the gap is left unfilled?

Do different types of graft material used in HTO result in osteotomy constructs that have different biomechanical properties?

↓

Chapter 6

Do HTO with allograft wedges affect the level to which patients return to physical activity after surgery?

↓

Chapter 7

What are the most common factors that influence patient decisions regarding their return to physical activity post-operatively; and how do they impact on the type and frequency of activity undertaken?

↓

Chapter 8

What are the points of consensus and contention among surgeons regarding the information given to prospective HTO patients and the management of post-operative expectations?

↓

Chapter 9

What is the relationship between pain and physical activity within the first 12 months after surgery?

How soon after HTO are patients able to return to different physical activities and what are the rates of participation?

↓

Chapter 10

Does the intensity of an activity affect residual pain levels after HTO?

Is there a difference in gait during high- and low-impact physical activities between HTO patients and healthy controls, and does this interact with reported pain levels?

Chapter 11 discusses how the findings of chapters 4 to 10 relate to one another, and compares them with relevant literature to demonstrate how the primary aim of this thesis was achieved. The implications of the overall results of this thesis – both clinical and theoretical – are considered, practical applications are recommended, and potential directions for future research are identified. Finally, this thesis concludes in Chapter 12 with a summary of all that precedes it, and a statement hinting at the ever more essential and prevalent role that knee osteotomy is likely to find itself having in the future.

CHAPTER 2 – REVIEW OF THE LITERATURE

"We must spend time in study and in the writings of wise men, to learn the truths that have emerged from their researches, and carry on the search ourselves for the answers that have not yet been discovered." -Lucius Seneca, circa AD 41 (translated by Robin Campbell, 1969)

2.1 Indications for HTO

The type of knee surgery a patient undergoes varies depending on the exhibited symptoms. Opting for an HTO depends on a number of factors that often include (but are not limited to): painful osteoarthritis in only one side of the knee (Kumagai *et al.*, 2017); tibial deformity (Khoshbin *et al.*, 2017); no extreme knee instability/laxity; no severe decrease in range of motion; age less than 60 years (Amendola and Bonasia, 2010); an active lifestyle (Meidinger *et al.*, 2011); body mass index (BMI) of 18.5-24.9 kg/m^2; malalignment of less than 15°; and being a non-smoker (Brinkman *et al.*, 2008). These indications are not exhaustive and the literature shows that HTO can be used in other circumstances such as in patients displaying symptoms in the ankle (Elson *et al.*, 2013). This is a rare occurrence, however, and so will not be further addressed here.

Contraindications for knee osteotomy surgery are normally the inverse of the aforementioned indications but can also include: having undergone prior meniscectomy (Khoshbin *et al.*, 2017) and having bi-lateral osteoarthritis of the knee (Brinkman *et al.*, 2008). There is also limited research showing that being female is a predictor of HTO patients requiring early conversion to total knee arthroplasty (TKA) (Niinimaki *et al.*, 2012; Keenan *et al.*, 2019), possibly suggesting that the sex of a patient should be taken into consideration when assessing treatment options. However, in studies where a majority of females constituted their cohorts (Yim *et al.*, 2013; Kim *et al.*, 2018) clinical outcomes were not necessarily worse than those reported in male-majority articles (Brinkman *et al.*, 2010; Cotic *et al.*, 2015). In summary, it appears that the sex of a patient does not impact upon the short- to mid-term[†] outcomes after HTO, hence the continued inclusion of females in the published literature. However, sex may influence the survivorship of the osteotomy in the long-term. Patients who are contraindicated for knee osteotomy but who still require surgical intervention may be more suited for a unicompartmental knee arthroplasty or total knee arthroplasty (Berger *et al.*, 2005; Mancuso *et al.*, 2016).

2.1.1 Age

The abovementioned indications and contraindications, although generally accepted, have been disputed in the literature due to factors including improvements in surgical accuracy and advancements in technology. Research has sometimes been conflicted with regards to HTO patients needing to be less than 60 years of age to avoid poor outcomes after surgery, although this is the generally agreed consensus. Studies by Trieb *et al.* (2006) and Khoshbin *et*

[†] Reflecting the way that terms are generally used in the literature, throughout this thesis "short-term" = <2 years post-op; "mid-term" = 3-8 years post-op; and "long-term" = >9 years post-op.

al. (2017) concluded that age was negatively associated with survivorship of the HTO. The former study showed a higher failure rate in patients older than 65 years, and the latter study showed a 5% increased risk of eventual total knee arthroplasty for each year above the age of 46 (the median age of their sample). Other research has challenged age as a point for consideration for HTO by showing that it is independent of the surgical outcome (Kohn *et al.*, 2013; Goshima *et al.*, 2017). It should be noted though that the study by Kohn *et al.* (2013) compared two age groups that were already below the recommended upper age limit for HTO of 60 years (median of 42 years and 57 years); so their conclusions do not persuasively challenge the common assertion that age can contraindicate surgery. Goshima *et al.* (2017) evaluated participants at a mean 51 months post-operatively. They found no significant differences in knee alignment or clinical outcomes between patients who were older or younger than 65 years at the time of surgery. This would suggest that age is not a factor that affects outcome in the mid-term. However, it is difficult to draw any concrete conclusions around the impact of age on the final outcome of surgery since positive results within the first 60 months after surgery are to be expected. This is demonstrated by recent studies that reported survival rates ranging from 89-96% at 60 months post-HTO (Hui *et al.*, 2011; Niinimaki *et al.*, 2012; Bode, von Heyden, *et al.*, 2015). To firmly conclude whether age matters for HTO, attention must also be paid to differences in the long-term survival of the procedure. Such research was conducted by Trieb *et al.* (2006) and Khoshbin *et al.* (2017). Both studies reported survivorship with a follow-up of at least 10 years, finding that age was inversely related to the need for a conversion to arthroplasty after HTO. Therefore, it appears that an age <60 years as an indication for HTO remains appropriate for the aim of delaying the need for arthroplasty in the long-term. However, in the short- to mid-term it is not an influencing factor on outcome.

2.1.2 Smoking

Research has shown that smoking negatively impacts bone healing and time-to-union (W-Dahl and Toksvig-Larsen, 2004; Meidinger *et al.*, 2011; Schröter *et al.*, 2015), due to factors such as reduced blood flow to the area and the toxic effect that nicotine has on osteoblasts (Sloan *et al.*, 2010). Conversely, other studies have found no significant differences in the rate of delayed healing or overall knee function between non-smokers and smokers (Niemeyer *et al.*, 2010; Floerkemeier *et al.*, 2014). W-Dahl and Toksvig-Larsen (2004) distinguished between delayed healing and pseudarthrosis (rapid loss of correction) when reporting their instances of non-union, whereas Floerkemeier *et al.* (2014) only reported rates of pseudarthrosis. This could explain why some studies have contradictory conclusions regarding the effects of smoking on bone healing. The results of Schröter *et al.* (2015) showed a trend of delayed healing in smokers compared to non-smokers, but the difference was not statistically significant.

Studies by Floerkemeier *et al.* (2014) and Niemeyer *et al.* (2010) measured knee function outcomes in smokers and non-smokers, with the former study finding comparable outcomes between groups in the short- to mid-term (2-5 year follow-up). The latter study reported that knee function was significantly worse in smokers in the first six post-operative months but that there was no significant difference after the first post-operative year. It is during the first few post-operative months that delayed healing mostly occurs (W-Dahl and Toksvig-Larsen, 2004), therefore the lower knee function in the smokers six months after surgery in the Niemeyer *et al.* (2010) study is unsurprising. As the post-operative follow-up increases, it is similarly unsurprising to see differences in knee function between smokers and non-smokers diminish because healing, including delayed healing, occurs within the first post-operative year (W-Dahl and Toksvig-Larsen, 2004; Han *et al.*, 2015). Overall, studies are equivocal regarding smoking as a contraindication for HTO. It affects outcomes in the short-term, but negative effects are not sustained in the mid- to long-term. Smoking is a factor that should be considered when selecting an appropriate surgical treatment for a patient. But it should not automatically preclude them from HTO if it is the only contraindication they present.

2.1.3 Body Mass Index (BMI)

Having a BMI >30 kg/m^2 is a generally accepted contraindication for knee osteotomy. Research has shown that instances of intra-operative fractures of the contralateral hinge, and post-operative delayed healing, are more common in obese patients than non-obese patients (Meidinger *et al.*, 2011; Yokoyama *et al.*, 2016). Functional outcome scores of HTO have also been shown to be significantly worse in obese patients (Floerkemeier *et al.*, 2014). Such findings suggest that patients with a high BMI, who would otherwise be indicated for an HTO, may benefit from losing weight to lower their BMI before undergoing surgery. Weight loss would reduce the forces exerted through the knee once the patient is able to fully bear weight after their operation, therefore decreasing the stress on the healing osteotomy and reducing the risk of failure (Spahn, Kirschbaum and Kahl, 2006; Hui *et al.*, 2011). Supporting the idea that a high BMI is detrimental to the knee, Jiang *et al.* (2012) conducted a systematic review and meta-analysis of the literature and found a significant increase in the risk of developing knee osteoarthritis for obese people. Additionally, the authors reported that lowering a patient's BMI to <30 kg/m² can reduce, and even prevent, pain and disability caused by osteoarthritis. From this it is logical to assume that obese patients already suffering from osteoarthritis may prevent or delay the worsening of symptoms by similarly lowering their BMI. Although a high BMI may accelerate the degeneration of an osteoarthritic knee, the preclusion of such patients from HTO should be re-evaluated. Recent research has demonstrated that modern types of internal plate fixation allow an osteotomy to be able to withstand forces that exceed those exerted through the knee during standing and normal walking without correction loss or failure of the construct (Maas *et al.*, 2013; Diffo Kaze *et al.*, 2015). Similar to the previously mentioned contraindications (relating to sex, age, and smoking status), a high BMI on its own should not necessarily automatically preclude a patient from HTO.

2.2 Methods of fixation

2.2.1 External fixators

Brinkman *et al.* (2008) and Zhim *et al.* (2005) suggested that the major advantage of external fixation is that the angle of correction can be adjusted post-operatively due to easy access to the external framework. This is particularly useful for large bony deformities that require a gradual correction over time. Studies into the clinical outcomes of knee osteotomy surgery using external fixators have had mostly positive results (Robinson *et al.*, 2011; Mondanelli *et al.*, 2017). They are comparable to studies where internal implants were used: concerning decreases in patient-reported pain, improved limb alignment, and short- to mid-term survival of the osteotomy (Sen, Kocaoglu and Eralp, 2003; Watanabe *et al.*, 2008). In contrast, Brinkman *et al.* (2008) and Rossi *et al.* (2011) highlighted some of the disadvantages of external fixation, which largely related to the impracticality of the device's large size (Figure 2.1). Consequently, the large proportions of external fixators pose an inconvenience for patients, who must deal with having the metal framework around their knee for up to 23 weeks (Viskontas, MacLeod and Sanders, 2006). While internal fixators (explained below) can be left attached to the tibia or femur for much longer periods – not necessarily requiring removal at all (Woodacre *et al.*, 2016; Grünwald *et al.*, 2018) – they are less of a hindrance for daily life than external fixators and are therefore likely to be preferable, particularly if a patient is physically active (Ekhtiari *et al.*, 2016).

The primary factor suggesting that external fixation may not be the optimal option for knee osteotomy is that it is biomechanically inferior to internal fixator plates. Zhim *et al.*

(2005) compared the Puddu Plate (Arthrex, Munich, Germany) (internal fixator) against a Hoffman II external fixator (Stryker Howmedica) by using sawbone tibiae, which each had an opening-wedge HTO performed on them, and was held in place using either device. The osteotomised tibiae were then compressed axially in a cyclical manner to imitate the forces created when walking. While neither the internal nor external devices broke during the testing, the sawbones with the internal device better maintained the correction angle of the osteotomy and could withstand twice as much force before the construct failed (due to fracture of the tibia). The biomechanical difference between fixator types is important as it can be inferred that the use of internal fixation may be beneficial when returning to physical activity post-operatively, particularly for activities that involve large forces being exerted through the knee. The disadvantages of external fixators presented here are likely a major reason as to why internal fixators are prevalent in the vast majority of recent knee osteotomy research (Lash *et al.*, 2015; Hoorntje *et al.*, 2017; Wu *et al.*, 2017; van Heerwaarden *et al.*, 2018; Liu *et al.*, 2019).

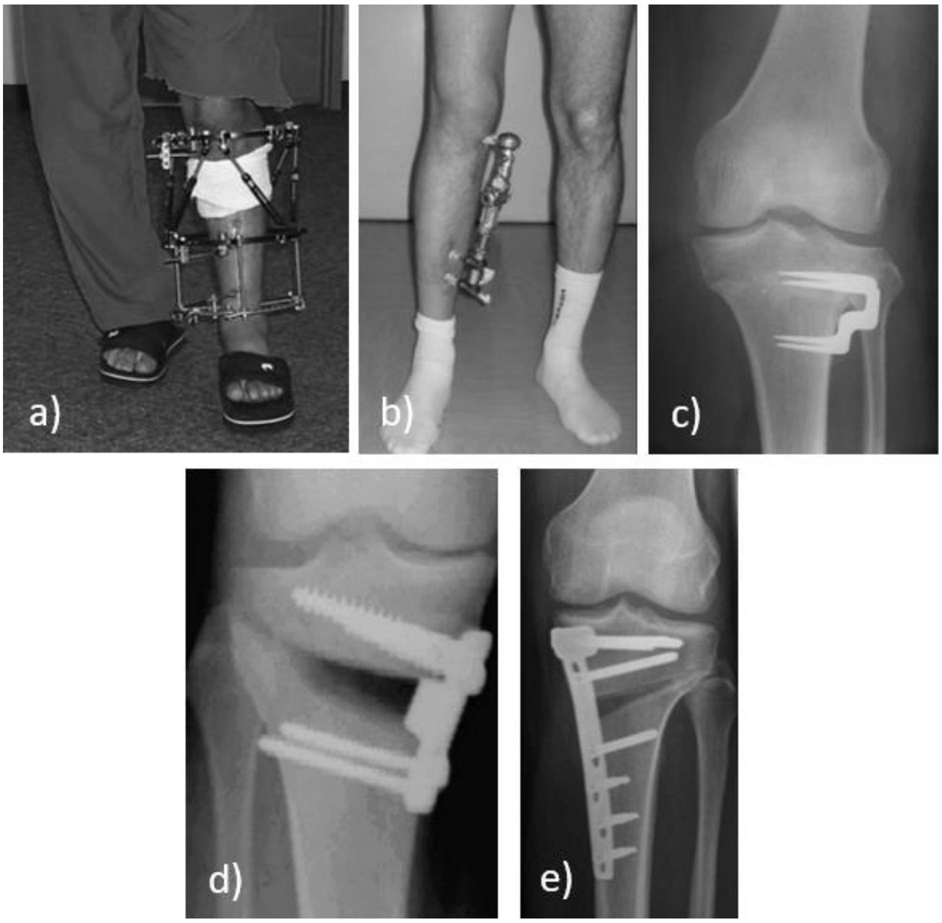

Figure 2.1: Examples of different methods of HTO fixation.

a) ring external fixator (image from Viskontas, MacLeod and Sanders (2006)); b) monoaxial dynamic external fixator (image from Mondanelli et al. (2017)); c) internal staple fixation (image from Brouwer et al. (2006); d) internal spacer plate (image from Nelissen, van Langelaan and Nelissen (2010); e) internal locking compression plate (image from Niemeyer et al. (2010)).

2.2.2 Internal fixators

There are many types of internal implant that have been used in the past including: staples, spacer plates, and locking compression plates (Figure 2.1). Since staples are most often used during closing-wedge HTO (Dowd, Somayaji and Uthukuri, 2006; Punwar and Haddad, 2007; Rossi, Bonasia and Amendola, 2011), and the present project focuses on the increasingly popular opening-wedge technique (Erak *et al.*, 2011; Bonasia *et al.*, 2014), the use of staples will not be further discussed here. Locking compression plates have become known as the gold standard for HTO fixation as many studies have shown them to perform the same or better than the other available options, both clinically (Egol *et al.*, 2004; Zhang *et al.*, 2009; Hernigou *et al.*, 2013; van Heerwaarden *et al.*, 2018) and biomechanically (Gardner, Helfet and Lorich, 2004; Agneskirchner *et al.*, 2006).

The three most researched HTO internal plate fixators are the Tomofix plate (Depuy Synthes GmbH, Oberdorf, Switzerland), and Arthrex's PEEKpower and Puddu plates. Of these, the Tomofix is regarded as the gold standard due to: its ability to allow early weightbearing post-surgery (Pape *et al.*, 2013; Diffo Kaze *et al.*, 2015); its lower associated instances of non-union; its lower complication rates (Cotic *et al.*, 2015); its effective performance when a lateral cortex fracture occurs intra-operatively (Amendola and Bonasia, 2010); and its performance biomechanically (Stoffel, Stachowiak and Kuster, 2004). However, there are other plates that have been shown to provide greater mechanical static and fatigue strength to an osteotomy construct in-vitro than the Tomofix (Table 2.1; Luo *et al.*, 2013; Diffo Kaze *et al.*, 2017).

It should be noted that a plate with higher mechanical strength does not necessarily always equal a superior outcome because a certain amount of micro-movement between the plate and the bone is needed to stimulate bone healing (Diffo Kaze *et al.*, 2018). This perhaps explains why the Tomofix is considered the gold-standard, despite not being the plate that provides the most strength to an osteotomy construct. The data in Table 2.1 were collated from a study by Diffo Kaze *et al.* (2017), where the standard Tomofix was tested against five other available plates. It was shown to be the third strongest plate under static strength testing, and only the fourth strongest during fatigue strength testing. Using a plate that provides suitable strength, while allowing adequate micro-movement between the plate and bone to occur, may have important implications for highly active patients, who require a swift and successful recovery from HTO to return to their chosen activities.

Table 2.1*: Mean vertical load at failure of specimens with various HTO plates (kN ± SD)**

Plate	Static strength testing	Fatigue strength testing
Size 2 Activmotion	8.2 ± 1.0	1.9 ± 0.3
iBalance	5.5 ± 0.2	1.8 ± 0.1
Tomofix (standard)	5.3 ± 0.1	1.5 ± 0.2
PEEKpower	4.4 ± 0.1	1.4 ± 0.1
ContourLock	3.6 ± 0.5	2.2 ± 0.4
Tomofix (small)	3.4 ± 0.3	1.4 ± 0.3

**data from Diffo Kaze et al. (2017)*

The position of the plate on the tibia affects its strength and stability. Blecha *et al.* (2005) found that a plate fixed anteromedially – as opposed to medially – was able to withstand higher axial forces. A new fixator plate, "ActivMotion" (NewClip Technics, Haute-Goulaine, France), is smaller than the Tomofix and is designed so that it can be affixed anteromedially. The previously mentioned study by Diffo Kaze *et al.* (2017) showed that an HTO fixed with an Activmotion plate was able to withstand the most force under static strength testing in comparison to five other types of internal fixation. Four out of the five comparison plates were fixed medially, and one (iBalance) was designed to be positioned within the osteotomy gap (Figure 2.2). The Activmotion plate also provided the highest stiffness to the osteotomy construct while under cyclical fatigue strength testing, which is intended to replicate the forces exerted on the knee during level walking. These findings support those of Blecha *et al.* (2005) regarding the superior biomechanical performance of an anteromedially positioned internal fixation device.

It is also important to consider the implications of an incorrectly positioned plate, since most implants, other than the Activmotion, are not designed to be affixed anteromedially to the tibial head. A recent study by Takeuchi *et al.* (2017) showed that the anteromedial positioning of a plate designed to be fixed medially was biomechanically inferior compared to when the plate was correctly positioned (medially). They noted that the insertion of synthetic bone grafts into the osteotomy gap helped to decrease the added stresses that were observed in an incorrectly anteromedially positioned plate. From the studies of Blecha *et al.* (2005) and Takeuchi *et al.* (2017) it is clear that plate position is important, and that it is necessary to ensure that plates are correctly positioned at the location for which they are designed. This is of particular relevance for plates intended for medial fixation as they appear to be biomechanically inferior to correctly positioned anteromedial plates (Blecha *et al.*, 2005). However, the Takeuchi *et al.* (2017) study showed that the inclusion of a graft material during surgery could help to mitigate any negative biomechanical effects that result from an incorrectly positioned plate designed for medial fixation.

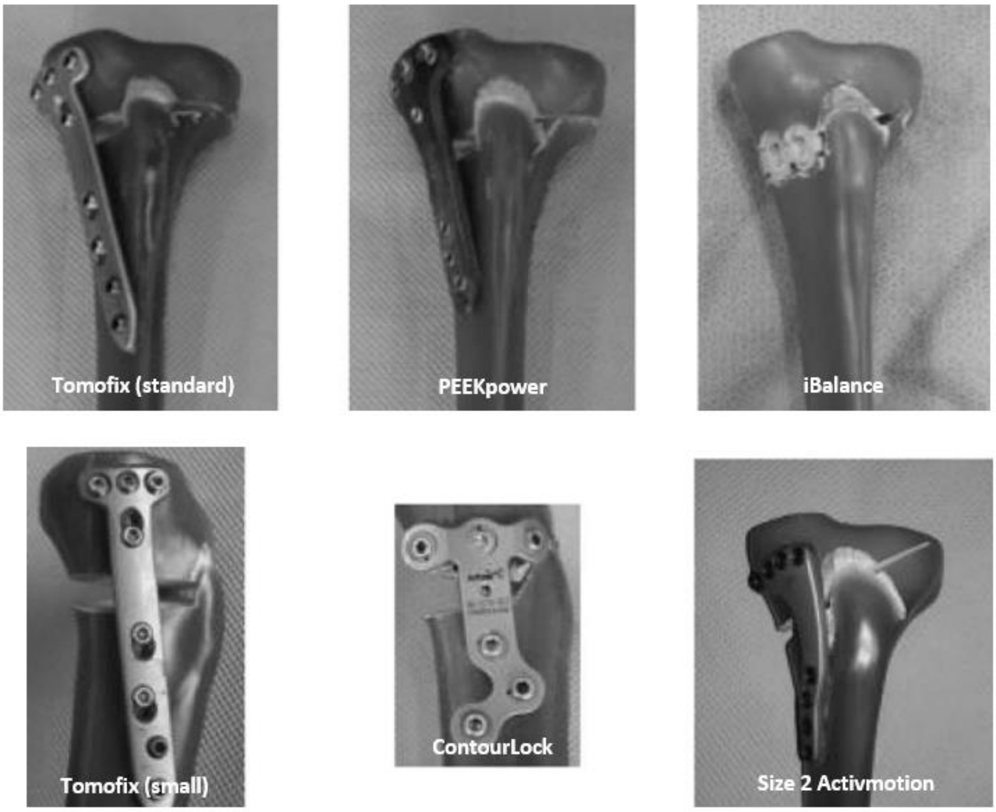

Figure 2.2: The six HTO plates subjected to biomechanical testing by Diffo Kaze et al. (2017)

Another type of internal plate fixator is one that incorporates a metal spacer, which fits into the osteotomy gap, to offer extra support. Multiple studies have shown that this type of plate allows much higher axial forces to be exerted through the knee before the osteotomy fails compared to plates with no spacer (Spahn and Wittig, 2002; Spahn *et al.*, 2006; Amendola and Bonasia, 2010; Han *et al.*, 2014). However, it could be argued that the spacer plate, although biomechanically superior, may inherently not allow complete healing of the osteotomy due to the metal spacer intruding into the gap. Further support is given to this argument by the results of Schröter *et al.* (2011), who reported abnormally high levels of plate-related complications (23%) in their investigation into the clinical outcomes of HTO with a spacer plate. While this type of plate may not be desirable from a clinical perspective, the improved biomechanical properties provided by spacer plates suggests that inserting a material into the osteotomy gap is beneficial. This notion is reinforced by the previously mentioned findings of Takeuchi *et al.* (2017) who found that the insertion of synthetic grafts into the osteotomy gap negated the disadvantages in biomechanical performance caused by an incorrectly positioned plate.

2.3 Bone grafting

Although it is possible for HTO to be performed without the inclusion of a graft material in the osteotomy gap, many surgeons opt to use fillers. Bone grafts for HTO come in a variety of forms; the most common of which include autografts (usually from the iliac crest), allografts (often from the femoral head), and synthetic grafts (generally composed of calcium and phosphate) (Lash *et al.*, 2015). Each graft type has its own advantages and disadvantages, which has led to much controversy in the literature regarding the optimal option; and indeed whether they are necessary at all.

2.3.1 An overview of the different graft types

Autografts are associated with faster healing compared to an unfilled osteotomy gap (Fucentese *et al.*, 2019; Jung *et al.*, 2020), and lower rates of correction loss and delayed- or non-union of the bone when compared to other graft types (Chernchujit *et al.*, 2009; Gouin *et al.*, 2010). Therefore, autograft wedges may be a preferable choice in patients with increased risk of complications or osteotomy failure: smokers and obese patients being two examples (Aryee *et al.*, 2008). The use of autografts, however, increases surgical time and patient-reported pain, as well as the risk of infection and intra-operative complications due to the need for an additional procedure to harvest the graft and its associated donor site morbidity (Amendola and Panarella, 2005; Duivenvoorden *et al.*, 2017). Chae *et al.* (2008) found that the use of autografts during HTO contributed to the prevention of change in posterior tibial slope – likely due to the added support the graft provided the osteotomy – helping to reduce the risk of post-operative loss of correction.

A systematic review by Slevin *et al.* (2016) found differences in the amount that the tibial slope was altered during surgery depending on the type of graft used. A mean increase in tibial slope of 1.4°, 1.6°, and 1.8° was found after HTO with auto-, allo- and synthetic graft, respectively. Slevin *et al.* (2016) also reported a smaller mean increase in tibial slope of 0.9° in HTO without a graft, however this result appeared to come from a single study (Kolb *et al.*, 2009). The authors cited a second study as having reported similar tibial slope changes in HTO without grafts (Jung *et al.*, 2013) but upon closer inspection it presented the data of patients who underwent HTO with either allo- or synthetic grafts. When looking at other studies not included in the Slevin *et* al. (2016) systematic review – which include cases of HTO without graft augmentation – pre- to post-operative mean tibial slope increases as high as 2.1°, 2.5°, and 3.6° can be found (Hoell *et al.*, 2005; El-Azab *et al.*, 2008, 2010). An unintentional change in the tibial slope during HTO can lead to future injury as a result of excessive strain being applied to the soft tissues around the joint: namely the anterior and posterior cruciate ligaments (Savarese *et al.*, 2011; Shelburne *et al.*, 2011; Petrigliano *et al.*, 2012; Amis, 2013; Feucht *et al.*, 2013). The abovementioned results suggest that the inclusion of graft materials during HTO allowed for better control of the tibial slope angle compared with HTO without grafting.

Not only do graft materials reduce unintentional changes in the tibial slope during HTO, there is also limited evidence to suggest that they have further biomechanical advantages (Takeuchi *et al.,* 2010). Takeuchi *et al.* (2010) found that synthetic grafts increased the strength and stability of an osteotomy construct compared to HTO with no graft. Under vertical loading, specimens that included synthetic grafts in the osteotomy gap failed at a mean 4.3 ± 0.4 kN; significantly higher than those without grafts, which failed at a mean 2.5 ± 0.3 kN. Under cyclical loading the specimens with grafts performed better, with the mean stress at the lateral hinge of the osteotomy being significantly lower (2.49 ± 0.2 MPa) than those without grafts (3.31 ± 0.5 MPa). The findings of Takeuchi *et al.* (2010) offer an initial insight into the potential biomechanical advantages of including bone grafts in HTO procedures and the extra protection they may provide to the lateral hinge of the construct. This is of significance for patients who are young or normally physically active – two of the surgical indications for HTO – since they are more likely to participate in activities (such as running) that involve movements involving the exertion of high loads through the knee joint (Besier *et al.*, 2001). As a result, it is crucial that unintentional changes in tibial slope, or a post-operative loss of correction, are avoided where possible. The study by Takeuchi *et al.* (2010) appears to be the first to investigate bone graft use in HTO from a biomechanical perspective and, because of the positive results, further investigation in this area is warranted. It is not known whether differences exist between graft type and the biomechanical support they provide an osteotomy. Such studies would help to better inform the decisions that surgeons make regarding the use of graft materials during HTO.

Synthetic grafts for HTO are generally made from a form of calcium phosphate, hydroxyapatite, bioglass, coralline, or a combination of these (Lash *et al.*, 2015). They may be preferred due to the absence of disease transmission risk that is normally associated with the use of allografts (Amendola and Bonasia, 2010; Hung and Noi, 2012). Regardless, research has shown this type of graft to be associated with higher rates of correction loss and hinge fractures when compared to autografts (Gouin *et al.*, 2010). Han *et al.* (2015) included the Gouin *et al.* (2010) study in their meta-analysis and interpreted this particular finding to mean that the synthetic material was less tolerant to higher stress than autologous bone.

Furthermore, due to the fact that synthetic grafts are not made from real bone, absorption during healing can be slower, and delayed- or non-union of the osteotomy gap occurs more frequently (Amendola and Bonasia, 2010; Gouin *et al.*, 2010; Lash *et al.*, 2015; Nha *et al.*, 2018). According to a systematic review by Lash *et al.* (2015) there is evidence to suggest that rates of superficial wound infection may be higher when certain synthetic grafts are used. A rate of infection of 6.2% was found with hydroxyapatite-tricalcium phosphate synthetic wedges compared with 0.6% for other graft types. However, the authors noted that all of the cases of infection came from one study of 24 knees. In the remaining 4 studies (89 knees) included in the systematic review, which used the same type of synthetic graft, no cases of superficial wound infections were reported.

The use of allograft wedges during HTO has various advantages and disadvantages. A major advantage of using allograft wedges instead of autografts is that the need for a simultaneous second procedure, in which the graft is harvested, is not required. As a result, disadvantages with the use of autografts such as donor site morbidity, severe pain immediately after surgery, greater blood loss, and longer operating time are avoided (Kuremsky *et al.*, 2010; Cho *et al.*, 2013; van Heerwaarden *et al.*, 2018). In addition, the rates of bony union in patients who undergo HTO with allograft wedges are predictable (Amendola and Panarella, 2005). Conversely, one study found rates of osteotomy failure (non-union or loss of correction) to be up to six times higher in patients who underwent HTO with allografts when compared to those with autografts (Kuremsky *et al.*, 2010). This seems to be an extreme anomaly when compared to the majority of the literature (Han *et al.*, 2015; Lash *et al.*, 2015; Slevin *et al.*, 2016). Furthermore, it is difficult to determine whether it was the graft type or size of the osteotomy gap that led to the failures in the Kuremsky *et al.* (2010) study because patients were not randomised into groups based on graft type, and 75% of the failures occurred in osteotomies 11 mm or greater. An alternative, and possibly more valid, interpretation of these findings would be to suggest that the use of allograft wedges may not be optimal for large corrections greater than 10 mm. Other research has supported this inference by showing a positive correlation between allograft wedge size and time-to-union (Jung *et al.*, 2010; Santic *et al.*, 2010), though it should be noted that they were not comparative studies and included no control groups. Further research is needed to determine whether this correlation is caused by the allograft wedges, the size of the gap, a combination of both, or some other factors.

2.3.2 Non-union, delayed union, and time-to-union

The sample in the abovementioned study by Kuremsky *et al.* (2010) resulted in failure due to non-union of the osteotomy in almost 30% of the 51 knees that underwent HTO with an allograft wedge, compared with 5.3% of the 19 knees included in the autograft group. While this finding alone is dramatic regarding the usefulness of allograft wedges in HTO, it is a rather extreme anomaly compared to the majority of the literature (Han *et al.*, 2015; Lash *et al.*, 2015; Slevin *et al.*, 2016). This claim is supported by a systematic review by Lash *et al.* (2015) who found that non-union occurred only 4.6% of the time in 895 knees that underwent HTO with allograft wedges compared with 2.6% of the 787 knees with autografts. While these results still showed a statistically significant difference between the non-union rates of allograft and autograft wedges, the difference was vastly lower than that reported by Kuremsky *et al.* (2010). Furthermore, a meta-analysis by Han *et al.* (2015) showed lower rates of non-union in HTO with both autograft (0/230 knees) and allograft wedges (2/402 knees). Despite the reported difference in rates of non-union between allograft and autograft, the systematic review of Lash *et al.* (2015) and the meta-analysis of Han *et al.* (2015) demonstrated that the likelihood of non-union occurring with an allograft wedge is extremely low. It could be argued that the slightly higher rate of non-union for allografts versus autografts is an acceptable risk – since it is still very low in absolute terms – and one that makes them preferable when considering the previously described disadvantages associated with the use of autografts (increased operating time, donor site morbidity, increased pain).

When observing rates of delayed- and non-union in HTO with synthetic augmentation, there is much variation in results depending on the synthetic compound of which a graft is composed. Lash *et al.* (2015) found non-union to occur 21.6% of the time with bioglass wedges, while hydroxyapatite had a non-union rate of 0%. On average, synthetic grafts, regardless of their material, exhibit higher rates of delayed- or non-union than auto- and allografts (Lash *et al.*, 2015; Slevin *et al.*, 2016). A final study recommended against the use of synthetic wedges in HTO based on results that showed statistically significant increased rates of non-union when synthetic grafts were used compared with HTO without grafting (Ferner *et al.*, 2016).

In cases where union does occur, HTO with autograft or allograft wedges heal at a similar rate: mean time-to-union in HTO with autografts was found to be 3.1 months, and for HTO with allografts it was 3.8 months (Lash *et al.*, 2015). However, Han *et al.* (2015) found slightly different results in their meta-analysis where time-to-union in HTO with allograft wedges was 4-6 months. Autografts, though, resulted in a similar union period of 3 months.

The apparent difference in findings for time to union in HTO with allograft wedges can be explained when looking at the individual studies from which the Lash *et al.* (2015) systematic review and the Han *et al.* (2015) meta-analysis drew their data. Two of the studies, only included in the Lash *et al.* (2015) review, found that 100% of osteotomies with autografts had healed within 3 months (Ribeiro *et al.*, 2009; Megied *et al.*, 2010). One further study that was included in both the Lash *et al.* (2015) review and the Han *et al.* (2015) meta-analysis reported the same time-to-union (3 months), but in just 95% of cases (Noyes *et al.*, 2006). A final study, only included in the Han *et al.* (2015) meta-analysis, reported time-to-union at a mean of 3 months (Shim *et al.*, 2013). To summarise, studies consistently reported a time-to-union of around 3 months where autografts were used.

When analysing studies that investigated time-to-union in HTO with allografts, one reported bony union at a mean of 3 months (Yacobucci and Cocking, 2008) and a second reported that healing occurred within 6 months (Santic *et al.*, 2010). Both studies were included in the Lash *et al.* (2015) review and the Han *et al.* (2015) meta-analysis. In the study by Santic *et al.* (2010), it was also reported that there was a positive correlation between healing time and osteotomy gap size. The authors furthered their analysis and found that bone grafts up to 9 mm in size healed within 3 months in 200/221 (90%) of cases. The mean osteotomy gap size in the Santic *et al.* (2010) study was 8.6 ± 2.0 mm, suggesting that mean time-to-union for the whole cohort may have been around 3 months. Additionally, 224/304 (74%) of the overall sample, regardless of gap size, had achieved union within 3 months. However, the Han *et al.* (2015) meta-analysis only reported the time it took for <u>all</u> cases in the Santic *et al.* (2010) study to achieve radiological union (6 months) rather than the likely average (3 months). Consequently, the data regarding time to union in the Han *et al.* (2015) meta-analysis only provide an estimate of the absolute maximum time to achieve union rather than the average.

The findings of Santic *et al.* (2010) were supported by another study included in the Lash *et al.* (2015) review that made similar associations between gap size and time-to-union (Jung *et al.*, 2010). The consolidation of a 7 mm gap, filled with an allograft wedge, occurred within 3 months in 91% of cases; whereas this was only the case 52.6% of the time in 13 mm osteotomies. One further study (Haviv *et al.*, 2012) reporting time-to-union in HTO with allograft wedges was included in the Han *et al.* (2015) meta-analysis but not in the Lash *et al.* (2015) systematic review. In the meta-analysis, it was reported that the Haviv *et al.* (2012) study found allograft time-to-union to be approximately 6 months. However, the Haviv *et al.* (2012) study, which had a mean follow-up of 6.3 years, only stated that "full incorporation" of the allografts had occurred by the final follow-up. It did not report on the actual time taken before the HTO with allograft augmentation achieved bony union and so it is therefore unknown where the Han *et al.* (2015) claim to that effect about the Haviv *et al.* (2012) cohort originated. This more detailed investigation of the papers included in the Lash *et al.* (2015) review and the Han *et al.* (2015) meta-analysis begin to demonstrate an explanation for their differing findings, particularly concerning the time-to-union of HTO with allograft augmentation. When considering all of these points, the findings of Lash *et al.* (2015) appear to better reflect the reality regarding mean time-to-union in HTO with autografts (3.1 months) or allografts (3.8 months).

Results of the time-to-union of HTO with synthetic grafts varies greatly, ranging from 2 months (Koshino, Murase and Saito, 2003) to 12 months (Ozalay *et al.*, 2009). Other studies have reported mean bony union occurring at 3 months (Hernigou and Ma, 2001), 4.5 months (Hernigou *et al.*, 2013), and 6 months (Gouin *et al.*, 2010). There are two main possible explanations as to why such variation is reported in the literature: 1) there is variation in the material of the synthetic graft; and 2) there is a variation in the definition of "union" across research studies. Despite the many types of material used to create synthetic grafts, results are often conflated under the umbrella term "synthetic grafts" when comparing them against auto- or allografts (Lash *et al.*, 2015; Slevin *et al.*, 2016). By doing this, conclusions drawn from such aggregated data perhaps lack efficacy and do not offer a true reflection of the performance of certain synthetic grafts. When looking at individual studies, it would seem that hydroxyapatite wedges could, in fact, be a viable competitor to allografts and autografts since 0% non-union (Lash *et al.*, 2015) and 2 months time-to-union (Koshino, Murase and Saito, 2003) are better than, or comparable to, results in some of the abovementioned studies involving auto- and allografts. Further research into the different types of synthetic graft is required to confirm this speculation.

The main goals of the use of bone grafting during HTO are to facilitate bone healing, decrease blood loss, and increase construct stability (Lash *et al.*, 2015; van Heerwaarden *et al.*, 2018), therefore it is not recommended to base graft selection purely on the results of time-to-union. The literature tends to show that autografts are appropriate to fill larger osteotomies (>10 mm) since they consistently heal within approximately 3 months. However, an argument can be made that allograft wedges are preferable because they perform reliably regarding bony union – similar to autografts and better than synthetic grafts – while avoiding the disadvantages associated with the other two types. Furthermore, the disadvantages associated with allografts – disease transmission and required access to a bone bank – are low risk in terms of patient wellbeing and outcome. For example, the risk of disease transmission from an allograft is 1:1,500,000 for HIV, 1:100,000 for Hepatitis B, and 1:60,000 for Hepatitis C (similar to the risks associated with blood transfusions) and is now considered to be a historical complication (Hung and Noi, 2012; Slevin *et al.*, 2016; van Heerwaarden *et al.*, 2018). Considering that the disadvantages associated with autografts (prolonged operative time, donor site morbidity) and synthetic grafts (increased rates of non-union) have been shown to be relatively common occurrences (Smith, Wilson and Thomas, 2013; Lash *et al.*, 2015; Slevin *et al.*, 2016; Sarman *et al.*, 2019), allograft wedges may be preferable alternatives with low risk disadvantages, assuming they are readily available to a surgeon.

2.3.3 Clinical outcomes

Regardless of graft type, or whether a graft is inserted in the osteotomy gap at all, the literature overwhelmingly suggests that clinical outcomes of the knee significantly improve pre- to post-operatively (Lash *et al.*, 2015; Slevin *et al.*, 2016). However, when examining differences in HTO without grafts and between graft types – notwithstanding the abovementioned issues regarding the umbrella term “synthetic grafts” – the data from two systematic reviews suggests that little-to-no difference exists in terms of outcome (Lash *et al.*, 2015; Slevin *et al.*, 2016). The mean follow-up times in the systematic reviews were 41 months (Slevin *et al.*, 2016) and 42 months (Lash *et al.*, 2015) so this conclusion should be refined to suggest that clinical outcome of HTO is not affected by graft type, or the absence of a graft, in the mid-term after surgery. Additionally, a single study found no association between the inclusion of a bone graft and long-term survivorship of the osteotomy (Khoshbin *et al.*, 2017). This suggests that outcomes in the longer-term are similarly not negatively affected by bone grafting during HTO. Given that bony union occurs within the first 12 months in the vast majority of cases, with the exception of when certain synthetic graft types are used (Lash *et al.*, 2015), it is unsurprising that differences in outcomes past this point tend to be insignificant. It is unclear which graft type was used in the Khoshbin *et al.* (2017) study and comparative investigations examining differences between graft type and HTO survivorship are lacking. By interpreting separate studies, it can be inferred that graft type probably does not impact survivorship of HTO – where a conversion to total knee arthroplasty is the endpoint – since findings show a 10 year survivorship of 83% in HTO with autograft (Ekeland *et al.*, 2017), 85% in HTO with synthetic (acrylic) grafts (Hernigou and Ma, 2001), and 88% in HTO without grafting (Darees *et al.*, 2018). There does not appear to be a similar long-term comparison for HTO with allograft wedges but one study reported survivorship at 8 years post-operatively as

70% (DeMeo *et al.*, 2010). Although this final figure is lower than those for the other graft options, a comparative study has yet to be conducted to specifically assess the impact that different graft types may have on survivorship, making it difficult to draw firm conclusions.

When analysing comparative studies that presented data based on a shorter term post-operative follow-up, differences between grafting options begin to emerge. Cho *et al.* (2013) compared outcomes between HTO with autografts and allografts, finding that the autograft group reported significantly higher pain levels immediately post-operatively (Table 2.2). However, no further difference in pain existed between groups after 2 weeks, 6 weeks, or at final follow-up (mean 28 months). Similarly, no difference between groups existed when assessing knee function using a Knee Society Score questionnaire. Pain was found to be a longer lasting symptom of the inclusion of calcium phosphate synthetic wedges versus autografts in a study by Gouin *et al.* (2010). Visual Analogue Scale pain scores were significantly worse (higher) in the synthetic graft group 3 months post-operatively, but this difference no longer existed at 6 months (Table 2.2). Knee Society Scores, which record changes in function, were also significantly worse (lower) in the synthetic group 3 months after surgery. No differences in knee function were apparent at final follow-up (mean 45 months), which is consistent with the findings of the systematic reviews of Lash *et al.* (2015) and Slevin *et al.* (2016). The differences found by Gouin *et al.* (2010) in the short-term lend further credence to the suggestion that graft type has the largest impact on outcome during the initial healing period. Additionally, Lind-Hansen *et al.* (2016) found generally worse (lower) scores after 12 months, according to the Knee Injury and Osteoarthritis Outcome Score (KOOS), in patients receiving injectable calcium phosphate cement into the osteotomy gap compared to those who received an autograft. Notably, a statistically significantly lower KOOS sub-score signifying “quality of life” was found in the synthetic graft group after 12 months (Lind-Hansen *et al.*, 2016).

Table 2.2: *Mean acute post-op Visual Analogue Scale pain scores with different graft types.*

Study	Graft type	Pre-op	Post-op	6 weeks	3 months	6 months
Gouin *et al.* (2010)	Autograft	5.8	5.6	2	2.1*	2
	Synthetic	5.6	5.5	2.1	3.1*	1.7
Cho *et al.* (2013)	Autograft	3.4	5.7**	2.1	not reported	not reported
	Allograft	2.7	4.5**	1.8	not reported	not reported

**significant difference (p=0.04)*
***significant difference (p=0.01)*

Clinical outcomes appear to be most affected by graft type within the first 12 months post-operatively. Past this point, differences tend to diminish (Gouin *et al.*, 2010; Slevin *et al.*, 2016). Synthetic grafts result in higher pain levels than autografts, which in turn are initially associated with higher pain levels than allografts. Improvement in knee function is typically similar in patients who undergo HTO with auto- or allografts, but is worse within the first 6-12 months in patients who receive a synthetic graft. Synthetic grafts are associated with lower reported quality of life in the first 12 months post-operatively, which may be linked to the observed poorer improvement in knee function. Quality of life and physical activity are positively associated (Bize, Johnson and Plotnikoff, 2007). Research is warranted to investigate the links between improvement in knee function, graft type (including the absence of a graft), physical activity levels, and quality of life in order to optimise reported outcomes during the acute post-operative period.

2.4 Post-surgery rehabilitation

Post-operative rehabilitation and physiotherapy is necessary for a prompt and full recovery after corrective surgery of the lower limbs (Schröter *et al.*, 2017). Concerning HTO, there has been a rapid improvement in (and increased number of) fixation methods that allow patients to fully bear weight on the operated leg sooner after surgery (Aalderink, Shaffer and Amendola, 2010; van Heerwaarden *et al.*, 2018). However, research into rehabilitation and early weightbearing after knee osteotomy is limited. Of the available research, findings showed earlier pre- to post-operative improvements in terms of knee function and pain (Schröter *et al.*, 2017), and positive radiological findings regarding maintenance of correction (Takeuchi *et al.*, 2009), where early weightbearing rehabilitation protocols were employed.

The study conducted by Schröter *et al.* (2017) sought to determine the differences in the reported clinical outcomes of patients who were allowed to fully bear weight 11 days post-surgery (*n*=49), and those who were instructed to partially bear weight on their treated knee for the first 6 weeks after HTO (*n*=48). The results showed greater improvements in patient-reported clinical outcomes in the early full weightbearing group. None of the osteotomies performed in the study included the use of a graft. A study by Takeuchi *et al.* (2009), however, did insert synthetic grafts into the osteotomy gap in their patient cohort. It found that a rehabilitation program focused on early weightbearing resulted in patients being able to fully bear weight as soon as two weeks after surgery without the occurrence of complications such as a loss of correction, implant failure, or lateral cortex fracture. Both studies showed similar results regarding full weightbearing post-HTO, despite differences in the operative procedure concerning the use of a graft material. It is not known if there is a significant difference between the use of graft materials and the time it takes to return to full weightbearing, however if the minimal differences between the results in these two studies are to be used as a guide, it could be hypothesised that the use of graft materials during HTO does not affect the time it takes for patients to be able to fully bear weight after surgery.

2.5 Loading of the knee during sport and physical activity

Peak ground reaction forces, and knee joint forces, differ depending on the type of physical activity performed (Cavanagh and Lafortune, 1980; Taylor *et al.*, 2004). Level walking has been found to involve forces of 2.5 to 3 times bodyweight (BW), with stair climbing and stair descending producing mean peak forces of 3 to 5.5 times BW (Taylor *et al.*, 2004) and 3.5 times BW (Kutzner *et al.*, 2010), respectively. In regard to the forces of more dynamic movements, mean vertical peak forces of running (Cavanagh and Lafortune, 1980), jumping and landing (Cleather, Goodwin and Bull, 2013) have been shown to be up to 3 times BW, 6.9 times BW and 7.6 times BW, respectively.

Since different movements in daily life and in sporting activities load the knees with varying levels of force, it is necessary to investigate and compare these with the forces that osteotomies can withstand. Diffo Kaze *et al.* (2017) showed that different internal fixation plates for HTO enable the construct to withstand static vertical forces higher than those generated through slow walking (approximately 2.4 kN). Under fatigue strength testing, each plate type (except one) provided enough support to the osteotomy construct to survive 80,000-173,000 cycles prior to failure. Considering that an average person produces one million cycles of the lower limb in a year (Baleani, Traina and Toni, 2003), this equates to most plates being able to support a fully-loaded osteotomy construct for 4-8 weeks post-operatively. It is important to note that this study was conducted *in-vitro*, using sawbone tibiae, meaning that no healing of the osteotomy had taken place prior to testing in conditions designed to simulate full weightbearing during dynamic activities. As previously discussed, *in-*

vivo studies only allowed full weightbearing activities 11 days after surgery at the earliest (Schröter *et al.*, 2017), suggesting that plates could provide increased structural support to an osteotomy for 4-8 weeks from this point. Given that healing begins to occur after 3-4 weeks (Marsell and Einhorn, 2011), it can be inferred that most HTO plates provide suitable support to the osteotomy construct during the initial phases of healing. The findings from Diffo Kaze *et al.* (2017) should only be used to approximate efficacy *in-vivo* since they resulted from an *in-vitro* investigation. The osteotomy gap was left unfilled in all cases in this study and, when considering the previously described work of Takeuchi *et al.* (2010), it may be possible that the insertion of a bone graft to the osteotomy increases stability enough to withstand loads comparable to the ones generated through more vigorous activities such as stair climbing or fast walking. If graft augmentation during HTO is able to provide greater axial strength and stability to the tibia while the osteotomy is healing (comparable to the forces involved in daily life activities and sporting movements) then physically active patients may be able to return to their activities more quickly, with a lower risk of post-operative complications such as a loss of correction or lateral cortex fracture. This speculation reflects a similar hypothesis noted in the concluding statements of Akiyama *et al.* (2016). They reported positive results using the novel technique of including autografts in the form of osteophytes about the knee joint rather than from the (gold standard) iliac crest. This method therefore avoided the added complications and initial increased pain associated with a second incision being performed when harvesting an autograft from the iliac crest. The study reported bone healing at a mean 5.3 weeks post-operatively and concluded with the suggestion that the quicker healing period allowed for earlier weightbearing and a sooner return to activities after surgery.

A further point for consideration is the ability for correction to be maintained in cases where lateral hinge fractures occur. Hinge fractures can occur either intra-operatively or post-operatively. Research suggests that intra-operative hinge fractures occur from 4% (Miller *et al.*, 2009) to 39% (Schröter *et al.*, 2015) of the time. The incidence of post-operative lateral hinge fractures ranges from 4% (Miller *et al.*, 2009) to 15% (Dexel *et al.*, 2017). Since it is not extremely rare for hinge fractures to occur – and since they impact primary stability of the construct, thereby increasing the risk of further complications (Meidinger *et al.*, 2011) – methods of optimising stability with the use of bone grafting in case of a hinge fracture should be investigated. This will be of particular benefit to patients wishing to resume physical activity sooner after surgery.

2.6 Gait

Gait is another physical variable affected by HTO and is therefore a factor to consider when examining a patient's ability to resume physical activity post-operatively. During normal walking, loads are largely exerted on the medial compartment of the knee (Amis, 2013). Since HTO achieves its goal of reducing the symptoms of medial osteoarthritis by shifting the weightbearing line laterally, thus unloading the medial compartment of the knee (Amendola and Bonasia, 2010), it is not illogical to expect changes in gait to occur after surgery. Measuring gait parameters in patients with knee osteoarthritis has been shown to be a reliable method of assessing surgical outcome (Fransen, Crosbie and Edmonds, 1997). Furthermore, gait analysis may be more sensitive to changes in surgical outcome in the acute post-operative period compared to the commonly implemented patient-reported outcome questionnaires (Borjesson *et al.*, 2005). However, it seems that only a small proportion of the literature includes gait measurements when reporting outcomes of HTO, despite having previously been recommended as a simple yet conclusive method of evaluation (Ivarsson and Larsson, 1989). This could be due to reasons such as the cost of purchasing equipment, or feasibility issues regarding the extra time commitments necessary from both staff and patients to analyse gait.

A systematic review and meta-analysis of changes in the gait of HTO patients (Lee *et al.*, 2017) found that walking speed and stride length generally increased, while knee adduction moments and lateral thrust decreased, pre- to post-operatively. Individual studies have demonstrated similar results and have additionally showed that the stride length and walking speed of patients, in the short- to mid-term after surgery, was similar to that of healthy controls (Wada *et al.*, 1998; Lind *et al.*, 2013; van Egmond *et al.*, 2017; Whatling *et al.*, 2019). Other studies demonstrated that further gait parameters such as knee adduction moments changed from being greater than control values pre-operatively to lower than control values post-operatively (Noyes, Barber-westin and Hewett, 2000; Lind *et al.*, 2013; Birmingham *et al.*, 2017). A recent study by Morin *et al.* (2018) found evidence to the contrary regarding adduction moments, however the patients in their series did not show significant pre- to post-operative changes in the spatiotemporal gait parameters, suggesting that no normalisation (compared to age-matched controls) occurred. Where a change in knee adduction moment is reported, studies have demonstrated that the surgery successfully reduced the contact pressure in the medial compartment of the knee (DeMeo *et al.*, 2010; Leitch *et al.*, 2015). Overall, the literature suggests that HTO causes a normalisation of spatiotemporal gait parameters compared to healthy controls (Lind *et al.*, 2013; van Egmond *et al.*, 2017), which comes at the expense of an overcorrection in the knee adduction moment.

2.7 Scoring patient-reported outcomes

Patient-reported outcomes for knee osteotomy are normally measured using different questionnaires, which help to determine clinical outcomes and the level of success of the operation. The Knee injury and Osteoarthritis Outcome Score (KOOS), the Hospital for Special Surgery (HSS), and the Oxford Knee Score (OKS) are questionnaires that are often used in the literature that help to assess a patient's post-operative symptoms, stiffness, pain, function, and quality of life (Pfahler *et al.*, 2003; Schallberger *et al.*, 2011; Floerkemeier *et al.*, 2013; Ferruzzi *et al.*, 2014; Sischek *et al.*, 2014; Bode *et al.*, 2015; Goshima *et al.*, 2017). They consist of questions pertaining to the previously mentioned aspects, and patients provide answers using a Likert-scale multiple choice system. From this, an overall score is calculated to determine the status of a patient regarding the condition of their knee and the outcome of the surgery.

The KOOS is also able to assess the extent to which patients participate in physical and recreational activities by subjectively measuring the difficulty a patient experiences while performing certain movements: squatting, running, and kneeling, for example. As such, the KOOS is a useful tool to use when investigating return to physical activity after HTO. Additionally, other patient-reported outcome scores aim specifically to determine the level at which a patient participates in physical activity: the Tegner activity scale and University of California, Los Angeles (UCLA) activity scale are commonly used. Like the KOOS, the Tegner and UCLA scores have been validated for use in clinical settings and are often cited in the literature (Salzmann *et al.*, 2009; Schröter *et al.*, 2013; Saragaglia *et al.*, 2014; Faschingbauer *et al.*, 2015; Nerhus *et al.*, 2017). They differ from the 5 point Likert-scales of the KOOS as they consist of a scale from zero (Tegner) or one (UCLA) to ten, where the lowest number denotes a patient being totally inactive because of their injured knee, and ten signifies either: competition at the elite or international level (Tegner), or regularly participating in impact activities (UCLA). Due to the sole focus of these scores on patient activity levels, they are a vital tool to be used during patient-involved investigations into physical activity after HTO.

The UCLA score is also commonly used with patients who have undergone knee arthroplasty. Recent systematic reviews investigating return to sport after unicompartmental and total knee arthroplasty reported that UCLA scores were used in 19 out of 39 (49%) included studies (Papalia *et al.*, 2012; Waldstein *et al.*, 2017). Whereas, in a systematic review into return to sport after HTO (Ekhtiari *et al.*, 2016), only one study of the 19 reviewed articles included the UCLA score within its clinical evaluation. Including the UCLA score as well as the

Tegner score more in HTO research would be useful to allow for estimated comparisons between the outcomes of HTO and unicompartmental knee arthroplasty to be made (in lieu of comparative studies). This is of particular importance since being physically active is one of the key differences in the classic indications for HTO and against arthroplasty (Zuiderbaan *et al.*, 2016); something that has been challenged more in recent studies (Pandit *et al.*, 2011; Campi, Pandit and Oosthuizen, 2018; Rogriguez-Merchan and Gomez-Cardero, 2018; Vasso, Antoniadis and Helmy, 2018). Currently, only limited data exist that have directly compared HTO and unicompartmental knee arthroplasty regarding physical activity outcomes, with varying results (Yim *et al.*, 2013; Krych *et al.*, 2017).

2.8 Physical activity and osteotomy

There is a positive correlation between health-related quality of life and physical activity (Vuillemin *et al.*, 2005; Acree *et al.*, 2006; Bize, Johnson and Plotnikoff, 2007; Filbay *et al.*, 2017), therefore it is of great importance for patients to have the option of being active post-operatively without being limited by their operated knee. Previous systematic reviews showed that 76-94% of patients returned to physical activity at a level equal to, or higher than, their pre-operative status (Ekhtiari *et al.*, 2016; Hoorntje *et al.*, 2017; Kunze *et al.*, 2019). The meta-analysis by Kunze *et al.* (2019) showed that this statistic largely consisted of patients who equalled their pre-operative activity levels (66%) where only a relatively small proportion of patients (10%) achieved a pre- to post-operative increase in activity levels at a mean 5.2 ± 5.1 years after HTO. In contrast, Hoorntje *et al.* (2017) conducted a meta-analysis and showed that the vast majority of patients (85%) did, in fact, achieve a pre- to post-operative increase in activity levels at a similar follow-up time (mean 4.8 years).

The stark difference in results between these two meta-analyses is likely explained by the definition of the word "level" when reporting physical activity levels. Hoorntje *et al.* (2017) observed a shift in high-impact to low-impact activities post-operatively, whereas Kunze *et al.* (2019) analysed data largely from activity scales (Tegner and UCLA). On the Tegner and UCLA scales, high-impact activities tend to equal higher levels of activity and low-impact activities tend to equal lower levels of activity. A pre- to post-operative shift from high- to low-impact activities – as observed by Hoorntje *et al.* (2017) – would therefore result in no increase (and probably a decrease) in Tegner or UCLA scores, as was observed by Kunze *et al.* (2019). This suggests that the two meta-analyses would probably have reported more similar "levels" of return to sport, had they used the same measuring tools or definitions. This is further supported by the reporting of the range of median pre- and post-operative UCLA scores in the

Hoorntje *et al.* (2017) meta-analysis, which suggested a slight decrease in pre- to post-operative activity levels (3.1 to 6.5 pre-operatively and 2.5 to 5.9 post-operatively). Based on the two meta-analyses, it can be concluded that only a small percentage of HTO patients experienced a pre- to post-operative increase in high-impact activities, but that the vast majority of patients nevertheless returned to some sort of physical activity, with a tendency towards performing low-impact activities. Consequently, it is important to determine whether this shift from high- to low-impact activities was due to the operated knee. If so, variables need to be identified that are able to reduce this effect as much as possible since HTO is specifically indicated in active individuals.

Bonnin *et al.* (2013) found that residual pain was common during physical activities and that high levels of discomfort in the operated knee were often the reason that patients did not participate in most activities. They found that patients motivated to participate in high-impact activities after surgery would return to them at a higher rate (66%) compared to the overall sample (28%). Although motivation influenced activity participation, the operated knee remained a common limiting factor despite the HTO. The fact that the operated knee continued to cause problems for physical activity after surgery – to the extent that patients generally did not perform the high-impact activities that they did pre-operatively – suggests that this may have limiting implications for health-related quality of life. Investigating this further would develop an understanding of the impact that HTO has on motivation and decisions regarding activity participation. In turn, this could increase the likelihood and degree to which patients return to physical activities post-operatively.

The study by Bonnin *et al.* (2013) also reported the frequency of post-operative sports participation and distinguished between different types of sport by splitting them into three groups: light, intermediate, and strenuous. The criteria to determine which sports belonged to which category were not disclosed. Additionally, the study did not distinguish between the levels of a given sport within the three groups (for example: recreationally, competitively, professionally), and did not include a pre- to post-operative comparison of changes in physical activity participation. Frequency of participation in sporting activities was either maintained or increased post-operatively in 65% of their cohort, but it is not known whether the level or type of activity changed. More discussion around the 56% of patients, whose outcome expectations were not met post-operatively, could have been made if a pre- to post-operative comparison had been assessed.

A study by Faschingbauer *et al.* (2015) provided results to this effect. It found that HTO patients returned to physical activity after surgery but that the type of activity performed was different. Fewer patients (82% decrease) returned to “ball games”, which came under the category “high impact activities”, and more patients (27% increase) participated in weight/fitness training. There was also a 25% decrease in post-operative participation in “low impact activities” such as cycling. A suggestion given for these changes was that patients were explicitly advised against participation in impact sports after HTO by their surgeon. This speculation could reasonably explain the dramatic pre- to post-operative decrease in high-impact activity participation and is something that should be investigated further.

Studies tend to show that most patients return to physical activity after osteotomy and, in some cases, without significant changes in the frequency of participation (Salzmann *et al.*, 2009; Gougoulias, Khanna and Maffulli, 2009; Saragaglia *et al.*, 2014). Most, however, did not account for operative variables such as opening- versus closing-wedge, or HTO with graft materials versus HTO without graft materials. In terms of returning to high-impact activities post-operatively, a case study by Boussaton and Potel (2007) showed that all six of the professional rugby players examined returned to their sport after a tibial osteotomy; at the same level of competition as before their operation. In contrast, a study into HTO in the United States military (Waterman *et al.*, 2015) showed mostly positive results at mid-term follow-up, concurrent with previous research (72% success rate), but only 43% of patients returned to their physical activity regime without restrictions relating to their knee. Those service members who were deemed to have a successful outcome – no need for arthroplasty or no knee-related medical discharge from the military – but who experienced physical activity restrictions, were limited to low-impact activities (cycling, swimming, walking). This prevented them from returning to their full duties as they were unable to satisfy some of the physical challenges expected of military service members (timed runs and carrying heavy loads). The studies of Boussaton and Potel (2007) and Waterman *et al.* (2015) suggest that it is possible for patients to return to high levels of physical activity after HTO, but the type, duration, and frequency of participation may change in the short-term. It should, however, be noted that both studies examined patients who are unlikely to be representative of the general population since professional sportsmen and military service members comprised their samples. This, combined with the small sample size (*n*=6) of the study by Boussaton and Potel (2007), means that these results only offer an insight into what is possible after HTO. They do not provide evidence that can be easily generalised to all HTO patients, so further research into high-impact activity participation after surgery is needed.

Numerous qualitative investigations have uncovered different factors that influenced patients’ return to physical activity after forms of knee surgery other than osteotomy. Tjong *et* *al.* (2014) showed that recommendations from surgeons not to participate in certain activities after anterior cruciate ligament reconstruction (ACL) existed but was one of the less common reasons as to why patients did not resume sporting activities post-operatively. This study found fear to be the most common factor attributed to the change in physical activity behaviour. Fear was an overarching theme that encompassed different elements: fear of pain, fear of debilitation, fear of the sport, fear of financial burden, as well as fear of reinjury. Fear of reinjury, specifically, was also cited as the most common reason to reduce post-operative physical activity in ACL patients by Ardern *et al.* (2011). Similarly, another study made a further distinction finding that a hyperawareness of the knee was a larger limitation to physical activity than the fear of reinjury itself (Burland *et al.*, 2018). Conversely, Ramanathan *et al.* (2015) found that fear of reinjury did not alter post-operative physical activity levels among ACL patients when exercise was considered to be of high importance by an individual. Similar to the correlation between motivation and activity participation found by Bonnin *et al.* (2013), these results suggest that the way in which patients prioritise physical activity is an influencing factor regarding the resumption post-operatively. The results of the abovementioned qualitative investigations show that the suggestion by Faschingbauer *et al* (2015), regarding surgeon recommendations and the post-operative reduction in impact-sport participation, is likely to be one of many contributing factors. While some studies have reported on pre- to post-HTO activity levels, research investigating the reasons behind such observations is lacking. Developing an understanding of the multiple factors that may influence physical activity participation after HTO will help to identify where current barriers lie, and would allow for future research to be conducted that aims to remove these barriers and improve the overall outcome for future patients.

Despite the literature generally demonstrating that HTO patients mostly return to an equivalent physical activity level compared to their pre-operative status (Ekhtiari *et al.*, 2016; Hoorntje *et al.*, 2017; Kunze *et al.*, 2019), one meta-analysis by Spahn *et al.* (2013) claimed that patients should expect a reduction in post-operative activity. The aim of the meta-analysis was to compare the impact of HTO and unicompartmental knee arthroplasty (UKA) on the treatment of knee osteoarthritis. The final analysis included 46 studies reporting on HTO and 43 that reported on UKA. Findings were presented relating to overall survival of the treatment (defined as the time until a total knee arthroplasty was performed) and outcome measures that were not physical activity-specific (through the implementation of various knee scores). No overall difference in survival rates was found between treatments, but UKA was shown to result in a better clinical outcome than HTO. However, since scores that specifically measure physical activity levels were not included in the analysis, claims about the effects of each procedure on physical activity cannot reliably be made; yet this is precisely something that was mentioned in the conclusion of the study. It stated that patients who undergo HTO should expect a slight overall decrease in their physical activity. This assertion does not appear to have emerged from the data in the meta-analysis itself, rather it mirrors an unsubstantiated claim made in the introduction of the article. Therefore, this conclusion should be queried, and the consensus reached among more recent systematic reviews and meta-analyses – that patients achieve a post-operative physical activity outcome at least equal to their pre-operative status – should be considered a more accurate reflection of the literature (Ekhtiari *et al.*, 2016; Hoorntje *et al.*, 2017; Kunze *et al.*, 2019).

2.9 Pain

As previously discussed, HTO aims to reduce painful unicompartmental knee osteoarthritis and its outcome can be influenced by factors such as operative technique and post-operative rehabilitation. Consequently, pain is a (subjective) measure commonly reported in the literature (Brouwer *et al.*, 2014). Despite multiple studies showing that HTO leads to an overall reduction in experienced pain over time (Kohn *et al.*, 2013; Cotic *et al.*, 2015; Faschingbauer *et al.*, 2015; Nerhus *et al.*, 2017), there appears to be no suggestion in the literature regarding the precise degree to which pain is reduced. Salzmann *et al.* (2009) reported that 75% of their sample required no pain medication to participate in physical activities and the remaining 25% required pain medication either occasionally (22%) or regularly (3%) before activity. In line with the literature, mean Visual Analogue Scale (VAS) pain scores decreased but remained above zero (6.9 ± 2.4 pre-operatively; 2.9 ± 2.2 post-operatively), demonstrating that total pain relief is not to be expected through HTO. These findings imply that patients tend to experience some level of residual pain in the knee after surgery, which can be managed through the use of medication rather than through the cessation of physical activity. Faschingbauer *et al.* (2015) similarly found that frequency of sports participation did not significantly change post-operatively, but that patients tended to change the type of activity they performed: shifting from high- to low-impact activities. It can be inferred from this that residual pain is sufficient to modify the activity behaviours of patients, despite generally returning to physical activity after HTO. Further evidence to support this claim can be seen in the study by Bonnin *et al.* (2013), who found that approximately 65% of patients achieved post-operative activity levels at least equivalent to their pre-operative status, but that residual pain was not uncommon. Additionally, the highest incidence of patients in this study reporting that their operated knee was the reason behind them not participating in certain activities was observed with reference to “strenuous activities” such as skiing, tennis, and running. This suggests that an observed change in the type of activity practised is not surprising. Based on the above, the role that pain plays in patient physical activity post-operatively, and the extent to which it is tolerated, is something that warrants further investigation.

Residual pain is also often present in the mid- to long-term after surgery (Marriott *et al.*, 2015; W-Dahl, Toksvig-Larsen and Lindstrand, 2017), and it has a large impact on, and negative correlation with, health-related quality of life (Pang *et al.*, 2015; Ihle *et al.*, 2016; Saier *et al.*, 2017). Conversely, a positive correlation exists between quality of life and participation in physical activity (Bize, Johnson and Plotnikoff, 2007) as well as activity intensity (Vuillemin *et al.*, 2005). Although HTO has been shown to improve the quality of life of patients (McNamara *et al.*, 2014; Bastard *et al.*, 2017), the research discussed in this section indicates that post-operative pain levels do continue to influence activity behaviours. Patients opted for lower intensity activities and tolerated mild discomfort, while avoiding higher intensity activities. In doing so, this could inadvertently limit overall health-related quality of life after surgery.

2.10 Patient Expectations

Much of the literature around the influences on HTO outcome centres around the variation in treatment that occurs perioperatively: opening- versus closing-wedge, fixation type, graft versus no graft, rehabilitative protocols etc. One of the lesser reported potential influences is patient expectation of the surgery. Studies presenting results of patient expectations with other forms of knee surgery tend to show that expectations are high pre-operatively but are often not met (Pellegrini *et al.*, 2017). There is also an apparent strong correlation between the accuracy of expectations and patient satisfaction with the actual outcome (Baker *et al.*, 2007; Scott *et al.*, 2010; Longo *et al.*, 2015).

Scott *et al.* (2010) found that expectations of outcome after knee arthroplasty was positively correlated to satisfaction (r=0.77), second only to pain relief (r=0.78), and ahead of functional ability (r=0.67). The influence of pain and expectation on patient satisfaction was also discussed in a study by Baker *et al.* (2007), who suggested that moderating pre-operative expectations of post-operative pain should be of great importance to reduce patient dissatisfaction. The study found pain to be more closely linked to dissatisfaction than other factors such as function, and that pre-operative patient expectations were often highest with regard to pain relief. As such, managing expectations around pain relief should be a high priority for surgeons to increase patient satisfaction. The study by Baker *et al.* (2007) only included arthroplasty patients, and while it is possible that this would not necessarily mirror the expectations of prospective HTO patients, a recent study by Grünwald *et al.* (2018) found that 74% of HTO patients rated pain relief as very important. Pain relief is therefore also a high priority for HTO patients, and when considering the aforementioned research by Baker *et al.* (2007) and Scott *et al.* (2010), more research in the area of expectation management within HTO patient populations is needed.

Return to work (Hoorntje *et al.*, 2017; Grünwald *et al.*, 2018) and health related quality of life (Zhou *et al.*, 2017) have also been shown to be associated with patient expectations. Grünwald *et al.* (2018) showed that returning to work was of highest importance for HTO patients with 86% expecting to do so with no, or minor, adaptations needed. They also found a negative correlation between the length of pre-operative inability to work and the expectations of returning to work post-operatively. A similar study by Hoorntje *et al*. (2017), but with arthroplasty patients, confirmed that those who were not working pre-operatively were more likely not to return to work post-operatively. 67% of patients who were working pre-operatively went on to return to full working capacity within 12 months of arthroplasty, with a further 22% partially returning to work within the same timeframe. If a similar trend is observed for HTO patients – that a return to work after surgery is a top priority for patients but only 67% are able to fully do so – there needs to be a focus on managing expectations in this area. This would improve not only satisfaction with outcome of surgery, but would reduce any negative effects on health-related quality of life, since that is also positively correlated with the accuracy of expectations (Zhou *et al.*, 2017). Research is required to confirm these suggestions since they are based, in part, on the results of arthroplasty patients (Hoorntje *et al.*, 2017) due to a lack of similar investigations involving HTO patients.

Regarding pre-operative expectations themselves, a qualitative study involving arthroplasty patients found that full restoration of knee function, pain relief, no further progression of osteoarthritis, and the ability to walk unimpeded were commonly mentioned by participants (Nyvang, Hedström and Gleissman, 2016). Concerning physical activity, participants also revealed an expectation to be able to partake in low-impact activities such as golf or swimming, but that high-impact activities such as running or jumping were not expected. Nyvang, Hedström and Gleissman (2016) also stated that a strong connection existed between patient expectations and physical activity. Total knee arthroplasty is not necessarily associated with patients aiming to return to high levels of physical activity, which may explain the lack of interest in high-impact activities – but HTO is traditionally indicated for active individuals (Amendola and Bonasia, 2010). The extent to which HTO patients expect to return to physical activity post-operatively is not known but it is not unreasonable to predict that expectations may be higher than for arthroplasty patients.

Although the literature tends to report that HTO patients are able to return to physical activity at least equivalent to pre-operative levels (Ekhtiari *et al.*, 2016; Hoorntje *et al.*, 2017; Kunze *et al.*, 2019), other research has demonstrated a tendency for patients to change the type of activity performed: from high- to low-impact activities (Faschingbauer *et al.*, 2015). Assuming pre-operative expectations have a similar influence in HTO patients as they do in arthroplasty patients, patient satisfaction and general outcome may be negatively affected if pre-operative expectations of physical activity are not accurately managed.

Of the few studies that have included a cursory insight into expectations and HTO, the percentage of patients reporting that their general outcome met their pre-operative expectations is good, ranging from 72% (Faschingbauer *et al.*, 2015) to 90% (Pfahler *et al.*, 2003). However, expectations regarding return to physical activity specifically have been shown to be met only 56% (Bonnin *et al.*, 2013) to 65% (Saragaglia *et al.*, 2014) of the time. A focus on the management of expectations for return to physical activity, a key indication for HTO, is perhaps warranted to further improve patient-reported satisfaction. It has been suggested that the creation of a timeline demonstrating return to sport after HTO would be beneficial in helping surgeons to better manage patient expectations (Ekhtiari *et al.*, 2016).

Grünwald *et al.* (2018) found that HTO patients reporting higher pre-operative pain and symptoms, and lower quality of life, had higher expectations for their post-operative outcome. Conversely, those patients who had previously undergone knee surgery had significantly lower expectations than those undergoing primary surgery in terms of physical activity, pain, risk of further osteoarthritis, comparison to a healthy knee, and conversion to arthroplasty. This study did not present any outcome scores with which the expectations could be compared. However, it would not be unreasonable to predict that previous experience of knee surgery is associated with more realistic expectations of the outcome of future procedures. Further research is needed to confirm this. The same study suggested that regardless of previous experiences with knee surgery, HTO patients had expectations of osteotomy survival that were in line with the literature: 42% expected a conversion in 15-20 years, while 25% expected it after 5-10 years (Grünwald *et al.*, 2018). There are individual studies reporting variable rates of survival ranging from 54.1% to 90.4% at 15-20 years after HTO (Tang and Henderson, 2005; Papachristou *et al.*, 2006; Akizuki *et al.*, 2008; Gstottner *et al.*, 2008; Hui *et al.*, 2011). A systematic review reported conversion to arthroplasty at a median 7 years after HTO (van Raaij *et al.*, 2009), whereas a meta-analysis showed 84.4% of

HTO patients not requiring an arthroplasty 9-12 years after surgery (Spahn *et al.*, 2013). Overall it appears as though survival of HTO beyond 15 years after HTO is possible in many cases, which matched the expectations of the largest proportion of patients (42%) in the Grünwald *et al.* (2018) study. However, it should also be noted that 32% of patients in the same study expected the HTO to completely prevent the need for a later conversion to arthroplasty (which is not supported by the literature), suggesting that expectations for significant numbers of patients were nevertheless unrealistic.

Pre-operative patient education has been shown to improve outcomes and satisfaction with surgical procedures (Cross *et al.*, 2009; Kruzik, 2009) and has been equated in importance to pre-surgical planning (Aalderink, Shaffer and Amendola, 2010). With regard to rehabilitation, patient goals and expectations should be viewed as the primary variable to assess (Oberg and Oberg, 2000). Despite their potential influence, and frequent appearance among the literature of other forms of knee surgery, studies involving the outcome expectations of HTO patients are lacking. Where studies do exist, expectations pertaining to physical activity and overall survival of the HTO tend be inflated in a significant proportion of patients. Research to improve patient expectations in these areas may result in higher reported satisfaction and better overall outcome.

2.11 Arthroplasty

Unicompartmental knee arthroplasty (UKA) and total knee arthroplasty (TKA) are both relevant to any project investigating HTO. UKA is often compared with HTO since both procedures share many of the same indications for surgery (as previously discussed), whereas the need for a TKA marks the endpoint for every HTO and UKA (Fu *et al.*, 2013). As such, the remainder of this chapter will present a brief overview of UKA and revision to TKA.

2.11.1 Unicompartmental knee arthroplasty

The incidence of UKA has been on the rise in recent years (Becker and Hirschmann, 2017; Kley, 2020), which has been coupled with a decrease in the number of HTO performed (Nwachukwu *et al.*, 2014; Kley, 2020). Nwachukwu *et al.* (2014) suggested that a surgeon's experience with UKA is an influencing factor in choosing it over osteotomy. The classic indications for UKA include: 1) unicompartmental osteoarthritis with intact lateral and patellofemoral compartments, 2) advanced age (>60 years), 3) low physical activity levels, 4) low BMI (<30 kg/m^2), 5) low pain during rest, and 6) range of motion arc of 90°, 7) malalignment <5° (Dettoni *et al.*, 2010; Fu *et al.*, 2013). In comparison, HTO has its own surgical indications – <60 years of age, physically active, 5-15° malalignment, range of motion of 120° – which distinguishes it from UKA (Marti *et al.*, 2001; Amendola and Bonasia, 2010; Fu *et al.*, 2013). However, recent research has broadened and challenged some of these indications, leading to an overlap (age 55-65 years, moderately active, range of motion around 100°, malalignment 5-10°) and much debate around the optimal method of treatment for those patients who fall within these parameters (Dettoni *et al.*, 2010; Fu *et al.*, 2013; van Heerwaarden *et al.*, 2018). Becker and Hirschmann (2017) suggested that a factor for consideration with this patient demographic should be the underlying cause of the malalignment or deformity. If the deformity was caused by osteoarthritis and a loss in cartilage, UKA is an appropriate course of action. However, if the malalignment is due to a deformity in the bone itself, a corrective osteotomy to unload the arthritic compartment is more suitable.

As a result of the inconsistency of indications for UKA and HTO between studies, there remains much controversy as to which procedure is best. One meta-analysis found that UKA resulted in better functional outcome scores when compared to HTO, but that physical activity levels were higher in patients who underwent osteotomy (Santoso and Wu, 2017). Conversely, two recent individual studies have shown UKA to yield better physical activity scores and rates of return to physical activity than HTO in the short-term (3 months to 2 years post-operatively) and mid-term (5-7 years post-operatively) (Krych *et al.*, 2017; Kim *et al.*, 2018). Kim *et al.* (2018) used Tegner and UCLA scores to measure physical activity outcomes, finding significantly better UCLA scores in UKA patients at 3, 6, and 12 months post-operatively. Differences in physical activity levels had disappeared between groups at 24 months post-operatively but a significant difference in the rate of return to sporting activity was noted (94% in UKA patients and 75% in HTO patients). Krych *et al.* (2017) used a Tegner score to measure physical activity, finding that UKA resulted in superior results at 3 months, 2 years, and 5 years.

The study by Krych *et al.* (2017) was included in the meta-analysis by Santoso and Wu (2017), which concluded that HTO resulted in better physical activity outcomes than UKA overall. However, reference to physical activity in the meta-analysis appeared to be limited to comparing the results of free walking speed, (which showed no significant difference between UKA and HTO) making it unclear as to where their conclusion regarding increased physical activity in HTO patients came from. A second meta-analysis (Fu *et al.*, 2013) also presented results regarding free walking speed, referencing the same three studies as Santoso and Wu (2017) but came to a different conclusion: that UKA resulted in significantly faster velocity than HTO. Santoso and Wu (2017) explained this conflict in findings by highlighting that Fu *et al.* (2013) included TKA data from one of the studies, rather than just UKA data, thereby challenging the validity and reliability of this result. Therefore, the results of the more recent meta-analysis should be used to draw conclusions about walking speed after UKA and HTO.

A third meta-analysis comparing UKA with HTO found that UKA was associated with lower post-operative pain, fewer complications, and a lower revision rate, but that HTO was associated with greater range of motion (Cao *et al.*, 2018). This meta-analysis also concluded that HTO was the preferred option for highly active patients, however their study did not assess physical activity outcomes, meaning that this statement is probably based on the indications for HTO rather than data in their analysis. In light of recent studies challenging physical activity as a relative contraindication for UKA (Krych *et al.*, 2017; Kim *et al.*, 2018), further research is required to establish whether HTO remains justifiably preferable to UKA in active patients.

2.11.2 Survivorship and revision to total knee arthroplasty

Spahn *et al.* (2013) showed similar survival rates of UKA and HTO after 5-8 years (91.5% and 91%, respectively) and 9-12 years (86.9% and 84.4%, respectively). The similarities in survivorship between the two techniques is supported by two other meta-analyses that showed no significant difference in the revision rates of UKA and HTO to TKA (Fu *et al.*, 2013; Santoso and Wu, 2017). The data presented by Spahn *et al.* (2013) showed that UKA demonstrated better clinical outcomes from 5-12 years post-operatively but that this difference disappeared after 12 years. Mean time to TKA conversion was 9.7 and 8.2 years for HTO and UKA, respectively.

Total knee arthroplasty is often the final surgical option for the treatment of osteoarthritis (Becker and Hirschmann, 2017) and is the endpoint after HTO or UKA (Santoso and Wu, 2017). One systematic review (van Raaij *et al.*, 2009) and one meta-analysis (Ramappa, Anand and Jennings, 2013) each found that TKA following previous HTO resulted in similar outcomes to patients who underwent primary TKA. An individual study showed that operating time was increased for TKA after HTO and the procedure had a complication rate of 21%; closer to that of a revision TKA (28%) and worse than a primary TKA (11%) or TKA after UKA (8%) (Cross *et al.*, 2014). However, multiple systematic reviews and meta-analyses agreed that TKA after UKA resulted in inferior outcomes compared to primary TKA (Siddiqui and Ahmad, 2012; Lee *et al.*, 2018; Sun and Su, 2018; Zuo *et al.*, 2018), so the result of Cross *et al.* (2014) should be interpreted with caution.

Overall, the literature suggests that UKA and HTO are both effective procedures with good clinical outcomes in the short-, mid-, and long-term. Despite traditionally having separate indications, recent research indicates that surgeons are expanding them to the degree where there is considerable overlap between the two procedures. Multiple meta-analyses show UKA and HTO perform differently regarding functional outcomes, but most state that HTO is more suited to active patients. The only parameter of physical activity that has been subjected to systematic review or meta-analytic comparison between the two procedures is free walking speed, which has shown no significant difference. It is not clear where the advocacy for HTO in active patients, mentioned in numerous meta-analyses, originates. It is likely that it is a reference to the traditional surgical indication, but this is not clear. Regardless, researchers and clinicians would benefit from a comprehensive review of the literature reporting the current situation concerning return to physical activity after HTO and UKA to confirm the appropriateness of this traditional indication.

2.12 Conclusion

Overall, it is apparent that HTO can be successful in its aim to correct tibial malalignment. thereby reducing the pain of osteoarthritis caused by the previously overloaded medial compartment of the knee. Despite the largely positive results of HTO that have been published, the incidence of osteotomies being performed is far lower than that of surgical alternatives such as arthroplasty (Hunt *et al.*, 2014; Elson *et al.*, 2015; Kley, 2020). Indeed, there is evidence to suggest that the incidence of knee osteotomies is decreasing in countries where the number of arthroplasties performed is growing (Koskinen *et al.*, 2007; Niinimaki *et al.*, 2012; Nwachukwu *et al.*, 2014). One reason for the expanding disparity between the incidence of HTO and arthroplasty may be demonstrated by recent studies showing positive results after UKA in patients that would not traditionally have satisfied the indications for the procedure: a physically active patient with an age less than 60 years (Fu *et al.*, 2013; Walker *et al.*, 2015; Krych *et al.*, 2017; Santoso and Wu, 2017). This has been complicated by a mix of industry pressure to perform more arthroplasties and the relatively low numbers of training initiatives dedicated to osteotomy (Kley, 2020).

Physical activity levels have been shown to be positively correlated with health-related quality of life in adults both under and over the age of 60 years (Vuillemin *et al.*, 2005; Acree *et al.*, 2006; Bize, Johnson and Plotnikoff, 2007; Filbay *et al.*, 2017). Therefore, it can be inferred that there is a need for a focus not just on whether patients can return to physical activity after surgery, but also the level of physical activity to which patients they return. The recent propensity to overlap the surgical indications of HTO and UKA, combined with the emerging suggestion that young and active patients can benefit from UKA, means that it is necessary to first determine where HTO stands in comparison to UKA regarding physical activity. This would clarify whether HTO remains an avenue worth pursuing for active patients. Consequently, before the empirical studies are presented in this thesis, the original research begins with a systematic review and pooling data analysis comparing both procedures regarding a return to physical activity after surgery (chapter 4).

This literature review also highlighted the need for further investigation into the operative variables that have resulted in controversy regarding the optimal strategy for the most predictable and beneficial surgical outcomes. Surgical technique, method of fixation, and the use of graft materials have all been subject to previous investigation with varying levels of resultant consensus and contention. Consequently, more research is needed to determine which combination of these variables reliably produces the best outcome for patients. Little difference in outcome has been demonstrated in HTO with and without graft materials once the osteotomy has healed. However, graft materials have a more positive impact on outcome in the immediate post-operative period prior to union occurring, compared to HTO without grafting. Allograft wedges are clinically preferable to synthetic grafts and are arguably preferable to autografts immediately after surgery. If allografts have similar biomechanical properties in HTO to synthetic grafts – which are biomechanically stronger than HTO without grafting – this may have consequences regarding a return to physical activity after surgery.

Finally, several systematic reviews have shown that patients are able to return to physical activity after HTO (Ekhtiari *et al.*, 2016; Hoorntje *et al.*, 2017; Kunze *et al.*, 2019), however there remains much controversy regarding the degree to which this is possible. Since being active is one of the traditional surgical indications for patients undergoing HTO, there is a need for more research into post-operative physical activity to address this controversy. As a result, this thesis aims to provide clarity not only regarding patients returning to activity after HTO; but also regarding the effect that different variables have on the time that patients can first perform different activities post-operatively. This literature review has served the purpose of identifying potential areas of investigation and has provided the basic justification for the present project in general. However, it has not provided the reasoning behind the methods chosen for each investigation. To fully understand the rationale for the approaches taken within this project, attention must first be drawn to the underlying philosophy behind them (Hubbard, 1983; Wilson, 1999). It is to the acknowledgement and understanding of this philosophy that this thesis will now turn.

CHAPTER 3 – METHODOLOGY

"[We live] in a world that doesn't like grey areas. But the grey areas are where you find the complexity. They are where you find the humanity. And they're where you find the truth."
-Jon Ronson, 2012

3.1 The importance of philosophical consideration

Before reporting the results of any research and discussing their meaning, it is necessary to acknowledge that the process of designing studies and interpreting data is inherently affected by the philosophy and underlying assumptions of the researcher (Greenfield, Greene and Johanson, 2007; Koshy, Koshy and Waterman, 2010). In doing so, the researcher is better able to justify decisions made in terms of the approaches employed to explore and answer research questions (Mackenzie and Knipe, 2006; Jackson, 2013; Gray, 2014). Similarly, understanding pre-existing ontological and epistemological assumptions about reality allows for compatible methodological approaches to be selected. Contradictions between the methodological approach of a study and the underlying worldview of the researcher result in suboptimal research practice as one attempts to apply an approach of which they are not convinced (Maxwell, 2011; Jackson, 2013; Ormston *et al.*, 2013).

Failure to reflect upon the underpinning philosophy for research increases the likelihood of unconscious bias, while reducing the transparency, rigour, and credibility of the eventual research output (Jackson, 2013; Ormston *et al.*, 2013). As a result, this chapter presents the philosophy and reasoning that underpinned the studies reported later in the thesis. Since philosophy and underlying assumptions about reality are inherently unique to an individual, relevant parts of the remainder of this chapter have been written in the first person.

3.2 Personal philosophy

This chapter has already established the importance of considering and disclosing the philosophical approach to research. It logically follows that the philosophical paradigms to which one aligns themselves for research purposes are informed by one's philosophical approach to life more generally. Therefore, my personal philosophy will now be briefly outlined before proceeding to discuss the philosophical justification for the study designs chosen in this thesis.

Prior to the beginning of this project I had never examined my worldview in any detail before and, although aware of the phenomenon of experimenter bias in research, I had not considered the impact that an individual's philosophy has on their scientific practice. Upon reflection it became very clear that my personal philosophy lies closely aligned to that of the ancient stoics (Campbell, 1969; Brown, 2016). Firstly, leading a considered life by striving for and practising self-control, self-sufficiency, and self-improvement has obvious benefits. Determining how to achieve these goals through reasoned logic, focusing on variables that can be controlled, and accepting the presence and consequences of variables outside of one's control, seem to me to be rational, realistic, and rewarding. Finally, deferring short-term gratification in exchange for long-term prosperity, and being materialistic in the classical sense – placing value only on the truly important things in life and not on things that can be easily taken away – has served me well thus far in terms of achievements, experiences, and personal fulfilment.

A detailed examination of my personal philosophy would be outside of the scope of this thesis. However, this brief insight into my underlying worldview has served to explain the basis from which my research philosophy stems. This will now be described more explicitly.

3.3 Research philosophy

Given my academic background, which is comprised of predominantly sports medicine, sports biomechanics, and sports physiology, it would be reasonable to assume that I would be a proponent of positivism who seeks to obtain knowledge through objective, quantitative means. It is the case that the vast majority of literature around which this project was based has employed quantitative approaches (Greenfield, Greene and Johanson, 2007; Petty, Thomson and Stew, 2012a). However, I find my approach to research to be guided more by the philosophical paradigms of pragmatism and post-positivism (Johnson, Onwuegbuzie and Turner, 2007).

Ontologically speaking, I view the world from the perspective of critical realism. I believe that there is an objective reality that exists independently of ourselves. However, the inherent subjectivity of how we perceive this reality means that we can only approximate our comprehension of the world and never fully understand it (Maxwell, 2011; Ormston *et al.*, 2013; Gray, 2014). Therefore, in order to achieve the most accurate understanding of the world as possible, investigations must be conducted from multiple perspectives and approaches (Guba and Lincoln, 1994). The natural sciences tend to follow this ontology insofar as they do not attempt to prove hypotheses to be true, rather they adopt an approach of falsification, which seeks to reject hypotheses that turn out not to be true (Popper, 1959; Guba and Lincoln, 1994; Ormston *et al.*, 2013; Gray, 2014).

The ontological position of critical realism is commonly linked to an objectivist epistemology: there is an objective reality, therefore research should endeavour to determine objective truths (Gray, 2014). While this provides the rationale for positivistic approaches, I maintain that the inherent subjectivity of individuals means that research only serves to approximate the truth about reality rather than provide infallible answers to questions (Guba and Lincoln, 1994). Regardless, objectivism is my predominant epistemological stance because it does not necessarily require the denial of subjectivity (Gray, 2014). Subjective views can be investigated but should be done so as objectively as possible (Creswell, 2003). Pragmatically speaking, this is not always possible to achieve so it is therefore important to highlight one's biases and influences when conducting and reporting subjective research. The belief that one can only approximate an objective reality means that one should be prepared to employ multiple approaches to provide a comprehensive insight and accurate estimate of the true nature of reality.

Since most of the literature in the field of orthopaedics and sports rehabilitation has used objective methods (Greenfield, Greene and Johanson, 2007; Petty, Thomson and Stew, 2012a), it is largely based on deductive reasoning. Methods based on inductive reasoning would provide extra insight into some of the lesser known or controversial areas of the literature, thereby improving the accuracy of the approximated reality that is being discovered in this field of research. This thinking puts research questions at the centre of the problem to be solved, allowing for data collection and analysis methods to be chosen based upon their applicability to the question rather than their conformity to any given philosophical paradigm (Mackenzie and Knipe, 2006). This pragmatic approach is why I do not consider myself to be exclusively adherent to post-positivism and is also why I believe that the studies presented in this thesis contribute some truly novel information for the field of HTO research.

In summary, my underlying assumptions and mostly post-positivistic philosophical approach to research alludes to a proclivity for mainly quantitative, deductive methods. However, I simultaneously remain pragmatic and have an appreciation for the subjective nature of individuals and the value that qualitative, inductive protocols can bring to the goal of improving our understanding of reality. This philosophy is evident in the variety of methods used for the studies presented in this thesis.

3.4 A mixed methods approach

Reflecting the underlying philosophy of this project, the studies within this thesis employed predominantly quantitative methods. However, the subjective experiences of the main actors involved in HTO – namely the surgeons and the patients – have not been discounted and qualitative approaches have been included (Chapters 7 and 8). Overall, this project took a mixed methods approach to answering its research questions. Mixed methods research acknowledges that there are different perspectives and methods that can be used in the search for truth and knowledge (Johnson, Onwuegbuzie and Turner, 2007). This means that both quantitative and qualitative approaches can be used by a researcher depending upon the research question to be answered, leading to research with greater impact (Mackenzie and Knipe, 2006).

As with solely quantitative or qualitative approaches, mixed methods research also has its own advantages and disadvantages that should be considered. One of the main advantages of a mixed methods approach to research is that it allows for triangulation, wherein the use of quantitative and qualitative methods cancels out the respective inherent biases of the other, leading to greater confidence that the conclusions are closer to the truth than if only one approach was employed (Johnson, Onwuegbuzie and Turner, 2007; Gray, 2014). Triangulation in mixed methods research can occur simultaneously – where data sources interact during the data collection phase of a study – or it can occur sequentially: where the direction of one approach is informed by the results of one that was previously used (Creswell, 2003; Johnson, Onwuegbuzie and Turner, 2007). Sequential triangulation is prominent in this thesis since each study, and its respective approach, was informed by the findings of those that preceded it.

A central disadvantage to a mixed methods approach is that it is time-intensive compared to solely quantitative or qualitative research due to the requirement to collect and analyse both types of data (Creswell, 2003). Similarly, conducting a high quality mixed methods approach requires in-depth experience with both quantitative and qualitative approaches, which can be a difficult task (Johnson, Onwuegbuzie and Turner, 2007). However, these disadvantages are largely superficial and can be treated with extra time and extra education. Therefore, the disadvantages of mixed methods research do not necessarily hinder progress towards the accurate approximation of objective reality in the same way that the solely quantitative or qualitative approaches do; restricted by their inherent rigidity and failure to acknowledge the value of the other.

3.5 Study designs

The biomechanical study presented in Chapter 5 was the only true experiment conducted as part of this project. The lab-based in-vitro nature of the study, and the inclusion of a control group, allowed for a high level of control over the dependent, independent, and confounding variables. Consequently, this study had high internal validity and reliability. However, the extra control that the in-vitro protocol brought to the study came at the cost of weakened external validity regarding the generalisability of the findings to HTO patients.

In order to determine whether the conclusions of the in-vitro in Chapter 5 were relevant to an in-vivo population, Chapter 6 employed a quasi-experimental observational approach that involved a retrospective analysis of two groups of HTO patients before and after surgery. The retrospective approach was taken since a prospective, randomised controlled trial was unfeasible due to numerous financial and temporal constraints. For similar reasons, a retrospective approach was also employed in Chapter 9. In contrast to the previously described in-vitro study, the results from Chapters 6 and 9 have greater external validity due to the "real-world" setting and the approach taken.

The results presented in Chapter 10 possibly have the greatest validity of the studies contained within this thesis since they stemmed from a protocol involving prospective data collection from an experimental group and from an age-matched control group. This approach was chosen because it allowed for greater control over confounding variables, meaning that conclusions were more likely to be accurate reflections of the interaction between the independent and dependent variables.

As previously discussed, the largely post-positivist philosophy that underpinned this project meant that mostly quantitative measures were used to collect and analyse data. However, as demonstrated by areas of controversy in the predominantly positivist HTO literature, quantitative measures have not been able to control for, or expose, hidden confounders. With the underlying assumption that the objective reality is subjectively perceived by individuals, it stands to reason that some of these hidden confounders may be a product of this inherent subjectivity. Therefore, Chapters 7 and 8 employed predominantly qualitative measures to investigate the subjective experiences of both HTO patients and surgeons. Although the qualitative approach used makes it difficult to generalise findings, these studies served to generate research questions for subsequent studies and ideas that otherwise have not yet emerged from the positivist methods that dominate the literature.

3.6 Conclusion

The decisions that are made at every step of the research process are influenced by, and are a product of, the underlying philosophy of the researcher. Therefore, it is essential to reflect upon one's ontological and epistemological perspectives to identify personal biases and to justify the methodological approaches and protocols eventually employed. This PhD project was undertaken from a pragmatic post-positivist perspective whereby primarily quantitative methods were used but qualitative approaches were also included where appropriate. As such, an overall mixed methods approach has been taken for this project to provide a holistic and complete answer to the research questions. This thesis also aims to demonstrate the value of such an approach to a body of literature that is predominantly quantitative.

Chapter 1 laid out the overarching research questions for this thesis, Chapter 2 provided a critical literature review to identify knowledge gaps and areas of controversy, and this chapter disclosed the underlying philosophy that guided the direction of the project. The remaining chapters report the studies that were conducted for the project along with the interpretation of the results and their implications. The literature review in Chapter 2 revealed many areas that require further research regarding physical activity and HTO. These areas mainly pertained to the impact that operative variables have on post-operative outcomes, and the degree to which patients return to physical activity after surgery. However, recent research reported that unicompartmental knee arthroplasty patients achieved better physical activity outcomes compared to HTO patients (Krych *et al.*, 2017; Kim *et al.*, 2018), and that indications for both procedures are becoming increasingly overlapped (Fu *et al.*, 2013; Santoso and Wu, 2017; Cao *et al.*, 2018). Therefore, it is first vital to determine whether HTO remains suitable as the preferred option for young, active patients. This question is addressed in the following chapter and, by doing so, provides a solid justification for embarking on this research project.

CHAPTER 4 – RETURN TO PHYSICAL ACTIVITY AFTER HIGH TIBIAL OSTEOTOMY AND UNICOMPARTMENTAL KNEE ARTHROPLASTY: A SYSTEMATIC REVIEW AND POOLING DATA ANALYSIS

The following chapter contains a systematic review that has been peer-reviewed and accepted for publication in the American Journal of Sports Medicine. (Appendix A)

Belsey J, Yasen SK, Jobson S, Faulkner J, Wilson AJ [2020] Return to physical activity after high tibial osteotomy and unicompartmental knee arthroplasty: a systematic review and pooling data analysis. *American Journal of Sports Medicine.*

4.1 Abstract

Background: The two most common definitive surgical interventions currently performed for the treatment of medial osteoarthritis of the knee are medial opening wedge high tibial osteotomy (HTO) and medial unicompartmental knee arthroplasty (UKA). Physically active patients may be suitably indicated for either procedure despite HTO being historically indicated in active patients and UKA being more appropriate for sedentary individuals. This systematic review aimed to consolidate the current indications for both procedures regarding physical activity, to ensure that they are based on the best information presently available.

*Methods***:** A search of the literature using MEDLINE, EMBASE and PubMed databases was conducted independently by two reviewers in accordance with the PRISMA guidelines. Studies that reported patient physical activity levels using the Tegner activity score were eligible for inclusion. Patient demographics, operative variables, and patient-reported outcome scores were abstracted from the included studies.

*Results***:** Thirteen eligible studies were included, consisting of 401 HTOs (399 patients) and 1,622 UKAs (1400 patients). Mean age at surgery was 48.4 years (HTO) and 60.6 years (UKA). Mean follow-up was 46.6 months (HTO) and 53.4 months (UKA). All outcome scores demonstrated an equal or improved score for activity and knee function regardless of the operation performed. Operative variables during HTO had a larger impact on outcome than during UKA.

*Conclusion***:** HTO patients were more physically active pre- and post-operatively, but UKA patients experienced an overall greater increase in their physical activity levels and knee function. Activity after HTO may be influenced by operative factors such as the implant used and the decision to include graft materials, though this requires further research. Some research has found that patients returned to physical activity post-operatively despite having an age or BMI that would traditionally be a relative contraindication for HTO or UKA.

4.2 Introduction

The two most common definitive surgical interventions currently performed for the treatment of medial osteoarthritis of the knee are HTO and medial unicompartmental knee arthroplasty (UKA). The traditional indications for HTO include: unicompartmental osteoarthritis; tibial deformity; no extreme knee instability; >120° range of motion; age <60 years; physically active; and a body mass index <30 kg/m^2 (Brinkman *et al.*, 2008; Amendola and Bonasia, 2010; Zuiderbaan *et al.*, 2016). The traditional indications for UKA include: unicompartmental osteoarthritis; age >60 years; angular deformity <15°; low functional demands; and body mass <82kg (Fu *et al.*, 2013; Zuiderbaan *et al.*, 2016; Hamilton *et al.*, 2017) However, a wide body of research exists to suggest that good outcomes can be achieved with either procedure, outside of these traditional indications. Specifically, physically active patients may be suitably indicated for either procedure (Dettoni *et al.*, 2010; Fu *et al.*, 2013).

Surgeons have historically favoured HTO when presented with physically active patients, and have opted for UKA in cases of more sedentary individuals (Spahn *et al.*, 2013). Recent research, however, showed that patients who underwent UKA for medial osteoarthritis participated in higher levels of post-operative physical activity, compared with those who underwent HTO (Krych *et al.*, 2017; Kim *et al.*, 2018). While it is well reported that HTO patients are able to return to physical activity post-operatively in most cases (Ekhtiari *et al.*, 2016), two recent reviews found the same to be true for UKA patients (Witjes *et al.*, 2016; Waldstein *et al.*, 2017). With more studies emerging that report positive results in UKA where the traditional indications regarding physically active patients have not been adhered to, a comparative overview of the current situation around return to physical activity after HTO and UKA would be timely. Such an analysis would allow for the review and consolidation of the current indications for both procedures to ensure that they are based on the best information presently available. Ultimately, this would serve to improve surgical patient selection to the benefit of future patients. Notwithstanding the aforementioned advantages of a review focused on return to physical activity after surgery, to our knowledge recent systematic reviews and meta-analyses comparing HTO and UKA have focused on issues such as survivorship/revision, pain, complications, and knee function; but have not focused sufficiently on return to physical activity (Gandhi *et al.*, 2009; Fu *et al.*, 2013; Spahn *et al.*, 2013; Mancuso, Hamilton, *et al.*, 2016; S. B. Han *et al.*, 2017; Santoso and Wu, 2017; Cao *et al.*, 2018; Liu *et al.*, 2018).

The implementation of patient-reported outcome questionnaires is common to assess the outcome of HTO and UKA and the Tegner activity scale is one such questionnaire that is often used to specifically assess patient physical activity levels after either procedure (Ekhtiari *et al.*, 2016; Waldstein *et al.*, 2017). The Tegner activity score comprises a 10-point scale where 0 represents a patient who is on sick leave from work as a result of their knee problems; 5 represents a job involving heavy labour or participation in activities such as competitive cycling or recreational jogging on uneven ground; and 10 represents a patient who plays competitive high impact sports such as football (soccer) at the national or international level (Tegner and Lysholm, 1985).

The purpose of the present study was to perform a systematic review of the literature to investigate patients' return to physical activity after HTO and UKA.

4.3 Methods

A search of the literature using MEDLINE, EMBASE and PubMed databases was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Figure 4.1) (Moher *et al.*, 2009; Shamseer *et al.*, 2015). A second independent reviewer also conducted the same search to ensure the validity of the choices made to include the finally selected articles. Basic, and Medical Subject Headings (MeSH), searches were performed within each database; the search terms for which can be found in Table 4.1. Articles were screened and assessed for eligibility for inclusion in the review by the two reviewers according to the following criteria: a) *in-vivo* study with human participants, b) full text in English, c) internal plate fixation (for HTO), d) medial opening-wedge HTO, e) medial UKA, f) Tegner activity scores reported. Additionally, articles were excluded from the review based on the following criteria: a) sample included revision surgery, b) ACL-deficient patients, c) use of a novel surgical technique (defined as being unique and experimental at the time of publication), d) unspecified type of osteotomy or arthroplasty. The reference lists of any previous reviews and meta-analyses were manually searched to identify any additional published studies for inclusion. Unpublished studies and conference abstracts were not included.

Table 4.1: *Basic and MeSH search terms used*

Basic search terms	Medical subject headings (MeSH) search terms
1. UKR	1. Knee arthroplasty [MeSH]
2. UKA	2. Knee replacement [MeSH]
3. Unicompartmental knee replacement	3. Arthroplasty, replacement, knee [MeSH]
4. Unicompartmental knee arthroplast*	4. (1 OR 2 OR 3)
5. Unicondylar knee replacement	5. Tibia osteotomy [MeSH]
6. Unicondylar knee arthroplast*	6. Osteotomy [MeSH]
7. Partial knee replacement	7. (5 OR 6)
8. Partial knee arthroplast*	8. Physical activity, capacity and performance [MeSH]
9. (1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8)	9. Return to Sport [MeSH]
10. Tibia* osteotom*	10. Exercise [MeSH]
11. Knee osteotom*	11. (8 OR 9 OR 10)
12. HTO	12. (4 AND 11)
13. (10 OR 11 OR 12)	13. (7 AND 11)
14. Sport*	
15. Phys* activ*	
16. (14 OR 15)	
17. (9 AND 16)	
18. (13 AND 16)	

*truncated term

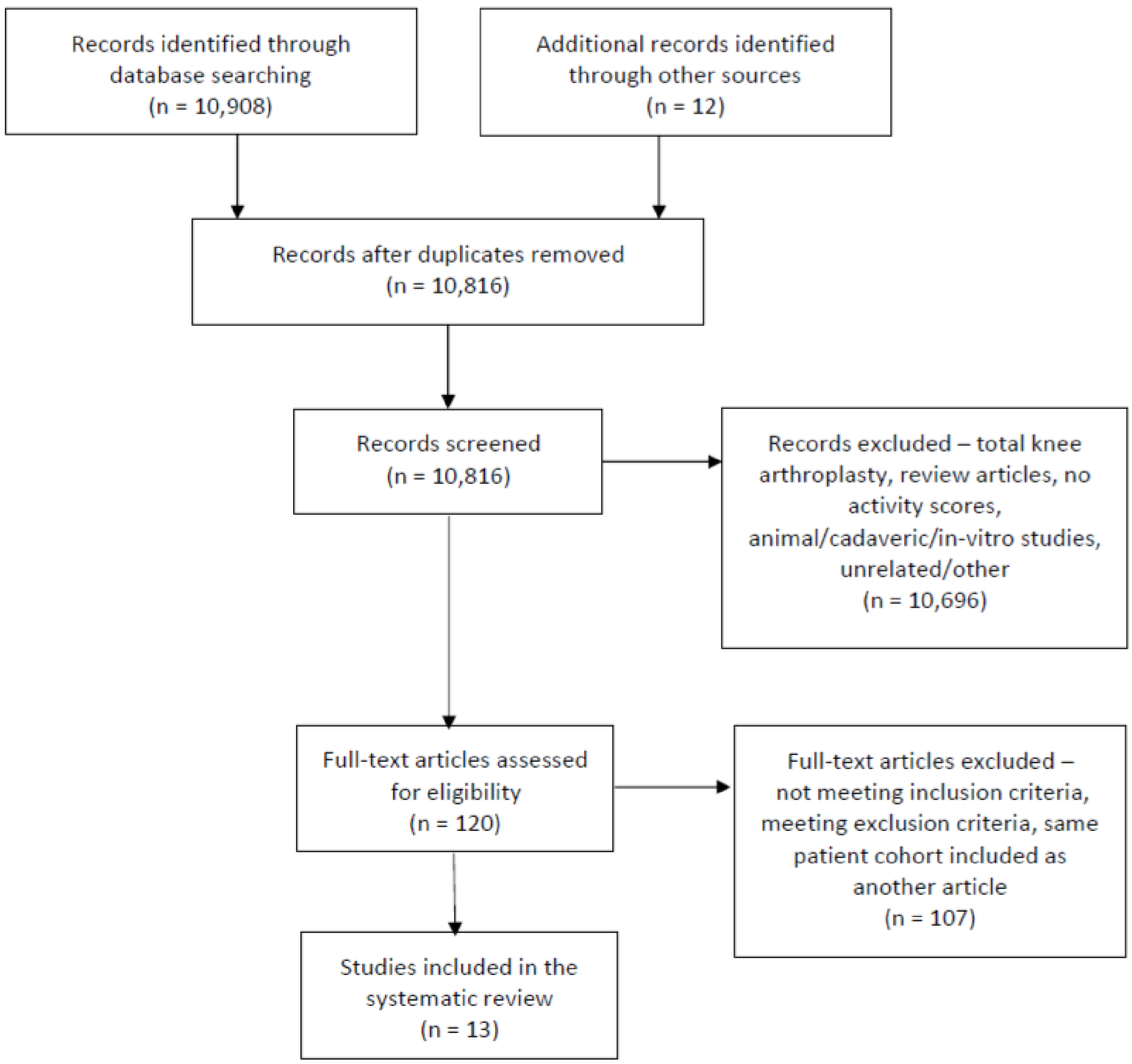

Figure 4.1: Search results flow chart following the PRISMA guidelines.

4.3.1 Methodological quality assessment

The methodological quality of each included article was assessed using the Methodological Index for Non-Randomized Studies (MINORS), a 12-point checklist that has been validated for use with non-randomised studies (comparative and non-comparative). Each item on the checklist was given a score between 0 and 2, where 0 indicates that the item was not reported in the article; 1 signifies that the item was reported in the article but was "inadequate"; and 2 denotes that the item was reported and was "adequate" (Slim *et al.*, 2003). The ideal global score for non-comparative studies was calculated using 8 of the items on the MINORS checklist, meaning that a maximum score of 16 was possible. All 12 items on the checklist were used to calculate a score for comparative studies, meaning that an ideal global score of 24 was possible. A study with high methodological quality was defined as one that satisfied at least 50% of the criteria (van Raaij *et al.*, 2009). Ten of the articles included in the final review were non-comparative studies and had a mean MINORS score of 11 ± 0.9. Two further articles compared HTO against UKA (Yim *et al.*, 2013; Krych *et al.*, 2017) and had a mean MINORS score of 19 ± 1.4. The comparative and non-comparative studies both had, on average, “fair” methodological quality (Lash *et al.*, 2015).

An additional two articles included in the present systematic review were randomised controlled trials (RCT) (Pandit *et al.*, 2013; Nerhus *et al.*, 2017). The methodological quality of these studies was assessed by comparing the articles against the revised Consolidated Standards of Reporting Trials (CONSORT) statement (Moher, Schulz and Altman, 2001), a 22 point checklist designed to guide authors of RCTs when writing up their findings in order to improve their reports; the higher the score, the better the methodological quality of a given study (Table 4.2).

Table 4.2: *Summary of articles included in systematic review (n=13)*

Author (year)	Study type	Technique	Implant	Knees at follow-up	Sex male:female	Mean age (years)	Mean BMI (kg/m2)	Follow-up (months)	Mean pre-op Tegner	Mean post-op Tegner	Methodological quality
Bastard et al. (2017)	Retrospective cohort	Medial OW HTO + synthetic graft	Limmed® locking plate	30	6:24	55.6 [27-59]	33.5 [22.9-41.6]	16 [12-18]	4 [3-6]	4 [3-6]	12/16 (MINORS)
Faschingbauer et al. (2015)	Retrospective cohort	Medial OW HTO + no graft	Tomofix	43	32:11	42 ±11.2	26.9 ±3.6	22 ±9.3	3.78 ±1.9	3.7 ±1.4	10/16 (MINORS)
Jahnke et al. (2014)	Prospective cohort	Medial UKA	Oxford	147	72:63	63.5 [36-86]	Not reported	24 ±17.6	4.06 ±1.4	3.9 ±0.96	12/16 (MINORS)
Krych et al. (2017)*	Prospective comparative	Medial OW HTO	Not reported	39	29:10	41	31.2	86	3.1 ±1.4	3.3 ±1.2	20/24 (MINORS)
		Medial UKA	Miller-Galante fixed bearing	183	82:101	49.2	32.4	70	2.6 ±0.9	4.5 ±0.9	
Nerhus et al. (2017)	Prospective RCT	Medial OW HTO	Puddu plate	35	20:15	51.3 [34-59]	Not reported	24	2.2 [2-3]	2.9 [2.4-3.3]	18/22 (CONSORT)

Table 4.2 *(continued)*

Author (year)	Study type	Technique	Implant	Knees at follow-up	Sex male:female	Mean age (years)	Mean BMI (kg/m2)	Follow-up (months)	Mean pre-op Tegner	Mean post-op Tegner	Methodological quality
Pandit et al. (2011)	Prospective cohort	MI medial UKA; cemented	Oxford Phase III	547	393:425	66 [32-88]	Not reported	60 [12-132]	2.3 ±1.1	2.8 ±1.1	11/16 (MINORS)
Pandit et al. (2013)	Prospective RCT	MI medial UKA; cementless	Oxford Phase III	27	16:14	64.7 [45-82]	27.9 [21-40]	60	1.9 ±0.7	2.9 ±0.6	19/22 (CONSORT)
		MI medial UKA; cemented	Oxford Phase III	32	20:12	63.8 [46-78]	28.9 [20-38]	60	1.9 ±0.8	2.6 ±0.8	
Panzram et al. (2018)	Retrospective cohort	Medial UKA; cementless	Oxford Phase III	27	15:12	62.5 [49-76]	Not reported	60 [47-69]	2.9 ±1.4	3.4 ±1.0	9/16 (MINORS)
Salzmann et al. (2009)	Retrospective cohort	Medial OW HTO + no graft	Tomofix	65	51:14	41.2 ±5.6 [19-65]	27.1 ±3.7 [20-34]	36 ±8.1 [14-84]	4.9 ±2.3 [1-10]	4.3 ±1.5 [2-9]	11/16 (MINORS)
Saragaglia et al. (2014)	Prospective cohort	Medial OW HTO	Not reported	62	39:23	50.5 ±10.3	27.06 ±4.6	69 ±15.6 [60-108]	4.6 ±1.7	4.2 ±1.4	11/16 (MINORS)

Table 4.2 *(continued)*

Author (year)	Study type	Technique	Implant	Knees at follow-up	Sex male:female	Mean age (years)	Mean BMI (kg/m2)	Follow-up (months)	Mean pre-op Tegner	Mean post-op Tegner	Methodological quality
Schröter et al. (2013)	Retrospective cohort	Medial OW HTO + autograft	Limited contact dynamic compression	32	22:10	47 ±9.0	28.6 ±4.7	77 ±19.0	30 ±1.4	4.1 ±1.3	11/16 (MINORS)
Walker et al. (2015)	Prospective cohort	MI medial UKA; cemented	Oxford Phase III	109	46:47	55 [36-60]	32 [20-58]	53 ±19.0 [28-101]	2.0 ±1.1 [1-6]	3.8 ±1.1	11/16 (MINORS)
Yim et al. (2013)*	Retrospective comparative	Medial OW HTO (+ allograft chips if gap >10 mm)	Two wedge plates	58	7:51	58.3 ±5.4 [43-65]	Not reported	43 ±5.0 [36-48]	3.1 ±1.1	2.5 ±1.2	18/24 (MINORS)
		Medial UKA	Miller-Galante fixed bearing	50	2:48	60.3 ±4.5 [47-65]	Not reported	44 ±5.0 [36-48]	3.2 ±0.9	2.6 ±0.9	

Note: *study comparing HTO and UKA groups

RCT = randomised controlled trial

OW = opening wedge; MI = minimally invasive

MINORS = Methodological Index for Non-Randomized Studies; CONSORT = Consolidated Standards of Reporting Trials

4.3.2 Data abstraction and analysis

The following data were extracted and recorded from each study: author, year of publication, study type, operation type (HTO or UKA), operative technique, implant type, sample size, mean age at surgery, sex, body mass index, mean follow-up, and mean pre- and post-operative outcome scores. In all studies (except one by Pandit *et al.* (2011)) where post-operative outcomes were reported at multiple time intervals (Pandit *et al.*, 2013; Krych *et al.*, 2017; Nerhus *et al.*, 2017), the most recent post-operative interval was included in the review. The study by Pandit *et al.* (2011) reported post-operative outcomes at one, five, seven, and ten years. It was noted in the article that only 156 of the original 1000 operated knees (a loss to follow-up of 84%) provided outcome scores at ten years. The overall loss to follow-up, and mean final follow-up, of the other studies included in the present review was 28% and 4.1 years, respectively. Therefore, the 547 knees that had outcome scores at 5 years in the Pandit *et al.* (2011) study were included in the final data synthesis to reduce the effects of attrition bias and skewed data.

Three studies reported the data of different HTO techniques: medial opening-wedge, lateral closing-wedge (Krych *et al.*, 2017; Nerhus *et al.*, 2017) or double (Saragaglia *et al.*, 2014) osteotomy. The study by Nerhus *et al.* (2017) included separate datasets for the demographics and outcome scores of its opening- and closing-wedge patients. In line with the inclusion criteria, only the data of the opening-wedge patients were included in the present review. It was not possible to separate the opening-wedge HTO data based on the articles in the studies by Saragaglia *et al.* (2014) and Krych *et al.* (2017). The authors were contacted and asked to provide this information, which was then included in the final review. Schröter *et al.* (2013) reported only median Tegner scores. As such, the lead author was contacted, and the mean values were obtained. A final HTO study met the inclusion criteria but reported only the mean change in pre- to post-operative Tegner scores, rather than separately stating the baseline and follow-up values (Kim *et al.*, 2018). As a result, this study was excluded from the overall review due to the unavailability of the required data.

A non-comparative UKA study met the inclusion criteria but the sample combined three lateral UKA patients with the results of 25 medial UKA patients (Schai *et al.*, 1998). It was not possible to extract the data relating to those patients who underwent medial UKA specifically. This study was therefore similarly excluded from the review. One RCT compared cementless versus cemented fixation during medial UKA (Pandit *et al.*, 2013), but no differences were found between the two methods pre-operatively or at final follow-up. Hence, this study was suitable for inclusion and the demographic and outcome data from both groups were included in the final review.

4.4 Results

4.4.1 Literature search

The titles and abstracts of the 10,908 studies resulting from the database searches, and 12 studies from the manual search, were first screened for duplicates. Any articles that did not satisfy the inclusion criteria were removed at this stage based on their title and abstract. The full texts of the remaining 120 articles were again screened according to the inclusion and exclusion criteria. A subset of patients constituting 74% of the overall cohort in one study (Liddle *et al.*, 2013) were part of a larger cohort of patients used in two other articles (Pandit *et al.*, 2011; Hamilton *et al.*, 2017). As such, this study was excluded from the final review. The study by Hamilton *et al.* (2017) did not include pre-operative Tegner scores and only included post-operative scores for various subsets of their cohort. This study was excluded from the final review. The study by Pandit *et al.* (2011) did include pre- and post-operative Tegner scores and was therefore included to represent this particular patient cohort in the final review. Pandit *et al.* (2009) included the same sample of patients as a subsequent report by the same author (Pandit *et al.,* 2013). Therefore, the earlier paper was excluded and the more recent article included. Details of the 13 studies included in the final systematic review can be found in Table 4.2.

A total of 2,097 knees (1,873 patients) were eligible for inclusion from 13 studies. Seventy-four knees (74 patients) underwent closing-wedge HTO or double osteotomy and were excluded from the present review. Of the remaining participants, 696 operated knees were lost to follow-up resulting in scores from 1,327 knees being pooled and reviewed. It was not possible to report the total number of patients who comprised the 1,327 knees at final follow-up as this was not reported in the study by Pandit *et al.* (2011), which accounted for 547 of the knees (40% of the overall sample). All studies included in the present review met the minimum requirement for methodological quality. The ten non-comparative studies scored a mean 10.9/16 (range: 9-12), and the two comparative studies scored 18/24 (Yim *et al.*, 2013) and 20/24 (Krych *et al.*, 2017), according to the MINORS criteria. The two RCT reports scored 18/22 (Nerhus *et al.*, 2017) and 19/22 (Pandit *et al.*, 2013) according to the CONSORT statement.

4.4.2 *Operative technique*

401 knees (399 patients) underwent medial opening-wedge HTO and 1,622 knees (1,400 patients) underwent medial UKA. Bone grafting was used in 62 HTO knees (Schröter *et al.*, 2013; Bastard *et al.*, 2017) and an unspecified number of knees in the study by Yim *et al.* (2013). Figures 4.2 and 4.3 show the total number of different types of HTO fixation plates and UKA prostheses that were used in the included studies. The Tomofix plate was the most used HTO fixation plate, comprising 32.7% (131 knees) of the included sample. The type of internal plate fixation used was not reported in two studies (Saragaglia *et al.*, 2014; Krych *et al.*, 2017), which constituted 25.2% of the total sample (101 knees). The remaining HTO studies each used different fixator plates. With respect to UKA, in 71.3% of the sample (1,157 knees), a cemented Oxford Phase III prosthesis was used. The 178 knees (159 patients) in the study by Jahnke *et al.* (2014) also received an Oxford UKA but it was not clear whether this was specifically a Phase III prosthesis. It is therefore possible that the overall percentage of patients that received a Phase III prosthesis was above 71.3%.

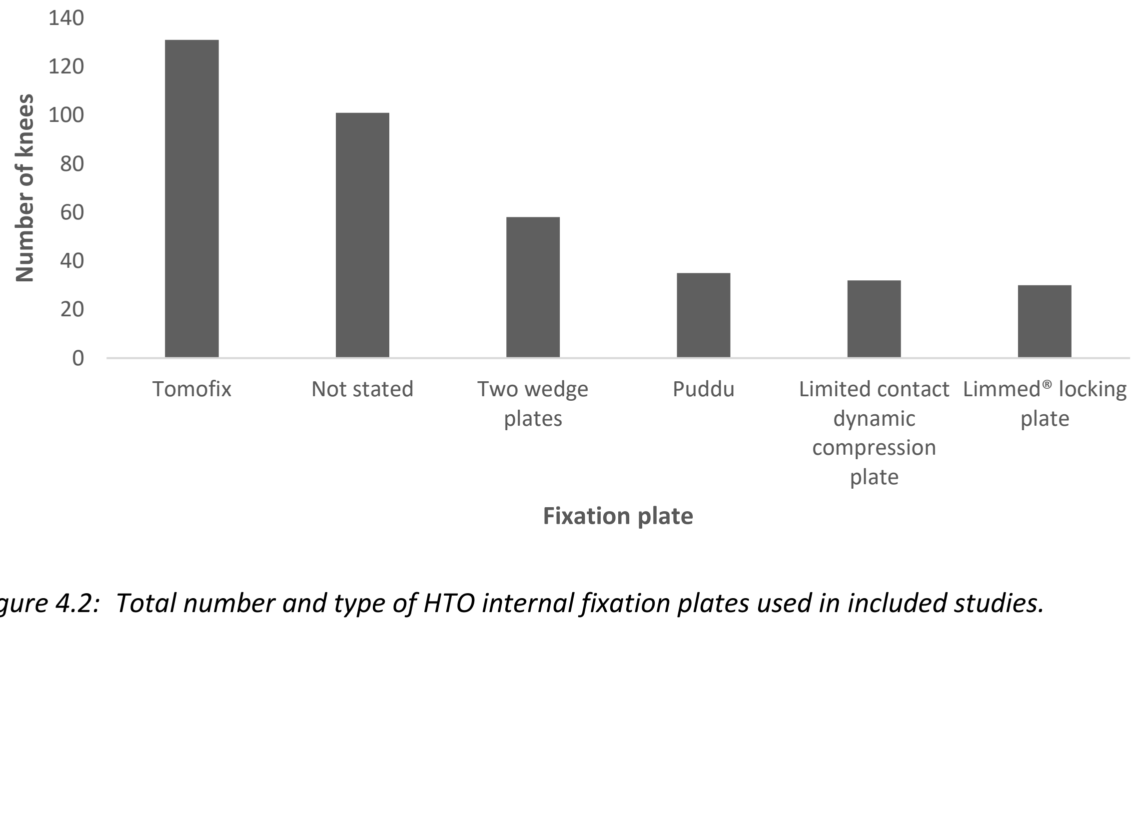

Figure 4.2: Total number and type of HTO internal fixation plates used in included studies.

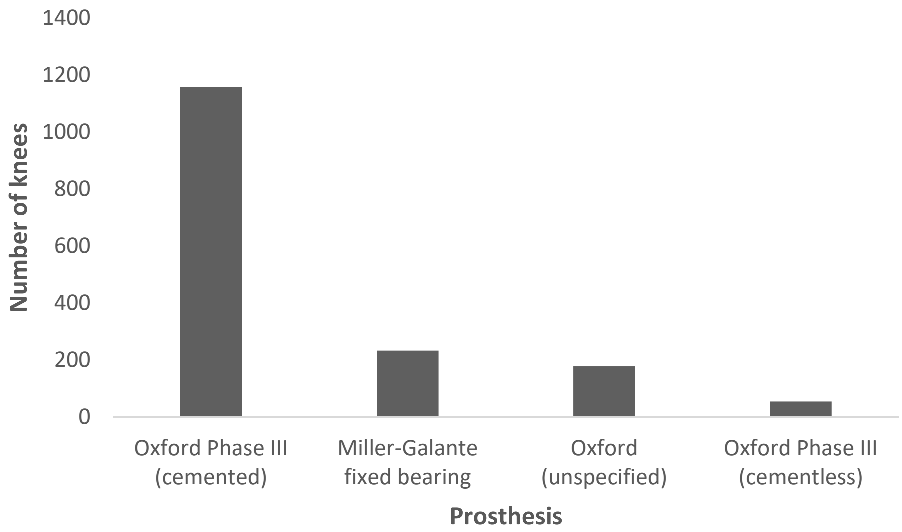

Figure 4.3: Total number and type of UKA prostheses used in included studies

4.4.3 Demographics

The mean age at surgery for all patients was 54.5 years and a total of 857 males and 875 females were recruited for these studies (excluding closing-wedge HTO and double osteotomies). The male-to-female ratio of patients that were lost to follow-up is not known. When stratifying patients according to the operation they underwent, the mean age at surgery for HTO and UKA was 48.4 years and 60.6 years, respectively. Additionally, where reported, more males underwent HTO than females (211:153), whilst the inverse was true for patients who underwent UKA (646:722). Of the nine studies that reported BMI, mean overall BMI was 29.56 kg/m^2 (29.06 kg/m^2 for HTO patients and 30.30 kg/m^2 for UKA patients). The mean overall follow-up was 50.3 months (46.6 months for HTO patients, and 53.4 months for UKA patients).

4.4.4 Patient-reported outcome scores

Outcome scores at final follow-up were available for 322 HTO knees and 1,005 UKA knees, representing an overall mean loss to follow-up of 34% (20% HTO; 38% UKA). In addition to the Tegner scores that were reported in each of the studies, additional patient-reported questionnaires were used to gather more clinical outcome data. The three most common of these additional questionnaires in the included studies were: the Lysholm score, Oxford Knee Score, and the University of California Los Angeles (UCLA) activity scale.

The Lysholm score is a subjective measure of patients' day-to-day knee function and general condition (Briggs *et al.*, 2009). Lysholm scores were reported for 322 HTO knees and 116 UKA knees in six HTO studies (Salzmann *et al.*, 2009; Schröter *et al.*, 2013; Saragaglia *et al.*, 2014; Faschingbauer *et al.*, 2015; Bastard *et al.*, 2017; Nerhus *et al.*, 2017) and two HTO/UKA comparative studies (Yim *et al.*, 2013; Krych *et al.*, 2017).

The Oxford Knee Score – designed to assess the overall outcome of knee surgery (Murray *et al.*, 2007) – was applied in one HTO study (Nerhus *et al.*, 2017) and three UKA studies (Pandit *et al.*, 2011; Pandit *et al.*, 2013; Jahnke *et al.*, 2014) representing 35 HTO knees and 753 UKA knees.

Similar to the Tegner score, the UCLA activity scale seeks to determine participation levels in various physical activities (Zahiri *et al.*, 1998). Two HTO studies (Saragaglia *et al.*, 2014; Nerhus *et al.*, 2017) and three UKA studies (Jahnke *et al.*, 2014; Walker *et al.*, 2015; Panzram *et al.*, 2018) reported UCLA scores, which corresponded to 97 HTO knees and 283 UKA knees. Table 4.3 shows the pooled mean reported pre-operative and post-operative levels for each of these clinical outcome scores. All scores demonstrated an equal or improved score for activity and knee function regardless of the operation performed.

Table 4.3: *Mean clinical outcome scores*

	Tegner		UCLA		Lysholm		OKS	
	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op
HTO	3.6	3.6	6.3	6.3	57.8	76.6	26.3	36.7
UKA	2.6	3.3	4.8	6.4	65.5	90.2	25.5	35.0
Overall	3.1	3.5	5.4	6.4	59.5	79.3	25.7	35.3

Note: HTO – high tibial osteotomy; UKA – unicompartmental knee arthroplasty
UCLA – University of California, Los Angeles activity scale; OKS – Oxford knee score

4.5 Discussion

HTO patients reported higher activity levels pre- and post-operatively compared to UKA patients, who in turn exhibited a greater overall pre- to post-operative improvement in physical activity (Tegner scores). Pooled analysis of the most commonly used outcome scores in the included studies showed that UKA patients experienced a greater improvement in the condition of their knee according to the Lysholm scores, but that knee function according to the Oxford Knee Score was similar between procedures. The pooled UCLA scores largely supported the pooled Tegner scores by showing that HTO patients were more physically active pre-operatively than UKA patients, and that a similar level of activity was maintained post-operatively. UKA patients exhibited a larger pre- to post-operative increase in physical activity than HTO patients. These findings demonstrate the propensity for HTO to be used in more active patients and for UKA to be performed in patients who are, pre-operatively, more sedentary.

The minimum clinically important difference (MCID) for the Tegner score has previously been estimated at 0.85 (Krych *et al.*, 2017; Kim *et al.*, 2018), which was not achieved pre- to post-operatively in either group in the pooled analysis. The MCID of the pre- to post-operative changes in the Lysholm (9.9 points) and Oxford Knee (5 points) scores was achieved in both groups (Clement, MacDonald and Simpson, 2014; Krych *et al.*, 2017; Kim *et al.*, 2018). The MCID of the UCLA score is not known. The mean pre-operative Tegner scores demonstrated that HTO patients were involved in light-moderate labour, competitive low impact sports (such as swimming), and recreational high impact sports (such as cross-country skiing or jogging on even ground). In comparison, mean pre-operative Tegner scores for UKA patients were equivalent to light labour and walking on uneven ground. Mean post-operative Tegner scores for both groups were similar to the mean pre-operative scores of the HTO group. A more highly active HTO patient group pre-operatively supports the traditional indications for both procedures regarding patient activity levels and suggests that they are being adhered to in most cases.

Other traditional indications such as HTO being better suited to younger patients than UKA, and HTO patients requiring a BMI lower than 30 kg/m^2, were reflected in the present review. A mean age difference of 12.2 years was observed between both patient groups, and the mean BMI of the HTO patients was 29.1 kg/m^2. However, cohorts in three of the studies were not consistent with the traditional indications (Walker *et al.*, 2015; Bastard *et al.*, 2017; Krych *et al.*, 2017). The study by Walker *et al.* (2015) specifically investigated patients under the age of 60 years who underwent UKA. Mean Tegner and UCLA scores improved significantly from 2.0 and 3.3 pre-operatively, respectively, to 3.8 and 6.8 post-operatively, respectively (mean follow-up 53 months). Similarly, the study by Krych *et al.* (2017), which included patients undergoing UKA with a mean age of 49.2 years, demonstrated an overall mean improvement in Tegner scores from 2.6 pre-operatively to 4.5 at a mean 70 months after surgery. The improvement in physical activity levels reported by Walker *et al.* (2015) and Krych *et al.* (2017) suggests that age may not be a limiting factor regarding return to physical activity after UKA. However, HTO has been shown to be more cost-effective than UKA in patients under 60 years of age (Bhandari *et al.*, 2012; Konopka *et al.*, 2015; Smith *et al.*, 2017; van Heerwaarden *et al.*, 2018).

If patients undergo UKA at a younger age than is traditionally indicated, attention must be paid towards the endpoint of such procedures and their impact on subsequent revision to total knee arthroplasty (TKA). A previous meta-analysis showed that revision to TKA after UKA occurred at a mean 8.2 years after surgery whereas revision to TKA after HTO occurred at a mean 9.7 years after surgery (Spahn *et al.*, 2013). Two review articles (including one meta-analysis) suggested that revising a UKA to TKA led to worse outcomes compared with primary TKA (Siddiqui and Ahmad, 2012; Sun and Su, 2018). Conversely, the literature tends to show that this was not the case for revising an HTO to TKA (van Raaij *et al.*, 2009; Dettoni *et al.*, 2010; Ramappa, Anand and Jennings, 2013). Additionally, a study by Robertsson and W-Dahl (2015) found that TKA after UKA had an increased risk of subsequent revision compared to TKA after HTO. High revision rates of UKA to TKA have also been shown in the United Kingdom's National Joint Registry – which records the outcomes of over 100,000 partial and total knee arthroplasties performed annually – leading to results based on very large sample sizes that support the previously mentioned literature (Reed *et al.*, 2019). There is some evidence to suggest that UKA performs well in the short- to mid-term after surgery in patients younger than the traditional indication for the procedure (Walker *et al.*, 2015; Krych *et al.*, 2017). However, the higher cost of UKA versus HTO, the shorter time until revision to TKA compared to HTO, the worse outcomes of the resultant TKA, and increased risk of subsequent revision of the TKA as reported in the literature suggests that caution should be exercised when offering UKA to patients <60 years.

In addition to age, the traditional BMI range for patients indicated for HTO has not always been strictly adhered to. In the HTO study by Bastard *et al.* (2017), the mean BMI of patients was 33.5 kg/m^2. Despite being higher than the traditionally recommended BMI threshold for HTO (<30 kg/m^2), patients equalled their pre-operative levels of physical activity at a mean 16 months follow-up according to the Tegner scores. This result was consistent with the pooled analysis of the other HTO studies in the present review.

The operative technique during HTO and UKA has many associated variables that could have an impact on outcome, which was also a major contributing factor to the heterogeneity of the reviewed studies. When pooling the Tegner data of the two HTO studies (62 knees) that reported that the osteotomy gap was filled with a graft material (Schröter *et al.*, 2013; Bastard *et al.*, 2017), a mean pre- to post-operative improvement in physical activity from 3.5 to 4.1 was observed. The five HTO studies (202 knees) that did not fill the osteotomy gap reported no change in physical activity levels with mean pre- and post-operative Tegner scores equalling 3.7 (Salzmann *et al.*, 2009; Saragaglia *et al.*, 2014; Faschingbauer *et al.*, 2015; Krych *et al.*, 2017; Nerhus *et al.*, 2017). These findings suggest that the inclusion of a graft during HTO may impact outcome and could allow for a return to physical activity at a level higher than pre-operative levels, though further investigation is required to confirm this.

Three HTO studies (Schröter *et al.*, 2013; Krych *et al.*, 2017; Nerhus *et al.*, 2017) showed a post-operative increase in physical activity, while one study (Bastard *et al.*, 2017) demonstrated no change, and the remaining four studies showed a decrease in physical activity levels, according to the Tegner scores. Conversely, five of the UKA studies included in the review showed a post-operative increase in physical activity, while two studies (Yim *et al.*, 2013; Jahnke *et al.*, 2014) resulted in a decrease according to the Tegner scores. The variation in HTO results compared with the more consistent pattern among most of the UKA studies suggests that UKA may lead to a more predictable increase in physical activity than HTO; but that patients who underwent HTO remained more active overall. It might equally demonstrate that the outcome of HTO is more sensitive to the surgical technique employed and equipment used than is the case with UKA. Due to the variation of results presented in the literature, these findings make evident the need for further investigation into return to physical activity after surgery, particularly in patients who undergo HTO.

Another study (Kim *et al.*, 2018) – which met the inclusion criteria for the present review but was unable to be included in the pooled analysis due to the use of graphs rather than numbers to present pre- and post-operative scores – demonstrated results that concurred with the main findings of this review. The authors performed a prospective comparative study of return to physical activity after HTO and UKA, where activity was measured using Tegner and UCLA scores pre-operatively and at 3, 6, 12, and 24 months after surgery. The findings showed that HTO patients were significantly more active than UKA patients pre-operatively but that UKA patients had a larger improvement in physical activity. The post-operative activity levels achieved by the UKA patients were not significantly different to their HTO counterparts after surgery.

Although previous systematic reviews have presented findings based on return to physical activity after HTO or UKA, none have compared the differences in activity levels between the two procedures. Ekhtiari *et al.* (2016) conducted a systematic review into return to work and sport after HTO and found that 85.2% of patients receiving opening-wedge HTO returned to a level of physical activity that was equal to, or greater than, their pre-operative status. These results were reflected in the findings of the present review. Waldstein *et al.*

(2017) conducted a similar systematic review (but with UKA patients) and found that participation in physical activity decreased up to 9% post-operatively. This is in contrast to the findings of the present review. It should, however, be noted that a decrease in activity participation does not necessarily equal a decrease in activity levels among the patients who remained active. This can be exemplified by further scrutinising the only study included in the present review that was also included in the Waldstein *et al.* (2017) review: Walker *et al.* (2015). Walker *et al.* (2015) found a 2% decrease in post-operative sports participation – defined as a patient being active in at least one physical activity prior to the onset of their symptoms – but simultaneously showed that mean pre- to post-operative patient Tegner and UCLA scores significantly increased. Based on this evidence, it can be inferred that UKA may lead to a decrease in the number of activities performed but that the level at which the remaining activities are performed, increases.

Four meta-analyses have compared outcomes of HTO and UKA but the only physical activity-related outcomes they examined was walking velocity. Two of the meta-analyses (Gandhi *et al.*, 2009; Santoso and Wu, 2017) found no significant differences between the procedures regarding walking velocity, whereas the remaining two meta-analyses (Fu *et al.*, 2013; Han *et al.*, 2017) found that UKA patients resulted in a faster walking velocity post-operatively than HTO patients. The finding of Gandhi *et al*. (2009) was criticised by its authors as being potentially underpowered since only two studies in their review reported walking velocity, constituting a total of approximately 30 HTO and 30 UKA patients. The meta-analysis by Santoso and Wu (2017) used the same studies as that of Fu *et al.* (2013) to assess walking velocity but came to different conclusions. This was explained by Santoso and Wu (2017) as being due to their analysis only including the HTO and UKA results in one particular study (Jefferson and Whittle, 1989), which also involved patients that had undergone total knee arthroplasty. In contrast Fu *et al.* (2013) included the results of the total knee arthroplasty patients with the UKA outcomes, thereby affecting the reliability of conclusions drawn specifically about UKA. There is conflicting evidence at best regarding walking velocity after HTO and UKA. Until further research is conducted it should not be used as a parameter for comparing the superiority of one procedure over the other regarding post-operative physical activity.

4.5.1 Strengths and limitations

The pooled analysis conducted on the demographic and operative data, as well as the most commonly used patient-reported outcome measures of the included studies, is a strength of this systematic review. The similar mean follow-up time between the pooled HTO and UKA groups allowed for a more reliable comparison of outcomes. However, the variation in the operative techniques and equipment used; the low numbers of prospective randomised controlled trials; and the high numbers of retrospective or non-comparative studies contributed to the heterogeneity of the included articles and the lack of statistical analysis performed on the data. Conclusions drawn based upon the pooled analysis in the present review only offer an approximate indication as to the current situation regarding HTO, UKA, and post-operative physical activity.

The results of the present paper were limited to patients who underwent HTO with internal plate fixators since this is the most common form of fixation used (Rossi, Bonasia and Amendola, 2011; Luo *et al.*, 2013). Alternative forms of fixation are available including external fixators, staples, or spacer implants (which are inserted into the osteotomy gap). Studies that included such fixation methods were not included in the present review as they could have confounded the overall results due to differences in their indications and fixation technique (Dowd, Somayaji and Uthukuri, 2006; Brinkman *et al.*, 2008; Lee and Byun, 2012), as well as in the clinical and biomechanical outcomes they achieve compared to internal plate fixation (Zhim *et al.*, 2005; Polyzois *et al.*, 2006; Anagnostakos, Mosser and Kohn, 2013; Belsey *et al.*, 2019a).

4.6 Conclusion

This systematic review showed that HTO and UKA are effective procedures that allow patients to return to an equal or greater level of physical activity post-operatively compared to their pre-operative status. Patients who underwent HTO were more physically active pre- and post-operatively, but UKA patients experienced an overall greater increase in their physical activity levels. Activity after HTO may be influenced by intraoperative factors such as the implant used and the decision to include a graft material, though this requires further research. Studies exist showing that patients were able to return to physical activity post-operatively despite having an age or BMI that would traditionally be a relative contraindication for HTO or UKA. Lastly, the relative cost-effectiveness and better implications for later conversion to total knee arthroplasty associated with HTO compared to UKA in younger patients suggests that the former procedure should retain its status as the preferred option for active patients under the age of 60 years.

Having come to the conclusion that HTO is a more appropriate procedure than UKA for young and active patients – one that was identified in Chapter 2 as necessary in order to cement the justification for this PhD project – attention should be drawn to the fact that HTO did not result in increased physical activity levels post-operatively but rather only equalled pre-operative ability. While this shows that HTO is not detrimental to physical activity, a research focus on further improving post-operative activity levels is warranted since patients are selected for this procedure largely due to them being active.

This systematic review highlighted that the outcome after HTO may be sensitive to variables in the surgical technique. Specifically, when the HTO data were stratified according to those that used bone grafting, a pre- to post-operative increase in Tegner activity scores was observed compared to HTO without grafting, where Tegner scores remained similar pre-operatively and at follow-up. This observation, combined with the suggestion based on the general literature review in Chapter 2 that the use of graft materials may improve the biomechanical performance of the osteotomy construct, provides the rationale for further investigation in this area. The use of graft materials during HTO and their impact on post-operative physical activity levels formed the basis for research questions from which the first empirical studies in this PhD project emerged.

CHAPTER 5 – IN-VITRO BIOMECHANICAL ANALYSES OF THE USE OF GRAFT MATERIALS DURING HTO

The following chapter has been published in the following journal articles (Appendix B):

Belsey, J., Diffo Kaze, A., Jobson, S., Faulkner, J., Maas, S., Khakha, R., Wilson, A.J. and Pape, D. (2019) Graft materials provide greater static strength to medial opening wedge high tibial osteotomy than when no graft is included. *Journal of Experimental Orthopaedics,* 6, 13. doi: https://doi.org/10.1186/s40634-019-0184-6.

Belsey, J., Diffo Kaze, A., Jobson, S., Faulkner, J., Maas, S., Khakha, R., Pape, D. and Wilson, A.J. (2019) The biomechanical effects of allograft wedges used for large corrections during medial opening wedge high tibial osteotomy. *PLoS One,* 14(5), 14. doi: https://doi.org/10.1371/journal.pone.0216660.

5.1 Abstract

Background: HTO with synthetic wedges is biomechanically stronger than to HTO without grafting. HTO with allograft wedges performs well clinically but its biomechanical performance is unknown. The purpose of this study was to compare the stability of HTO with and without different graft materials.

Methods: A 10 mm HTO was performed on 15 artificial sawbone tibiae, which were fixed using the Activmotion 2 plate. Five bones had OSferion60 wedges (10 mm synthetic group), five had allograft bone wedges (10 mm allograft group), and five had no wedges (10 mm control group) inserted into the osteotomy gap. A 12 mm HTO was performed on ten further sawbone tibiae, which were fixed using a Tomofix plate. Five bones had allograft wedges (12 mm allograft group) and five had no graft inserted into the gap (12 mm control group). Specimens underwent either static or fatigue strength testing until construct failure. Ultimate load, and horizontal and vertical displacements were measured and used to calculate construct stiffness and valgus malrotation of the tibial head.

Results: The 10 mm synthetic group failed at 6.3 kN after static strength testing, followed by the 10 mm allograft group (6 kN), and the 10 mm control group (4.5 kN). The most valgus malrotation of the tibial head was observed in the 10 mm allograft group (2.6˚). The 10 mm synthetic group showed the highest stiffness at the medial side of the tibial head (9.54 kN·mm^{-1}), but the lowest stiffness at the lateral side (1.59 kN·mm$^{-1)}$. The 10 mm allograft group showed high stiffness on the medial side of the tibial head (7.54 kN·mm^{-1}) as well as the highest stiffness on the lateral side (2.18 kN·mm^{-1}). Under static compression, the 12 mm allograft group withstood higher peak forces (6.01 kN) compared with the 12 mm control group (5.12 kN). Valgus malrotation was lower, and stiffness was higher, in the 12 mm allograft group. During cyclical fatigue testing, results within the 12 mm allograft group were more consistent than within the 12 mm control group.

Conclusion: The use of graft materials in HTO resulted in higher structural strength and stiffness compared to HTO without grafting. The construct strength of HTO was highest when synthetic grafts were inserted into the osteotomy gap. Allograft wedges provided higher mechanical strength and performed more consistently than HTO without grafting. In comparison to the synthetic grafts, allograft wedges resulted in more even levels of stiffness at the medial and lateral cortices.

5.2 Introduction

As discussed in Chapter 2 and 4, medial opening-wedge HTO has been shown to have promising clinical and radiological outcomes in the short- and mid-term irrespective of whether graft materials were (Lee *et al.,* 2010; Ganji *et al.,* 2013; Saito *et al.,* 2014) or were not (El-Assal *et al.,* 2010; Floerkemeier *et al.,* 2013; Saier *et al.,* 2017) used during the procedure. Clinically, a greater incidence of post-operative complications have been previously reported in larger corrections (>10 mm opening) and the inclusion of a bone graft, preferably autograft, has been recommended (Lobenhoffer and Agneskirchner, 2003; Yacobucci and Cocking, 2008; Jung *et al.*, 2010; Santic *et al.*, 2010). Lateral cortex fractures in particular have been reported to occur more frequently in HTO openings >10 mm, either intra-operatively or post-operatively (Spahn, 2004; Miller *et al.*, 2009), which lead to greater instability of the overall construct (Miller *et al.*, 2005; El-Assal *et al.*, 2010; Meidinger *et al.*, 2011; Takeuchi *et al.*, 2012). This can negatively influence certain clinical outcomes such as correction accuracy and time-to-union (Miller *et al.*, 2005; van Raaij *et al.*, 2008; Yacobucci and Cocking, 2008; Meidinger *et al.*, 2011; Takeuchi *et al.*, 2012). Furthermore, studies have shown a negative correlation between the size of an osteotomy gap and time-to-union (El-Assal *et al.*, 2010; Jung *et al.*, 2010). However, the insertion of an allograft wedge into the osteotomy gap seems to facilitate time-to-union in larger corrections to a degree comparable to smaller osteotomies (Jung *et al.*, 2010; Lee *et al.*, 2010; Nawas *et al.*, 2016).

Biomechanically, when considering the properties of the newly operated osteotomy construct, there is limited evidence to suggest that the inclusion of graft materials during HTO is preferable to leaving the osteotomy gap unfilled (Takeuchi *et al.*, 2010). Takeuchi *et al.* (2010) compared synthetic grafts versus no graft in a 7.5 mm HTO and found that synthetic grafts provided greater axial stability to the operated tibia. The in-vitro nature of the study – meaning no healing had taken place – represented how osteotomy constructs might perform biomechanically at a time equivalent to the first few post-operative weeks: before healing noticeably begins. This was the only study to have investigated the biomechanical differences of HTO with a graft compared to a control group where no graft was used. It is unknown whether the differences observed were specific to synthetic grafts or if the results represented a common advantage for the various graft types that can be used during surgery over HTO without grafting. There is a clear disparity in what is known about the biomechanical properties of graft materials used during HTO compared to their clinical effects.

The different types of graft material that are most used during HTO can be divided into three general categories: autograft, allograft, and synthetic. The pros and cons of each graft type was discussed in more detail in Chapter 2. As a brief overview: autografts offer the most reliable healing properties (Han *et al.*, 2015; Lash *et al.*, 2015), but patients often suffer increased pain in the immediate post-operative period as a result of the harvesting procedure, often performed at the iliac crest (Kuremsky *et al.*, 2010; Chae *et al.*, 2011; Pornrattanamaneewong *et al.*, 2012). Increased pain in the longer term has been a reported criticism of the use of synthetic grafts during HTO (Gouin *et al.*, 2010; Lind-Hansen *et al.*, 2016). A higher incidence of delayed- or non-union when synthetic grafts were used has also been noted (Lash *et al.*, 2015; Ferner *et al.*, 2016; Slevin *et al.*, 2016). The main benefit of synthetic grafts is that they do not carry the risk of disease transmission, which is inherent in the use of allografts – albeit a low risk that is often considered a "historical complication (Amendola and Bonasia, 2010; Hung and Noi, 2012; Han *et al.*, 2015; Lash *et al.*, 2015; Slevin *et al.*, 2016).

Allograft wedges have better osteoconductive properties than synthetic grafts, resulting in low rates of delayed- or non-union in HTO (Lash *et al.*, 2015; Slevin *et al.*, 2016). Allografts simultaneously maintain an advantage over autografts in terms of lower pain in the immediate post-operative period since no secondary procedure to harvest the graft is necessary (Amendola and Bonasia, 2010; Hung and Noi, 2012). On balance, allograft wedges could be the optimal material to fill an osteotomy gap in reference to clinical outcome. It is not known how they perform biomechanically with regard to the strength and stability they provide to an osteotomy construct in the same way that synthetic grafts have been shown to (Takeuchi *et al.*, 2010). Equally, no information exists pertaining to the biomechanical properties of a large (>10mm) HTO opening with and without graft materials. If the inclusion of a graft material provides more stability in HTO >10 mm – which are more likely to experience hinge fractures that reduce overall construct stability – then HTO with grafting could be recommended from a biomechanical perspective as well as from the already-accepted clinical perspective.

A high level of physical activity is one of the key surgical indications that separates HTO from UKA (Dettoni *et al.*, 2010; Fu *et al.*, 2013). As the systematic review in the previous chapter showed, patients were able to return to a level of physical activity after HTO that equalled or exceeded their pre-operative levels. The inclusion of a bone graft during HTO appeared to coincide with patients who experienced a pre- to post-operative increase in activity levels. In contrast, HTO without grafting resulted in patients only equalling their pre-operative activity ability. This was a secondary observation of the systematic review and, as such, cannot be confirmed to be true without further research. Nevertheless, it suggested that the outcome of HTO may be impacted by the presence of a graft material. Considering that an osteotomy construct has been shown to be biomechanically more stable in the (simulated) early post-operative period when synthetic grafts were used (Takeuchi *et al.*, 2010), there may be implications of a sooner return to activity after surgery when the osteotomy gap is filled. This would be particularly relevant if other graft materials – which perform better than synthetic grafts clinically – also share the biomechanical advantage of synthetic grafts over an unfilled HTO.

Understanding whether differences in graft type result in differences in biomechanical performance will help to inform clinical practice regarding the selection of an appropriate material for certain patient demographics. For example, patients who exert high forces through their knee – because of factors such as high body mass or high physical activity levels – may benefit from an HTO that confers greater resistance to mechanical loads. This could reduce the risk of post-operative complications such as loss of correction or a lateral hinge fracture – associated with an inferior clinical outcome (Spahn, Kirschbaum and Kahl, 2006; Schröter *et al.*, 2015) – and could translate to a sooner return to physical activity for patients.

The purpose of this study was to investigate the static strength (load to failure, stiffness, and valgus malrotation) of HTO with allografts, synthetic grafts, or no grafts. The availability of resources and materials meant that a secondary aim of this study was to also investigate the biomechanical differences in strength and stability between HTO with and without graft materials where an opening >10 mm was performed. It was hypothesised that: 1) both allografts and synthetic grafts would provide greater static strength to HTO compared to when no graft was used; 2) there would be a difference in performance between the two graft types; and 3) in gap sizes >10 mm, HTO with grafting would provide greater static and fatigue strength compared to HTO without grafting.

5.3 Methods

25 medium-size 4th generation analogue composite tibiae were used (Sawbones, Pacific Research Laboratories, Inc., Vashon Island, Washington, USA). These sawbone models have been validated and shown to have similar biomechanical properties to human bone while having significantly lower inter-specimen variability in comparison to cadaveric specimens (Heiner, 2008; Gardner *et al.,* 2010). Ethical approval for this study was granted by the University of Winchester Faculty of Business, Law & Sport ethics panel (Appendix C).

5.3.1 Specimen preparation

A 10 mm HTO was performed on 15 specimens by an experienced orthopaedic surgeon and fixed with a size 2 ActivMotion HTO plate (NewClip Technics, Haute-Goulaine, France) positioned antero-medially on the tibial head. The remaining 10 specimens received a 12 mm HTO, which was fixed medially with a standard Tomofix plate (Depuy Synthes GmbH, Oberdorf, Switzerland). Each osteotomy was performed in the same way, using the biplanar technique, with the plate fixed according to the standard technique of the implant (Diffo Kaze *et al.,* 2017). Performing a biplanar osteotomy has been shown to promote bone healing with increased stability, both rotationally and antero-posteriorly, compared to the uniplanar technique (Lobenhoffer and Agneskirchner, 2003; Pape *et al.*, 2010; van Heerwaarden *et al.*, 2018). A variety of plates exist for internal fixation of an osteotomy, of which the TomoFix plate is considered the gold standard (Diffo Kaze *et al.,* 2015). Alternative internal fixators are gathering popularity with varying degrees of success regarding clinical outcomes (pain and knee function) (Cotic *et al.,* 2015) and structural properties (construct strength and stiffness) (Diffo Kaze *et al.,* 2015; Luo *et al.,* 2015). The size 2 ActivMotion plate has been shown to allow an HTO to resist the greatest load until failure under static compression testing. It also provides the highest construct stiffness under cyclical testing, compared to the standard Tomofix plate and four other commercially available HTO plates (Diffo Kaze *et al.*, 2019).

In five of the 10 mm HTO specimens, a 10 mm (height) x 72mm (depth) bone wedge allograft (RTI Surgical Inc., Alachua, Florida, USA), sourced from the proximal tibia of a donor, was inserted prior to the fixation of the plate (10 mm Allograft Group; Figure 5.1a). The width of each allograft wedge was cut so that the graft matched the size of the osteotomy gap; as would be the case in-vivo. In the 10 mm Synthetic Group, two 10 mm x 10 mm x 50 mm β-tricalcium phosphate wedges (OSferion60, Olympus Terumo Biomaterials, Tokyo, Japan) were inserted into another five sawbone tibiae, prior to plate fixation of the osteotomy (Figure 5.1b) as previously reported (Takeuchi *et al.,* 2010). Five of the 12 mm HTO specimens were filled with a 12 mm x 72 mm allograft wedge (12 mm Allograft Group; Figure 5.1d). Each allograft and synthetic bone wedge was held in place using an ethyl cyanoacrylate glue to prevent the risk of them slipping or falling out of the osteotomy gap during testing. The remaining five 10 mm and five 12 mm HTO specimens had no graft inserted into the osteotomy gap (10 mm Control Group and 12 mm Control Group, respectively; Figures 5.1c and 5.1e).

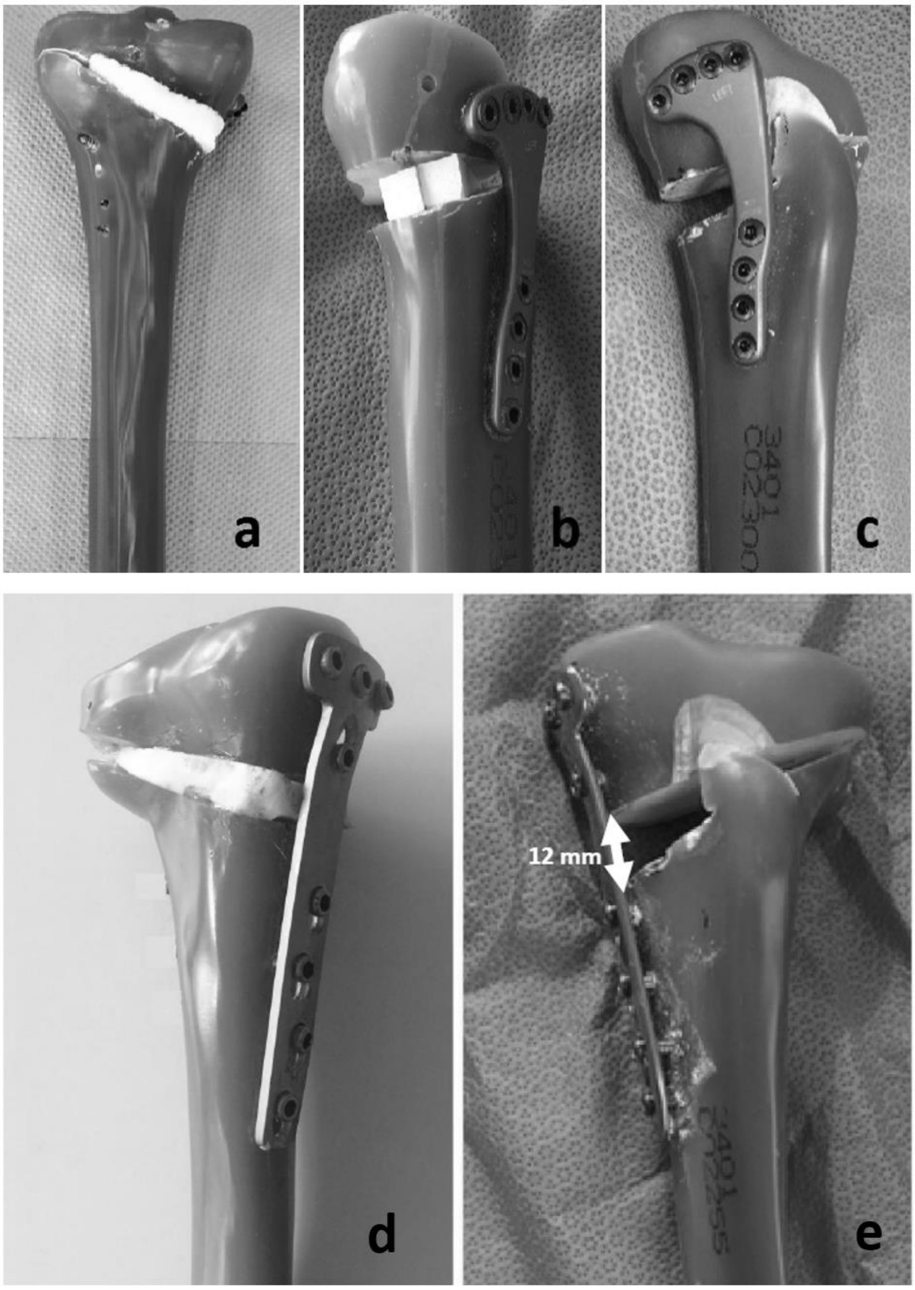

Figure 5.1: Example specimens from each group

a) 10 mm Allograft Group, b) 10 mm Synthetic Group, c) 10 mm Control Group, d) 12 mm Allograft Group, e) 12 mm Control Group

Each specimen was prepared for testing using a previously described method (Maas *et al.,* 2013; Diffo Kaze *et al.,* 2015). Specimens were cut 300 mm distal to the tibial plateau and placed inside a deep cylindrical mould (Figure 5.2a). A scaffold was mounted around the mould, with a centrical pinion on the inside base of the mould to ensure that the specimens were identically positioned for each test. A two-part polyurethane casting resin (FC-52, Huntsman Advanced Materials GmbH, Basel, Switzerland), created by mixing equal parts of an isocyanate and a polyol, was then poured into the cylindrical mould to better secure the specimen (Figure 5.2b). Once the resin hardened, the scaffold was removed and the specimens were rotated 180°, allowing the tibial head to be placed upside down inside a shallow cylindrical mould, in which more of the casting resin was then poured. Before the resin was added to the shallow mould, two small metal plates were appended to the medial and lateral sides of the mould, to which the displacement sensors were then attached during testing (Figure 5.2c). Finally, a custom-made sensor clamp was attached to the tibial shaft for the vertical displacement sensors to be held in place (Figure 5.2d).

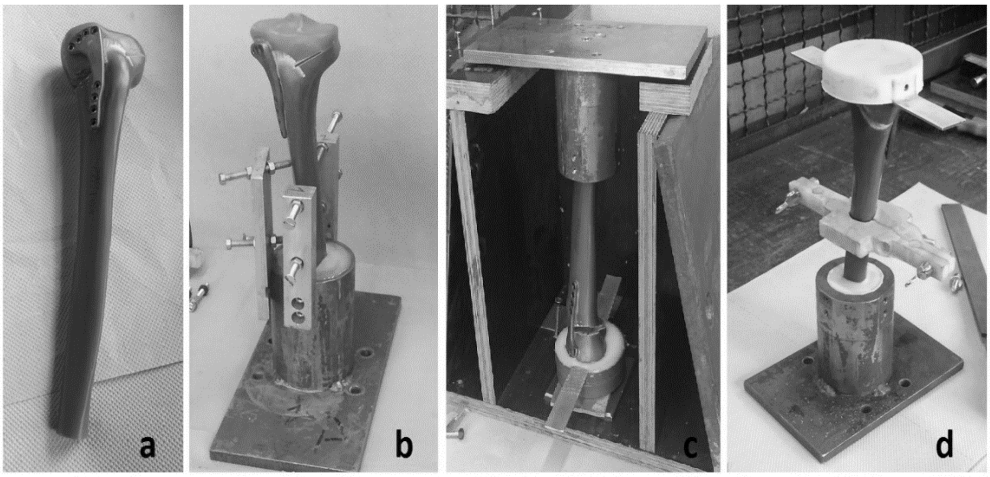

Figure 5.2: Specimen preparation

a) specimen cut 300 mm distal to tibial plateau; b) specimen placed inside cylindrical mould and casting resin added; c) tibial head placed in shallow mould and casting resin added; d) custom-made sensor clamp attached to tibial shaft.

5.3.2 Static strength test protocol

Following a previously published protocol (Maas *et al.,* 2013; Diffo Kaze *et al.,* 2015) all fifteen 10 mm specimens, and four of the 12 mm specimens (two per group), underwent static testing. Each specimen was loaded onto a 10 kN hydraulic piston (INSTRON, Darmstadt, Germany), which applied a pure vertical load to the tibial head through a moveable support. The support was able to move freely in the transverse plane by way of three moving metal balls. The distal end of each specimen was screwed to the piston, preventing any movement of the deep cylindrical mould in the transverse plane. Six displacement sensors were used to capture the deformation of each specimen at different positions around the tibial head during each test. With reference to the transverse plane, five of the displacement sensors were positioned as follows: lateral to the tibial head in the x-axis (LSX); medially and laterally to the tibial head in the y-axis (labelled "MSY" and "LSY" respectively); and medially and laterally to the tibial head in the z-axis (labelled "MSZ and LSZ" respectively). A final vertical displacement sensor (VS) was contained within the testing machine, which measured the vertical displacement of the hydraulic piston (Figure 5.3).

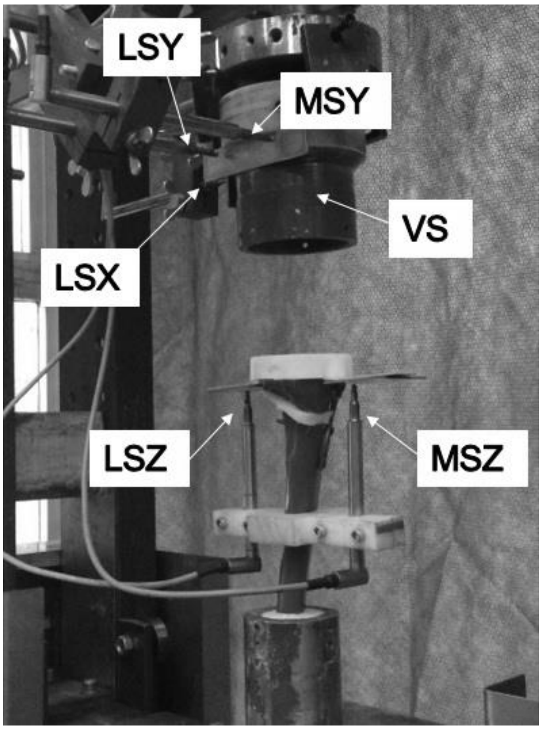

Figure 5.3: Positioning of displacement sensors around the tibial head (posteromedial view)

VS = vertical sensor; LSX = lateral sensor x-axis; LSY = lateral sensor y-axis; MSY = medial sensor y-axis; LSZ = lateral sensor z-axis; MSZ = medial sensor z-axis.

Once the setup was complete, the piston applied static compression to the specimens under displacement-controlled conditions, following a ramp protocol, with single loading to failure at a speed of 0.1 mm·s^{-1}. Failure was determined as being the point at which a simultaneous audible and visible collapse of the lateral cortex of the tibial head occurred (Figure 5.4), which has previously been described as a "Type 2 Failure" (Takeuchi *et al.*, 2012; Diffo Kaze *et al.*, 2015). In all cases, the point of failure was also signalled by a sudden drop in the force being applied to the tibial head by the piston as the collapse occurred.

Figure 5.4: Example of lateral cortex fracture and osteotomy collapse

5.3.3 Fatigue Strength Test Protocol

The remaining six 12 mm HTO specimens (3 per group) underwent fatigue strength testing. Each specimen was loaded onto the piston, and displacement sensors were attached, in a similar fashion as described above.

Sinusoidal loading at a frequency of 5 Hz was then applied by the piston to each specimen. Compression was increased stepwise until the point of failure at the lateral cortex of the tibial head (Figure 5.5). The lower compressive force limit remained constant at 0.16 kN throughout each load step. The upper compressive force limit for the first step was 0.8 kN, which was then increased at a constant rate of 0.16 kN after every 20,000 cycles (one load step), if the specimen remained intact.

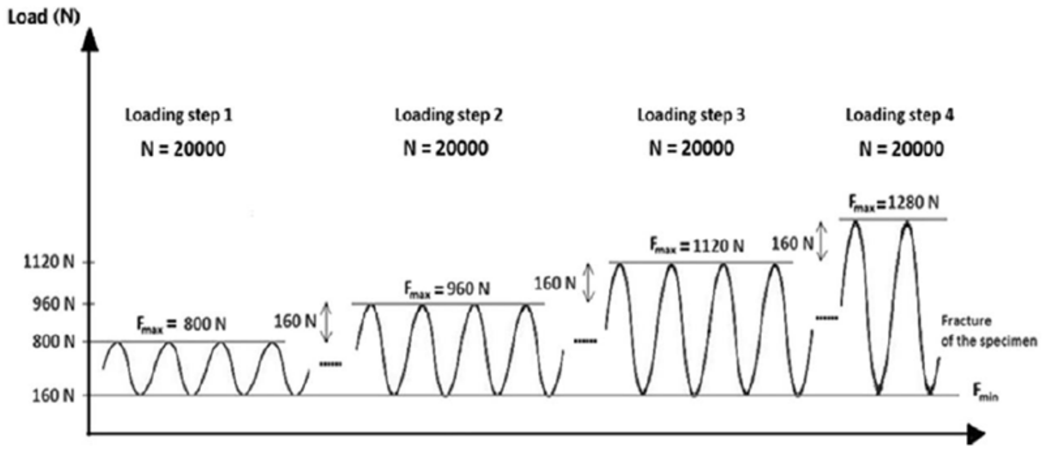

Figure 5.5: Applied vertical sinusoidal force step loading (Maas et al., 2013)

Loading frequency remained constant at 5 Hz and the upper force limit increased 0.16kN stepwise every 20,000 cycles until failure.

5.3.4 Analysis

The small sample size per group, which was limited due to financial reasons, meant that statistical tests were not performed on the data and only the means are presented. However, it should be noted that the group sizes were similar to, or larger than, those in the related literature (Takeuchi *et al.,* 2010; Diffo Kaze *et al.,* 2015). The peak force (kN) and displacement (mm) of all sensors at specimen failure were recorded. Displacements were recorded as either positive or negative values, indicating direction of the displacement. Following the protocol of a previous study (Diffo Kaze *et al.,* 2015), the stiffness (kN·mm^{-1}) of each specimen that underwent static strength testing (at each of the sensor positions) was calculated using the ratio of the measured force and displacement at the point of failure. Prior to calculating stiffness, any negative displacement values were multiplied by -1 to make them positive so that only absolute values were used, since the direction of each displacement was irrelevant for this calculation.

Dynamic stiffness of the six 12 mm HTO specimens that underwent fatigue strength testing was calculated using the ratio of the peak-to-peak force (ΔF) and peak-to-peak displacement (ΔX) from the same period of time at each sensor position around the tibial head (Figure 5.6; Maas *et al.*, 2013; Diffo Kaze *et al.*, 2015, 2017). Similar to the static tests, any negative displacement values were multiplied by -1 prior to calculation of stiffness to make them positive, since the direction of the displacement was equally irrelevant.

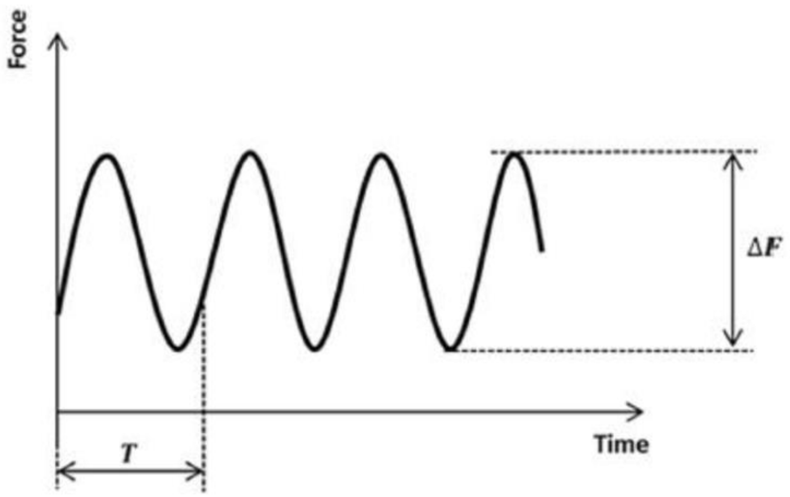

Figure 5.6: ΔF and ΔX used to calculate dynamic stiffness during fatigue strength testing (Maas et al., 2013)

Valgus malrotation of the tibial head in the frontal plane was calculated using the following formula (Diffo Kaze *et al.,* 2015):

$$\alpha = \frac{|d_L - d_M|}{D}$$

Where "α" was the valgus malrotation (rad), "dL" was LSZ displacement (mm), "dM" was MSZ displacement (mm), and "D" was the distance between the two sensor positions. The value α was then converted from radians to degrees by multiplying α by 180˚/3.14 rad.

Since different plates were used for the 10 mm HTO groups compared to the 12 mm HTO groups – due to limited available resources – analysis of differences between the two osteotomy sizes was not conducted. The different plates would likely have confounded any comparisons since they have both been shown to perform differently under biomechanical testing (Diffo Kaze *et al.*, 2017).

5.4 Results

5.4.1 Static strength testing in 10 mm HTO specimens

The data from one specimen in the allograft group and one specimen in the synthetic group were not included in the final analysis due to them accidentally being loaded prior to testing, resulting in the specimens failing abnormally early during their tests. Four specimens in the allograft group, four in the synthetic group, and five in the control group were analysed. All specimens, except for two in the allograft group, experienced an intra-operative lateral hinge fracture.

During testing all specimens failed in similar fashion due to a fracture of the lateral cortex of the tibial head (Figure 5.4). Prior to failure cracks were observed in the bones for all specimens, except two in the control group. Table 5.1 shows the mean force (kN) and time (s) at the point of failure for each group. The synthetic group failed at a higher ultimate load than the allograft and control groups, respectively.

Table 5.1: *Mean force and time at point of failure*

Group (10 mm HTO)	**Mean ± SD force at time of failure (kN)**	**Time until point of failure (s)**
Control	4.5 ± 1.6	20
Allograft	6.0 ± 1.8	25.8
Synthetic	6.3 ± 2.4	37.9

Figure 5.7 shows the mean displacements at each sensor position around the tibial head. A lateral-medial displacement of the tibial head during testing, as shown by a negative LSX value, was observed across all groups. Mean displacement values at positions LSY and MSY (anterior proximal tibial head) were negative, indicating an overall posteroanterior movement of the tibial head. The smallest difference between values at LSY and MSY was seen in the allograft group, followed by the control group and the synthetic group, respectively. In each group the mean absolute vertical displacement at the lateral cortex of the tibial head, position LSZ (1.1 mm, 2.8 mm, and 4.5 mm in the control, allograft, and synthetic groups respectively), was greater than at the medial cortex, position MSZ (-0.3 mm, -0.9 mm, and -0.9 mm in the control, allograft, and synthetic groups respectively). Values recorded at the lateral cortex were negative and those recorded at the medial cortex were positive (Figure 5.8). This indicated a valgus malrotation of the tibial head across all groups (since positive values equalled a downward motion and negative values equalled an upward motion). The amount of valgus malrotation of the tibial head was also measured, with the allograft group exhibiting the highest value (2.6˚), followed by the synthetic group (1.8˚) and the control group (0.7˚).

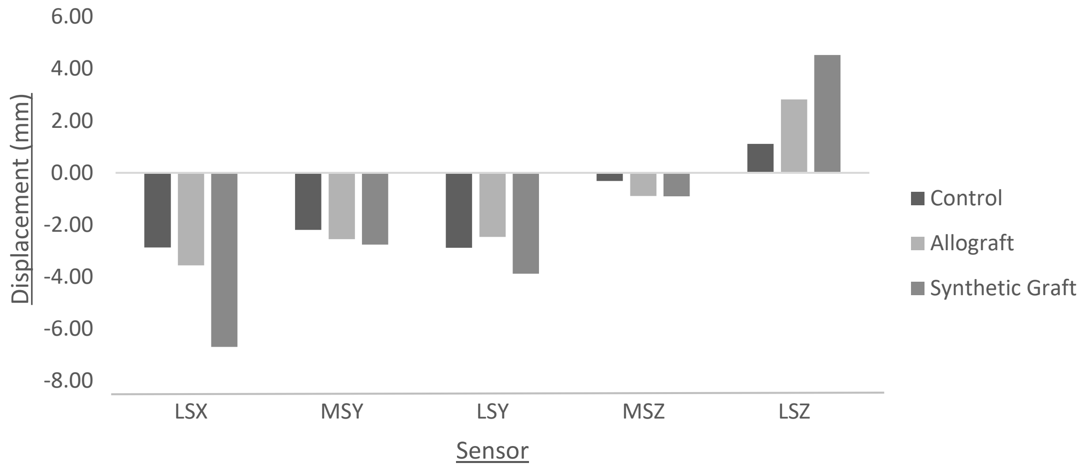

Figure 5.7: Mean displacement (mm) at each sensor position around the tibial head

Negative LSX values indicate lateromedial movement; negative MSY and LSY values indicate a posteroanterior movement; negative MSZ values indicate upward vertical movement; positive LSZ values indicate downward vertical movement. Allograft group (n=4), Synthetic group (n=4), Control group (n=5).

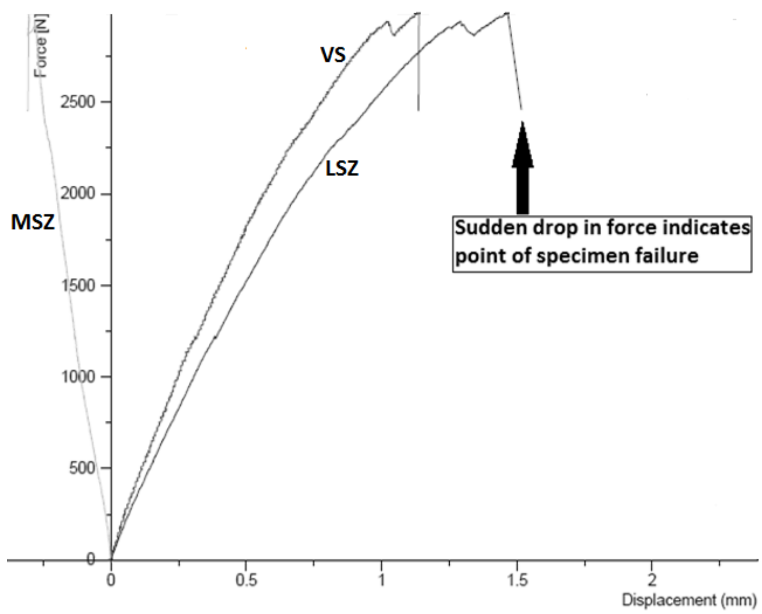

Figure 5.8: Example of vertical displacements

"VS" is positive, indicating the downward vertical motion of the piston. "MSZ" is negative and "LSZ" is positive, indicating a valgus malrotation of the tibial head.

Figure 5.9 shows the mean stiffness for each group at each sensor position around the tibial head. The lateral side of the tibial head was stiffest in the allograft group and weakest overall in the synthetic group; except for position LSY, where the synthetic group showed higher stiffness. The synthetic group was also the stiffest at the medial positions around the tibial head, followed by the allograft group and control group, respectively.

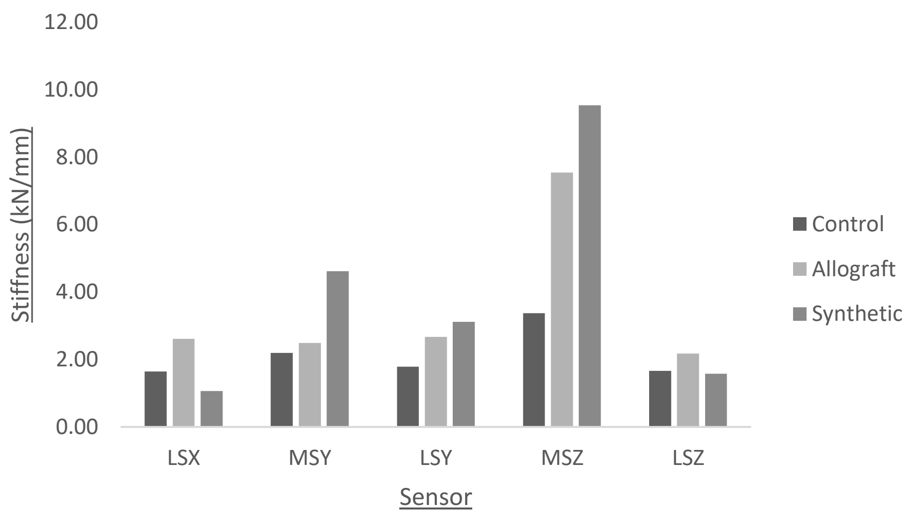

Figure 5.9: Mean stiffness at each sensor position for all groups at time of failure Allograft group (n=4), Synthetic group (n=4), Control group (n=5).

5.4.2 Testing of 12 mm HTO specimens

All 12 mm HTO specimens exhibited a lateral hinge fracture intraoperatively. A system malfunction during a fatigue test destroyed one tibia (specimen 1) from the Allograft Group, meaning that the data from this specimen could not be used in the analysis. In all tested specimens – except one (specimen 3) in the Allograft Group that underwent fatigue strength testing – construct failure occurred due to further fracture of the lateral cortex of the tibial head. Testing of specimen 3 from the Allograft Group was halted due to excessive valgus malrotations causing the lower safety limits to be tripped on the test machine. This was considered a specimen failure, and the data were included in the analysis. Since the specimen was not visibly damaged (other than the intra-operative hinge fracture), it also underwent static compression to failure. Consequently, the following results were based on: 3 specimens with an allograft, and 2 specimens with no graft that underwent static strength testing; and 2 specimens with an allograft, and 3 specimens with no graft that underwent fatigue strength testing.

5.4.3 Static strength testing in 12 mm HTO specimens

Cracking was observed in one specimen from each group prior to the final failure of the specimen. This cracking was first observed at a force of 3.78 kN in the control group, and at 3.12 kN in the allograft group. Table 5.2 shows the mean peak force (kN) and time (s) at the point of failure for each group. The allograft group withstood higher loads until construct failure than the control group.

Table 5.2: *Mean force at time of failure in each 12 mm HTO group.*

Group (12 mm HTO)	Mean ± SD force at failure (kN)	Time at failure (s)
Control	5.12 ± 0.7	40.36
Allograft	6.01 ± 0.7	44.54

Figure 5.10 shows the mean displacements at the point of failure at each sensor position around the tibial head. The largest absolute displacement in both groups was seen at position LSX. This is explained by the fact that the tibia head could move freely in the transverse plane. The negative LSX values indicated movement in a lateromedial direction. Values in both groups at position MSY and LSY were negative, indicating a posteroanterior movement of the tibial head. Since the values at these two sensor positions were not similar within groups, a slight axial rotation of the tibial head was also indicated. The allograft group showed a positive displacement at position MSZ, whereas the control group showed a negative displacement, indicating vertical downward and upward movements, respectively. LSZ displacement values were positive for both groups, indicating an overall vertical downward displacement. The difference in values within groups at position LSZ also indicated valgus malrotation of the tibial head. Since the control group displayed a negative displacement at MSZ but a positive displacement at LSZ – and the allograft displayed positive values at both positions – larger valgus malrotation of the tibial head was indicated in the control group. This was confirmed upon calculating the valgus malrotation of the tibial head where it was lower in the allograft group (2.22˚) than in the control group (2.85˚).

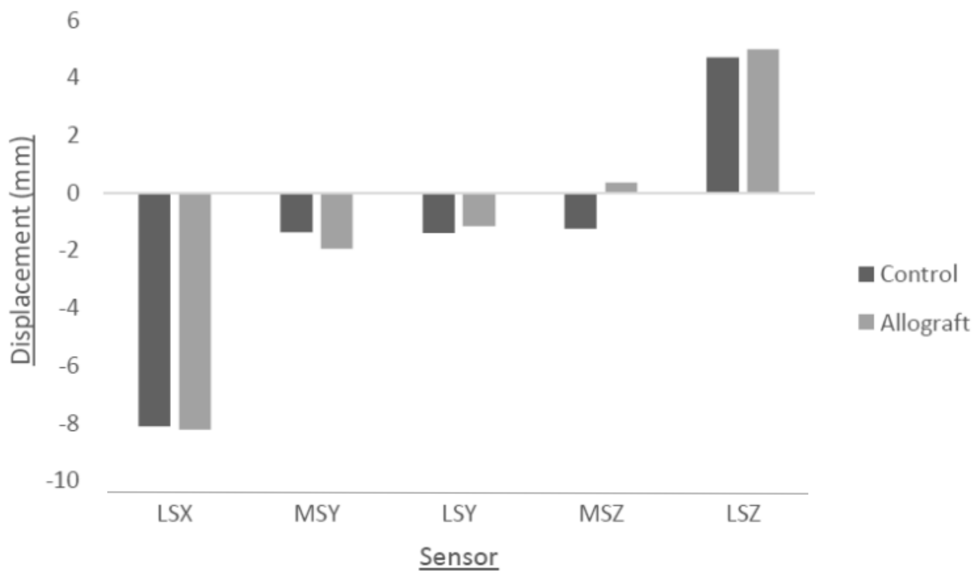

Figure 5.10: Mean displacement (mm) at each sensor position at specimen failure

Negative values at LSX indicate lateromedial movement. Negative values at MSY and LSY indicate posteroanterior movement. Negative and positive values at MSZ and LSZ indicate valgus malrotation.

Figure 5.11 shows the mean stiffness for each group at each sensor position around the tibial head. The allograft group exhibited higher specimen stiffness than the control group. The largest difference in stiffness between groups was seen at position MSZ. The lateral side of the tibial head showed the lowest overall stiffness in both groups compared to the medial side.

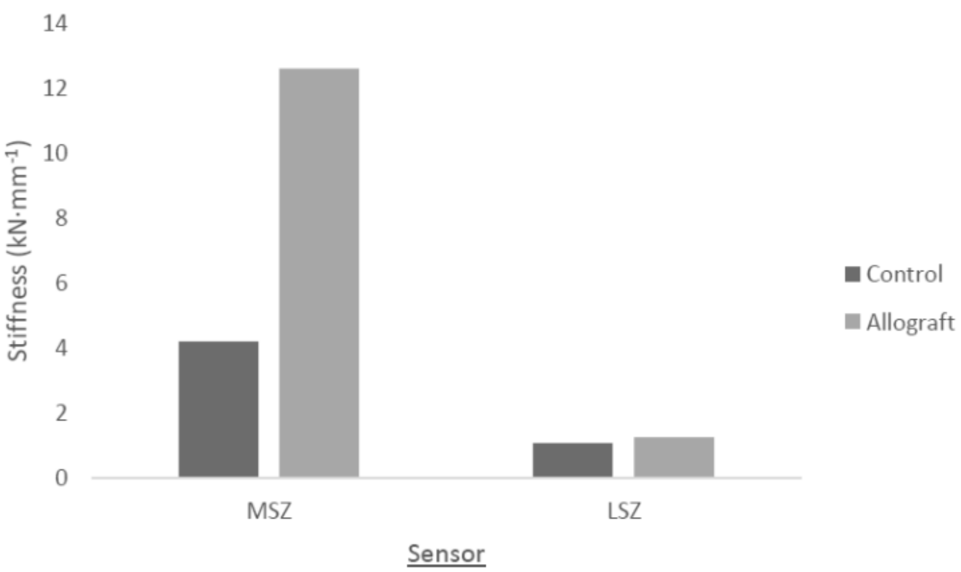

Figure 5.11: Mean specimen static stiffness around the tibial head at the point of failure.

5.4.4 *Fatigue strength testing in 12 mm HTO specimens*

Table 5.3 shows the load step, the approximate number of cycles, and maximum sinusoidal force that was applied to each specimen at the point of failure. Specimen "control 1" performed better than all other specimens: reaching the highest load step and therefore withstanding more cycles and higher forces. The remaining specimens from the control group, performed inferiorly to those in the allograft group.

Table 5.3: *Load step, approximate number of cycles, and maximum sinusoidal force at failure.*

12 mm HTO specimen	Load Step in which Fracture Occurred	Approximate Number of Cycles Until Failure	Maximum Sinusoidal Force (kN)
Control 1	4	67, 308	1.12
Control 2	2	37,974	0.80
Control 3	2	20,037	0.80
Allograft 1	3	42,630	0.96
Allograft 2	2	39,341	0.80

The vertical (VS) and lateral (LSZ) dynamic stiffness of each specimen that underwent fatigue strength testing was analysed, following the protocol of Diffo Kaze *et al.* (2015). A trend towards the lateral side of the tibial head being stiffer than the overall vertical dynamic stiffness was observed in the control group, whereas the opposite was true for the allograft group. Specimen 3 in the control group exhibited weaker lateral dynamic stiffness in comparison to the other control specimens.

5.5 Discussion

The key finding of this study was that an HTO with a graft material was able to withstand more vertical compressive force than an unfilled HTO, suggesting that a filled HTO was more stable and a mechanically stronger construct. HTO with a 12 mm gap resulted in a more predictable biomechanical performance when a graft was used compared to when the gap was left unfilled. During static strength testing, all groups – irrespective of gap size or grafting – fractured at a force greater than the physiological knee loads during normal, level walking (approximately 3 times bodyweight) (Taylor *et al.*, 2004). Only one other study has compared the biomechanical effects of synthetic augmentation in HTO against controls with no graft (Takeuchi *et al.,* 2010). While a direct comparison of results between that study and the present one is not possible due to differences between the methods employed and materials used, the findings are similar. Both studies demonstrated that synthetic grafts provided higher stability to an HTO under static compression than when no graft was inserted into the osteotomy gap. The present study was the first to compare multiple graft types against HTO without grafting using a biomechanical analysis.

5.5.1 Static strength of HTO

Each graft group withstood higher forces than their respective control group prior to construct failure during static strength testing, which may be explained by the increased medial and lateral stiffness of the tibial head provided by the wedges (Figures 5.9 and 5.11). This added static stiffness reduced valgus malrotation of the tibial head, which likely helped to distribute the vertical force more evenly across the tibial head and lowered the stress on the weakest point of the HTO: the lateral hinge (Watanabe *et al.*, 2014; Diffo Kaze *et al.*, 2015, 2017). A recent study used a 3D finite element model to find that the way that loads are balanced between the medial and lateral compartments of the knee may be key in optimising the clinical outcome of the procedure (Zheng *et al.*, 2017).

The highest mean stiffness value was recorded at the medial cortex in the 10 mm Synthetic Group. There is a limit to the beneficial amount of stiffness within an HTO construct because a certain level of elasticity is required to promote osteogenesis (Staubli and Jacob, 2010) and because too much stiffness can have deleterious effects on bony union (Röderer *et al.,* 2014). This is further supported by research showing that the current gold standard plate – Tomofix – is not the one that provides the highest construct stiffness (Maas *et al.,* 2013; Diffo Kaze *et al.,* 2017). The largest difference in stiffness between graft groups and their respective control groups was observed at the medial side of the tibial head. This is also the position where the fixation plates were situated and where the grafts were at their thickest, which explains the large discrepancy between the medial and lateral cortices of the tibial head. The specimens in the 10 mm Allograft Graft group exhibited higher stiffness at the lateral cortex compared to the 10 mm Synthetic Group and 10 mm Control Group. This may indicate that their inclusion better distributes compressive and shear forces across the knee, leading to better outcomes clinically. This would be particularly relevant for larger correction angles, which have been previously associated with inferior outcomes (van Raaij *et al.*, 2008; Yacobucci and Cocking, 2008; Nawas *et al.*, 2016).

A breaking up of the lateral side of the synthetic grafts was observed during testing, which supports the above indication that allograft wedges better support the lateral cortex.

Such concerns over the performance of synthetic grafts under compressive loads have been discussed in previous research (Amendola and Bonasia, 2010). It is also possible that the increased force distribution provided by the allograft wedges could be attributed to the differences in their shape compared to the synthetic grafts. The allograft wedges spanned the height, width, and depth (in the sagittal plane) of the osteotomy gap, whereas the synthetic grafts did not fully span the width of the opening. Despite these findings, the synthetic group withstood higher peak forces before failure of the osteotomy construct than the allograft group, which may suggest a link between high medial stiffness and the maximum force required to cause a fracture of the contralateral cortex of the tibial head.

The differences in vertical displacement values of the lateral and medial cortices, despite being compressed evenly by the piston, were mostly due to the presence of the fixation plate on the medial side. The plates did not lose their shape or weaken when the static forces were applied, since they are able to withstand much higher peak axial forces (Diffo Kaze *et al.*, 2017) . In contrast to the medial cortex, the lateral cortex of the tibial head had no such support from the plates. Given that the lateral cortex is the weakest point of an HTO, the discrepancy in vertical displacements between the medial and lateral cortices was to be expected (Maas *et al.,* 2013; Watanabe *et al.,* 2014; Diffo Kaze *et al.,* 2015). In descending order, absolute displacements tended to be largest in the Synthetic group, both Allograft groups, and both Control groups, respectively. This was due to the displacement-controlled nature of the ramp protocol (with the piston moving at a constant rate of 0.1 $mm \cdot s^{-1}$), meaning longer tests resulted in larger displacements than in specimens that failed at lower loads. However, the fact that displacements were observed in the x, y, and z-axes of the transverse plane, suggests that the tibial head moved and rotated in multiple directions as forces were applied to it. Therefore, it can be inferred that providing as much stability as possible to the construct is of vital importance in the earlier stages of healing, particularly given that more evidence is emerging that advocates for the use of early weightbearing protocols for knee osteotomy patients (Takeuchi *et al.*, 2009; Brinkman *et al.*, 2010; Brosset *et al.*, 2011; Hernigou *et al.*, 2015; Schröter *et al.*, 2017).

Although early full weightbearing after surgery has shown promising results in tibial osteotomies with (Takeuchi *et al.,* 2009; Brinkman *et al.,* 2010; Hernigou *et al.,* 2015) and without bone grafting (Brosset *et al.,* 2011; Schröter *et al.,* 2017), the added stability that a graft provides may reduce the risk of correction loss. However, it must be remembered that the present study was conducted in-vitro and that these results only approximate in-vivo efficacy since full weightbearing of the knee would only occur at least 11 days after surgery in patients specifically undergoing an early weightbearing rehabilitation protocol (Takeuchi *et al.*, 2008, 2012; Brinkman *et al.*, 2010; Schröer *et al.*, 2017). Moreover, in cases where an intraoperative lateral hinge fracture occurs – as was the case with specimens in the present study – weightbearing post-surgery may be delayed to allow some healing to take place (Takeuchi *et al.*, 2009). Previous research suggested that there is a substantial risk of construct failure if the intended angle of the osteotomy is not accurately achieved (Coventry, Ilstrup and Wallrichs, 1993). It can therefore be inferred that a loss of correction, or deviation from an accurate correction, should be avoided. Considering the results of the present study, this would be possible by including graft materials. Additionally, Spahn, Kirschbaum and Kahl (2006) found that patients who suffered a loss of correction after surgery had an inferior clinical outcome (according to the Knee Injury and Osteoarthritis Outcome Score) compared to patients who exhibited no post-operative change in the achieved correction. These findings could also have implications for patients desiring to return to physical activity, who require the ability to exert higher forces through the knee sooner after surgery.

The trend of positive displacement values for 10 mm and 12 mm HTO specimens at position LSZ, and negative values at position MSZ, indicated a valgus malrotation of the tibial head. Previous studies that utilised a similar test protocol on HTO without grafting have reported similar findings (Maas *et al.,* 2013; Diffo Kaze *et al.,* 2017). The highest valgus malrotation of the tibial head in the frontal plane prior to failure was observed in the 10 mm Allograft Group. This was the only group in which not all specimens experienced an intra-operative lateral hinge fracture. Intra-operative fractures of the lateral hinge occur frequently and have been labelled as inevitable in corrective osteotomies >8 mm (Maas *et al.,* 2013). Since the specimens in the present study involved such corrections, the number of hinge fractures in all groups prior to testing is not surprising. The fact that half of the specimens in the 10 mm Allograft Group did not experience intra-operative hinge fractures seems to be the only difference between the groups that may explain the increased level of valgus malrotation, although this does require further investigation. Intraoperative hinge fractures negatively influence construct stability (Staubli and Jacob, 2010), causing a higher rate of correction loss and non-union to occur (van Raaij *et al.*, 2008; Dexel *et al.*, 2017). This, combined with the number of specimens that experienced an intraoperative hinge fracture in the present study, suggests that maximising construct stability in large corrections or cases with hinge fractures is advisable, not only for biomechanical reasons but also from a clinical perspective.

5.5.2 Fatigue strength of HTO

Despite the abovementioned findings from the specimens that underwent static compression, the differences between groups after fatigue strength testing were subtler. There did not appear to be any significant differences between the 12 mm HTO groups in the data displayed in Table 5.3, however there were far more variations in performance between specimens in the 12 mm Control Group than within the 12 mm Allograft Group. It could therefore be inferred that HTO with grafting resulted in a more predictable biomechanical performance, which may be preferable in terms of clinical outcome.

The purpose of the fatigue strength testing was to simulate and approximate the oscillating stresses exerted upon an osteotomy construct during normal walking. Previous studies have shown that in level walking (Morrison, 1970), an axial force of around three times bodyweight is applied through the knee (Taylor *et al.,* 2004; Heinlein *et al.,* 2009). Forces of around 5.5, 6.9, and 7.6 times bodyweight have been shown to be exerted through the knee during more strenuous activities such as stair climbing (Taylor *et al.,* 2004), jumping, and landing (Cleather, Goodwin and Bull, 2013), respectively. Although osteotomy failure was not inevitable in HTO without grafting, the present study showed that the use of a graft material during HTO provided added stability to the construct. This may help to reduce the risk of failure during physical activity while healing is still taking place. If it is assumed that a person moving without restriction will perform approximately 1 million cycles of the knee in a year (Baleani, Traina and Toni, 2003), the specimens in the present study survived the equivalent of around 2 weeks (12 mm Allograft Group) and 1-4 weeks (12 mm Control Group) before failure. Given that it takes approximately 2 weeks for soft callus formation to begin to occur (Diffo Kaze *et al.*, 2017), the fatigue tests demonstrated the importance of restricting the forces applied to a large osteotomy where no healing has taken place, due to the high likelihood of construct failure. This may be particularly relevant for obese patients (Meidinger *et al.,* 2011), or in patients who perform physical activities that are more vigorous than level walking (e.g. stair climbing), where high forces through the knee are likely.

A disturbance was observed at ~4000 seconds in the vertical dynamic stiffness of the 12 mm Allograft Group but not in the 12 mm Control Group. 4000 seconds was the point at which the second load step began. The disturbance at this point suggests that the graft was resisting the increase in the maximum force being applied to it. Specimen 1 from the Allograft Group also displayed a large and sudden increase in dynamic stiffness at approximately 6500 seconds, before returning to previous levels. This may indicate that the graft was cracking or breaking. This is further supported by the fact that this phenomenon occurred towards the end of the test.

5.5.3 *Strengths and Limitations*

To better contextualise the results presented, the strengths and limitations of the study should be considered. This study was conducted in-vitro, which could be a limitation. However, the loading of each bone during the test protocol has been shown to correspond to the loading of the lower limb in-vivo at about 18% of the gait cycle with around 22 degrees of knee flexion (Diffo Kaze, 2016). Additionally, the standardised artificial sawbone tibiae that were used perform biomechanically similarly to human bone while reducing the issue of inter-specimen variability inherent in cadaveric studies (Heiner, 2008; Gardner *et al.,* 2010). However, since testing was conducted with only vertical force being applied perpendicular to the tibial plateau, the multi-axial forces that would be applied by the surrounding soft tissue in-vivo were not considered. Consequently, these results can be said to approximate the in-vivo efficacy of graft materials in HTO and caution should be exercised when applying these findings to clinical settings.

The findings in present study were further limited by the small sample size and, as such, further research into this area is recommended. For the same reason, statistical analyses were not relevant in the present study. However, the sample size used was reflective of previous studies and the findings presented build upon the small body of research in this area (Takeuchi *et al.,* 2010; Diffo Kaze *et al.,* 2015; Diffo Kaze *et al.,* 2017).

Finally, intra-operative lateral hinge fractures were a confounding variable in the present study, but it is unlikely that they had a significant effect on the results regarding the load at failure or construct stiffness. The hinge was compressed together prior to, and during testing, meaning that no excess movement of the lateral part of the construct could occur. Additionally, all specimens that suffered an intra-operative hinge fracture failed during testing due to further fractures of the lateral cortex. These fractures occurred in a similar manner to those in the specimens that did not experience an intra-operative fracture. Bone grafting of any sort during HTO is often used in larger osteotomies of 10 mm or more (Aryee *et al,* 2008; Ozalay *et al.,* 2009), hence why 10 mm and 12 mm osteotomies were investigated in the present study. This did, however, increase the likelihood of an intra-operative hinge fracture occurring (Miller *et al.*, 2009; van Heerwaarden *et al.*, 2018), which explains the high incidence that was observed.

5.5.4 Clinical implications and future research

The more predictable biomechanical performance of HTO with bone grafting lends support to current recommendations that graft materials should be used in corrections >10 mm (Aryee *et al.*, 2008; Yacobucci and Cocking, 2008; Santic *et al.*, 2010). The added support that the allograft wedges provided the lateral cortex of the tibial head implies that their inclusion offered greater protection of the overall osteotomy construct. This is of particular relevance to cases of intra-operative hinge fractures, which are more likely to occur during large corrections (Maas *et al.*, 2013; MacDonald *et al.*, 2019). A hinge fracture of the lateral cortex weakens the osteotomy structure and results in a worse biomechanical (Miller *et al.*, 2005; Nelissen, van Langelaan and Nelissen, 2010; Han *et al.*, 2013) and radiological outcome (van Raaij *et al.*, 2008; Schröter *et al.*, 2015; Kumagai *et al.*, 2020). Based on the results of this chapter, research is needed to determine whether the added support and consistent biomechanical performance of HTO with allograft bone wedges can help to offset the negative consequences of intra-operative hinge fractures.

The results presented may also have implications for patients returning to physical activity after surgery. Chapters 2 and 4 introduced the notion that the inclusion of graft materials during HTO could be a key variable regarding the degree to which patients are able to perform physical activities after surgery. The findings support this hypothesis with the added evidence that HTO with allograft wedges was biomechanically more stable than HTO without graft materials, which also better protected the vulnerable lateral cortex in comparison to HTO with synthetic grafts. As a result, it is not illogical to infer that this could translate clinically to a decrease in the time taken after surgery for patients to return to physical activity. Since being physically active is one of the key indications for HTO over other treatments for medial osteoarthritis (such as arthroplasty), there is a need for future research to improve and optimise practice in order to provide the best results possible with regard to patient physical activity after surgery.

5.6 Conclusion

The use of graft materials during HTO provided greater stability and strength to the osteotomy construct compared to when the gap was left unfilled. During testing, all specimens failed due to a fracture of the lateral cortex of the tibial head. Synthetic wedges provided the greatest overall strength to an HTO, however the highest medial stiffness exhibited may restrict micromovements of the plate-osteotomy construct. This would have implications for the stimulation of bone healing and may account for previous clinical studies that have reported a higher incidence of delayed- or non-union when synthetic wedges were used. Allograft wedges provided increased mechanical strength and stiffness compared to HTO without graft materials. Valgus malrotation of the tibial head was reduced when an allograft was inserted into the osteotomy gap, which may help to protect the lateral cortex post-operatively. Increased and more consistent biomechanical properties were observed in 12 mm HTO with allograft wedges compared to unfilled osteotomies, which could lead to more predictable outcomes in clinical settings.

The findings presented in this chapter have multiple clinical implications, and numerous research questions for future studies into the use of graft materials during HTO have been identified. However, the focus of this thesis is on patient physical activity specifically. It is the inference made above – that HTO with graft materials may be beneficial for a return to physical activity after surgery – that will be pursued in the next chapter.

CHAPTER 6 – PHYSICAL ACTIVITY LEVELS AND CLINICAL OUTCOME AFTER HTO WITH AND WITHOUT ALLOGRAFT BONE WEDGES

6.1 Abstract

Background: The inclusion of bone graft materials during HTO has been shown to positively impact on clinical outcome criteria such as complication rates, delayed union, and correction loss. Graft materials also result in a biomechanically stronger construct compared to HTO without grafting but it is unknown whether this affects physical activity levels. The purpose of this study was to investigate the difference that allograft bone grafting has on the post-operative activity levels of HTO patients.

Methods: 56 patients (38 males; mean age 50.6 ± 8.8 years; mean BMI 28.8 ± 4.5 kg/m2), who underwent HTO either with an allograft wedge (n=27) or without grafting (n=29), participated in this retrospective study. Pre-operative and post-operative Tegner, UCLA, and KOOS scores were used to estimate physical activity levels and knee function. Data were analysed to detect pre- to post-operative significant differences within and between groups ($p<0.05$).

Results: Both groups achieved a significant pre- to post-operative improvement in KOOS scores with no difference detected between groups (allograft group: 53.7 ± 15.2 pre-op to 75.2 ± 16.3 post-op; control group: 53.5 ± 17.6 pre-op to 68.5 ± 20.7 post-op). The allograft group achieved the minimum clinically important difference for each of the six KOOS subscales, whereas this was only true for four of the subscales in the control group. A significant improvement in physical activity scores was observed in the allograft group (Tegner: 2.7 ± 1.6 pre-op to 4.2 ± 1.7 post-op; UCLA: 4.7 ± 2.1 pre-op to 6.8 ± 1.8 post-op) but not in the control group (Tegner: 3.3 ± 1.6 pre-op to 3.4 ± 1.8 post-op; UCLA: 5.7 ± 2.5 pre-op to 6.0 ± 2.0 post-op).

Conclusion: HTO with allograft wedges resulted in a larger pre- to post-operative increase in physical activity levels than HTO without graft augmentation. Both operative techniques resulted in similar improvements in reported knee function. However, HTO with allograft wedges was preferable to no grafting due to more consistent and clinically important improvements in post-operative KOOS scores. The use of allograft wedges during HTO is recommended; especially for physically active patients or those with a desire to become more active after surgery.

6.2 Introduction

Chapter 5 demonstrated that the inclusion of graft materials during HTO resulted in a stronger and more stable construct than an HTO with an unfilled gap. Of the two graft materials tested, allograft wedges better distributed vertical forces across the tibial head and offered more protection to the lateral cortex (the weakest part of the structure) than synthetic grafts. It was suggested that this may have implications for patients returning to physical activity after surgery. An investigation into the effect of including allograft wedges during HTO on post-operative physical activity levels will now be presented.

Recent systematic reviews and meta-analyses have demonstrated that around 80% of patients were able to return to physical activity after HTO at a level that at least equalled their pre-operative status (Ekhtiari *et al.*, 2016; Hoorntje *et al.*, 2017; Kunze *et al.*, 2019). However, there is evidence to suggest that only arounds 10% of these patients returned to a level of activity that was greater post-operatively than pre-operatively (Kunze *et al.*, 2019). Furthermore, individual studies have reported a mean decrease in the post-operative activity levels of HTO patients compared to their pre-operative status (Salzmann *et al.*, 2009; Yim *et al.*, 2013). A study by Bonnin *et al.* (2013) found that 33% of patients were less active at follow-up than prior to surgery. Each of the abovementioned studies, reviews, and meta-analyses identified (but did not account for) potential confounding intra-operative variables such as technique, the inclusion of graft materials, and concurrent procedures performed. The systematic review presented in Chapter 4 highlighted a potential difference in post-operative activity levels between patients that underwent HTO with graft materials versus those where the osteotomy gap was unfilled. However, this trend was based on limited data, which remains unconfirmed due to a lack of comparative studies from which to draw firm conclusions.

The inclusion of bone graft materials during HTO has been shown to impact certain clinical outcome criteria such as complication rates, delayed union, and correction loss (Lash *et al.*, 2015; Slevin *et al.*, 2016). As the previous chapter demonstrated, the use of bone grafts as gap fillers during HTO is biomechanically stronger than HTO without grafting in reference to vertical loading (Belsey *et al.*, 2019a). It is unknown whether this translates to allowing patients to be more highly active as result of their knee being able to withstand higher stresses. Clinically, comparative studies have shown the use of synthetic grafts to be unfavourable compared to other graft types (or to no augmentation) regarding factors such as time to union, infection rates, and loss of correction (Gouin *et al.*, 2010; Lash *et al.*, 2015; Ferner *et al.*, 2016; Slevin *et al.*, 2016). Allograft wedges can perform similarly to autografts radiographically and clinically (Cho *et al.*, 2013). Despite possessing lower osteoconductive properties than autografts, allografts may be preferable overall since the consequences of donor site morbidity that are associated with an autograft harvesting procedure are not applicable (Amendola and Bonasia, 2010; Kuremsky *et al.*, 2010; Han *et al.*, 2015).

One of the indicative criteria for HTO is a patient who is physically active (Amendola and Panarella, 2005; Cao *et al.*, 2018). As mentioned above, it is common for patients to be able to return to activity levels that at least equal their pre-operative status (Ekhtiari *et al.*, 2016; Hoorntje *et al.*, 2017; Kunze *et al.*, 2019). However, the pre-operative activity status of patients does not necessarily reflect the level at which patients would choose to perform if they did not have a symptomatic knee in need of surgical intervention. The controversy in the literature around the likelihood of patients being able to exceed their pre-operative activity levels after surgery may be due to confounding variables such as the use of graft materials during the procedure. Further research is therefore required to assess the impact of such variables on physical activity to improve activity-related outcomes after HTO, and to further assert that the surgical indication of an active patient remains appropriate.

HTO with allograft wedges is biomechanically stronger than HTO without augmentation (Belsey *et al.*, 2019a), clinically superior to HTO with synthetic grafting (Slevin *et al.*, 2016), and preferable to HTO with autografts (Younger and Chapman, 1983; Sgaglione, Moynihan and Uggen, 2007) but it is not known whether their inclusion during HTO affects the physical activity levels of patients. Therefore, the purpose of this study was to investigate the difference that allograft bone grafting has on post-operative activity levels of patients who underwent HTO. It was hypothesised that patients who underwent HTO with allograft bone wedges inserted into the osteotomy gap would return to a higher level of physical activity than those who underwent surgery without graft augmentation.

6.3 Methods

6.3.1 Study design

This study was originally intended to be prospectively conducted, involving both subjective (patient-reported questionnaires) and objective measures (accelerometry). However, due to a combination of unforeseen circumstances – delays with ethical approval, a decline in patient numbers, a postponement of elective procedures at the study hospital, and extended delays due to the SARS-COV-2 pandemic – the study was not able to be completed within the timeframe of this PhD project. It is ongoing and will be recontinued once restrictions are lifted. A summary of the procedures and results based on the prospective data collected thus far can be viewed in Appendix D. The following retrospective study of subjective self-reported outcomes was designed and conducted once it became apparent that the originally planned investigation would not be possible to complete in time for the submission of this thesis. The purpose remained the same.

6.3.2 Participants

121 adult patients who underwent HTO with either allograft bone wedges or with no augmentation between November 2013 and December 2018 were eligible to participate in this multicentre, multi-surgeon study. Patients who underwent simultaneous procedures (other than arthroscopy) at the time of the HTO were excluded from participation. Eligible patients were identified from a prospectively maintained database and ethical approval for the study was attained from the University of Winchester and NHS review panels (Appendix E). Demographic and surgical information for each participant was recorded and analysed to check for potential confounding personal and intra-operative variables that may have influenced the eventual outcome of the surgery. A power analysis based on results from a previous study (Nerhus *et al.*, 2017) was conducted *a priori* to determine that a minimum sample size of 54 (27 per group) was required to achieve a power of 0.8 and an effect size of 0.78, with an α-error of 0.05.

Eligible patients were identified and contacted with a postal invitation to participate. An information sheet was given to potential participants and a consent form was signed by those who responded and indicated their interest in participating (Appendix E). Of the 65 responders, 56 returned completed questionnaires for the data that were analysed and presented in this paper. Patients were divided into two groups depending on whether they underwent HTO with allograft wedges (allograft group) or whether they underwent HTO without graft augmentation (control group).

6.3.3 Surgical technique

All procedures were performed under general anaesthesia by one of three experienced surgeons according to a standard protocol, and based on careful pre-operative planning undertaken digitally using long-leg full weightbearing radiographs (Ellis *et al.*, 1999; Schröter *et al.*, 2013). Arthroscopy was performed in 24 patients (Control group n=11; Allograft group n=13) for cartilage evaluation prior to the osteotomy.

A biplanar osteotomy was performed following the protocol previously described by Staubli *et al.* (2003). A small, longitudinal (1 surgeon) or oblique (2 surgeons) incision was made over the proximal tibia and a careful dissection down to the pes anserinus, followed by a release of the medial collateral ligament, was conducted. Under image intensifier guidance, two guide wires were placed from the level of the pes anserinus to the lateral tibial cortex, in line with the tip of the fibula head. A blunt Hohmann retractor was then inserted and placed posteriorly to avoid accidental neurovascular injury. The first osteotomy was then made distal to the guide wires and parallel to the tibial slope, beginning at the medial cortex and ending within approximately 10 mm of the lateral cortex. A second osteotomy at an angle of 135 ° to the first cut, moving proximally towards the tibial plateau, was then performed to create a biplane. A precision saw and chisels were used to complete both cuts. Osteotomes and a laminar spreader were then used to gradually open the osteotomy to the desired gap size according to the pre-operative planning; taking care not to fracture the lateral cortex. In patients who received allograft augmentation (*n*=27), the bone wedge was created from a donor femoral head to match the dimensions of the osteotomy, which was then impacted into the gap. Finally, the internal fixation plate was positioned and fixed according to their respective designs: medially for Tomofix and PEEKpower plates, and anteromedially for Size 2 ActivMotion plates.

6.3.4 Outcome measures

To assess overall knee function at the time of follow-up, a Knee Injury and Osteoarthritis Score (KOOS) was completed by all participants at follow-up (Roos and Lohmander, 2003). Pre-operative KOOS scores for all but four patients were taken from the prospectively maintained database from which the participants were originally identified. The remaining four patients had no prospectively recorded pre-operative KOOS scores, so these were estimated retrospectively by the patient at the point of follow-up. Changes in physical activity levels were recorded through the use of a Tegner activity score (Tegner and Lysholm, 1985) and a University of California, Los Angeles (UCLA) activity score (Zahiri *et al.*, 1998). Since pre-operative Tegner and UCLA scores were not recorded on our prospectively maintained database, they were retrospectively estimated by participants at the point of follow-up.

The self-administered KOOS score is commonly used to report changes in patient knee function after HTO, and has been validated for use in the short- and long-term follow-up of patients who undergo surgical intervention for osteoarthritis (Roos and Lohmander, 2003). The self-administered Tegner and UCLA scores have been validated for the clinical assessment of physical activity levels (Tegner and Lysholm, 1985; Zahiri *et al.*, 1998). The Tegner score is commonly used in the literature to report changes in activity before and after HTO surgery (Ekhtiari *et al.*, 2016; Kunze *et al.*, 2019). While the UCLA score has been used in the HTO literature to a lesser degree than the Tegner score, it is more commonly implemented in the reporting of outcomes after unicompartmental knee arthroplasty (UKA) (Waldstein *et al.*, 2017). Recent studies have demonstrated that the indications for HTO and UKA increasingly overlap (Dettoni *et al.*, 2010; Fu *et al.*, 2013), and that patients are able to return to physical activity after either procedure (Schröter *et al.*, 2013; Walker *et al.*, 2015; Krych *et al.*, 2017). To begin to allow for comparative estimates to be made between the present study and similar studies involving UKA patients, the UCLA score was implemented and included in the analysis.

6.3.5 Data analysis

Independent samples t-tests were performed to determine differences in demographic information and outcome scores between the Allograft group and the Control group. Paired samples t-tests were performed to determine whether the surgery resulted in pre- to post-operative changes in outcome measures for each group. Mean values in each test were calculated with a corresponding 95% confidence interval (CI). Statistical significance was defined at $p < 0.05$ for all tests and the whole analysis was conducted using the software package IBM SPSS Statistics 25 (IBM corporation, Armonk, New York). The minimum clinically important difference (MCID) for each KOOS subscale was determined in line with a previously published evaluation (Table 6.1; Jacquet *et al.*, 2020). MCID for the total KOOS score has not been assessed but previous research estimated it as approximately 10 points with the mean difference having a standard deviation of approximately 15 (Roos and Lohmander, 2003; Nerhus *et al.*, 2017).

Table 6.1: *The minimum clinically important difference (MCID) for each KOOS subscale* (Jacquet *et al.*, 2020)

KOOS subscale	MCID
Symptoms	15.1
Pain	15.4
Activities of daily living	17.0
Sports & recreation	11.2
Quality of life	16.5

6.4 Results

6.4.1 Demographics

Data from 56 patients were available for analysis. The baseline characteristics and operative information of the participants can be found in Table 6.2. The standard Tomofix plate was the most used plate in both groups, though more were used in the Control group than the

Allograft group. The second most used plate was the Activmotion plate, which was used more in the Allograft group than in the Control group. The only significant difference in demographic and operative data between groups was for mean follow-up time ($p < 0.05$). This was explained by the fact that the use of allograft bone wedges during HTO was introduced more recently than HTO without grafting at the hospitals involved in this study. The mean osteotomy gap size was significantly larger ($p<0.01$) in males (9.3 ± 3.0 mm; 95% CI: 8.2-10.3 mm) than females (6.4 ± 2.3 mm; 95% CI: 5.2-7.6 mm). In the overall cohort, no differences in outcome were detected between smokers and non-smokers ($p > 0.05$). However, when limiting the analysis of smoking solely to the Control group – which contained all of the smokers – the pre-operative Tegner scores of non-smokers (3.5 ± 1.4; 95% CI: 2.9-4.1) were significantly higher than for smokers (2.0 ± 1.2; 95% CI: 0.5-3.5).

Table 6.2: *Baseline demographic and operative information*

Participant characteristics	Allograft group (mean ± SD)	Control group (mean ± SD)	Overall (mean ± SD)
No. of patients	27	29	56
Males:females	19:8	19:10	38:18
Smokers:non-smokers	0:27	5:24	5:51
BMI (kg/m^2)	27.8 ± 3.4	29.7 ± 5.2	28.8 ± 4.5
Age at surgery, (years)	48.8 ± 10.5	52.2 ± 6.7	50.6 ± 8.8
Follow-up (months)	28.4 ± 14.3*	37.4 ± 12.9	33.1 ± 14.2

Operative information	Allograft group (mean ± SD)	Control group (mean ± SD)	Overall (mean ± SD)
Operated knee, right:left	14:13	14:15	28:28
No. of simultaneous arthroscopies performed	13	11	24
Gap size (mm)	8.4 ± 3.2	8.3 ± 3.1	8.3 ± 3.1
Standard Tomofix HTO plate	13	25	38
Small Tomofix HTO plate	0	1	1
Size 2 ActivMotion HTO plate	12	3	15
PEEKpower HTO plate	2	0	2
No. of plates removed (*n*)	15	18	33
Time from surgery to plate removal (months)	14.2 ± 5.1	18.3 ± 7.9	16.2 ± 7.0

*significant difference versus Control group ($p < 0.05$)

6.4.2 Surgical complications

Four patients in the Control group (14%) and one in the Allograft group (4%) experienced complications. Two patients in the Control group reported severe pain related to the standard Tomofix plate at 11 months and 19 months after surgery; one of whom also experienced nerve pain on the lateral side of the knee. Both patients subsequently had their plates removed. There was one case of infected haematoma and one case of non-fatal pulmonary embolism in the Control group, which were resolved through a washout and Rivaroxaban, respectively. In the Allograft group, one patient experienced extreme pain in the medial compartment of the knee due to a prior medial meniscectomy. This was resolved through the removal of the PEEKpower plate implant 6 months after HTO, plus meniscal transplant surgery. There were no instances of non-union, lateral hinge fracture, correction loss, or implant failure in either group.

6.4.3 Changes in knee function and physical activity

Mean pre- to post-operative KOOS scores significantly increased within both groups ($p < 0.05$; Table 6.3). The MCID of the total KOOS score was achieved in both groups (Roos and Lohmander, 2003; Nerhus *et al.*, 2017). The MCID for each KOOS subscale was achieved in both groups except for “Pain” and “ADL” in the control group (Jacquet *et al.*, 2020). There was no significant difference in KOOS scores between groups pre-operatively or at follow-up ($p > 0.05$). Post-operatively the Allograft group consistently achieved higher mean scores in all KOOS subscales versus the Control group, whereas pre-operatively the Allograft group only scored higher for the “Symptoms” subscale.

Table 6.3: *KOOS scores (Mean ± SD) within groups pre-operatively and at final follow-up*

KOOS subscale	Allograft group			Control group		
	Pre-op	Follow-up	Pre- to post-op 95% CI diff.	Pre-op	Follow-up	Pre- to post-op 95% CI diff.
Symptoms	57.9 ± 18.1	76.5 ± 16.5*	10.3-26.8	50.8 ± 18.2	70.0 ± 20.3*	12.0-26.4
Pain	53.8 ± 16.7	76.5 ± 16.3*	13.4-32.1	54.9 ± 19.0	69.0 ± 22.2	5.8-22.3
ADL	64.4 ± 17.9	84.2 ± 16.9*	11.5-28.1	63.6 ± 17.8	75.3 ± 21.4	5.3-18.0
Sport	24.1 ± 19.1	48.9 ± 23.6*	12.9-36.7	34.3 ± 26.2	47.2 ± 28.7*	1.7-24.2
QoL	31.0 ± 19.5	58.6 ± 21.9*	15.2-39.9	35.0 ± 19.5	51.7 ± 25.3*	8.4-25.1
Total	53.7 ± 15.2	75.2 ± 16.3*	13.5-29.5	53.5 ± 17.6	68.5 ± 20.7*	8.8-21.3

Note: *pre- to post-operative change exceeded the minimum clinically important difference
KOOS = Knee injury and Osteoarthritis Outcome Score; ADL = Activities and Daily Living
QoL = Quality of Life; CI diff. = Confidence Interval of the difference (95%)
SD = Standard Deviation

There were no significant differences in mean Tegner and UCLA scores between groups pre-operatively or at follow-up (Figures 6.1 and 6.2). However, the Allograft group showed a significant pre- to post-operative increase in physical activity from 2.7 ± 1.6 to 4.2 ± 1.7 ($p < 0.01$; 95% CI of the difference: 0.8-2.1) for the Tegner score, and from 4.7 ± 2.1 to 6.8 ± 1.8 ($p < 0.01$; 95% CI of the difference: 1.1-3.1) for the UCLA score. The Control group also exhibited a pre- to post-operative increase in physical activity: from 3.3 ± 1.6 to 3.4 ± 1.8 according to the Tegner score, and from 5.7 ± 2.5 to 6.0 ± 2.0 according to the UCLA score, but neither were statistically significant ($p > 0.05$). A post-hoc calculation of Cohen's *d* (Cohen, 1992) resulted in d=0.42 and d=0.41 for post-operative Tegner and UCLA scores, respectively, indicating a small-to-medium effect size. Pre-operatively, mean Tegner and UCLA scores were significantly higher in males (3.4 ± 1.5; 95% CI: 2.9-3.9, and 5.7 ± 2.3; 95% CI: 5.0-6.5, respectively) than females (2.3 ± 1.6; 95% CI: 1.5-3.1, and 4.1 ± 2.1; 95% CI: 3.1-5.2, respectively). However, no significant difference between the sexes existed at final follow-up ($p > 0.05$).

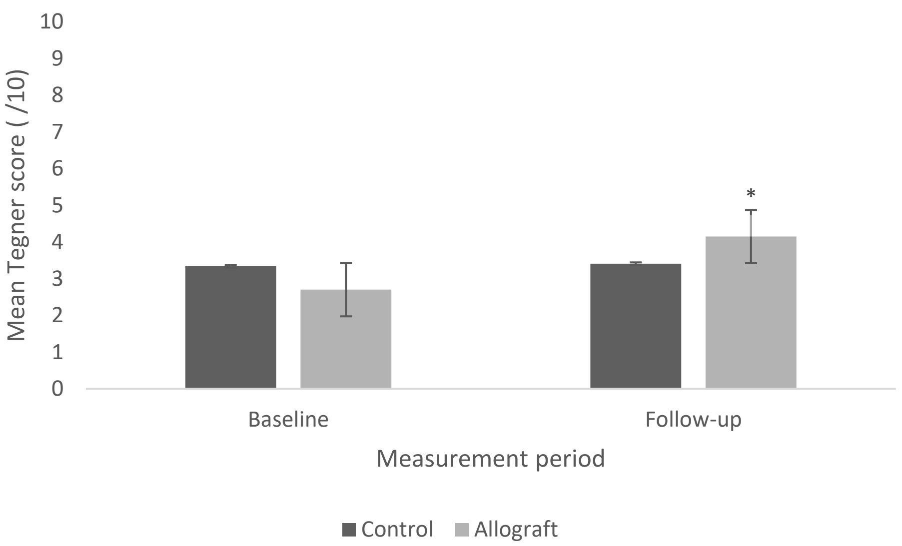

Figure 6.1: Mean Tegner scores per group pre-operatively (baseline) and at follow-up

**significant difference versus pre-operative value (p < 0.01).*

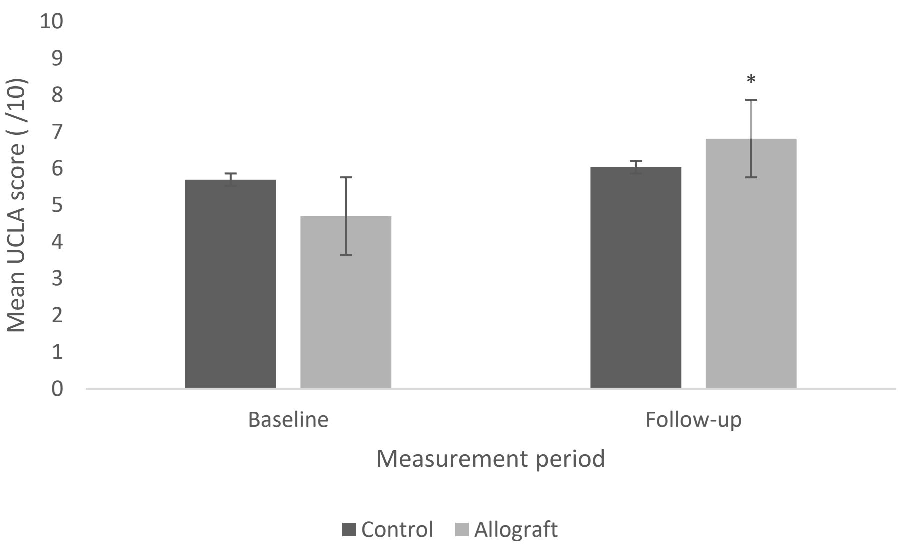

Figure 6.2: Mean UCLA scores per group pre-operatively (baseline) and at follow-up

**significant difference versus pre-operative value (p < 0.01).*

6.5 Discussion

The possibility of a return to physical activity after HTO to a level at least equal to the pre-operative status of a patient has been widely reported in the literature (Ekhtiari *et al.*, 2016; Hoorntje *et al.*, 2017; Kunze *et al.*, 2019). However, a comparative study investigating the impact of graft inclusion during HTO on post-operative activity levels has been lacking. The purpose of this study was to determine whether the inclusion of allograft bone wedges during HTO affected pre- to post-operative changes in patient physical activity levels. The results showed that patients who underwent HTO with allograft bone wedges displayed a significant pre- to post-operative increase in physical activity levels, according to Tegner and UCLA scores. Patients who underwent HTO without augmentation reported no significant pre- to post-operative difference in activity levels. The inclusion of allograft bone wedges during HTO can therefore be recommended to increase the likelihood of a better physical activity outcome after surgery. This is of particular relevance when considering that a key difference in the indications for HTO over other surgical treatments for medial osteoarthritis (such as UKA) is an active patient (Amendola and Panarella, 2005; Cao *et al.*, 2018).

KOOS results significantly increased from baseline to follow-up within both groups, but no significant differences between groups were detected at either time point. The MCID for each KOOS subscale was achieved in the allograft group but was not achieved for "Pain" and "ADL" in the control group (Roos and Lohmander, 2003; Jacquet *et al.*, 2020). Furthermore, upon examining the corresponding 95% confidence intervals of the pre- to post-operative differences for each KOOS subscale, patients who underwent HTO with allograft wedges were more likely overall to achieve the MCID than the control group. This is with the exception of the "Symptoms" subscale, where the control group was more likely to achieve the MCID. This suggests that HTO with allograft wedges resulted in a more predictable and consistently good outcome compared to HTO without grafting. Consequently, the inclusion of allograft wedges during HTO is preferable for the improvement of overall knee function as well as for physical activity levels after surgery.

No other study has reported changes in physical activity levels before and after HTO with allograft wedges. Separate non-comparative studies have tended to show similarly significant pre- to post-operative increases in KOOS scores for HTO without augmentation (Saragaglia *et al.*, 2014) and HTO with a graft material (Brinkman *et al.*, 2010; Lind-Hansen *et al.*, 2016; Ekeland *et al.*, 2017; Nerhus *et al.*, 2017). Additionally, in order to better establish whether the results of the present study were in accordance with those in the literature, the data of the Allograft group and Control group were combined for comparison against two studies that reported the KOOS scores of a cohort of patients that underwent a mix of HTO with and without graft materials (Birmingham *et al.*, 2009; Marriott *et al.*, 2015). In the prospective cohort study by Birmingham *et al.* (2009) patients who underwent HTO with a gap >7.5 mm received an allograft wedge and the remaining patients had no graft. The pre- and post-operative (24 months) KOOS scores of the overall cohort were similar to those of the overall cohort in the present study. Similar findings were evident in the pre-operative to 24 months comparison of KOOS results presented in the prospective cohort study of Marriot *et al.* (2015), who inserted graft materials (either allo- or autograft) into gaps >7.5 mm, while leaving the gap empty in smaller openings. The results of the KOOS questionnaires in the present study support the literature.

The increase in Tegner and UCLA scores in the Allograft group similarly appear to support the literature. Studies in which graft materials were used during HTO mostly reported increases in Tegner and UCLA scores from baseline to 12 months (Brinkman *et al.*, 2010; Nerhus *et al.*, 2017), 24 months (Nerhus *et al.*, 2017), and 77 months (Schröter *et al.*, 2013). There is one retrospective study that assessed patients who underwent HTO with synthetic grafts and found no change in Tegner scores at 12 months (Bastard *et al.*, 2017). The latter study notwithstanding, an overall improvement in physical activity after HTO with graft materials is the general consensus in the literature.

Studies in which HTO was performed without graft augmentation are more equivocal regarding conclusions based on Tegner and UCLA results (Salzmann *et al.*, 2009; Saragaglia *et al.*, 2014; Faschingbauer *et al.*, 2015; Krych *et al.*, 2017). A prospective study by Krych *et al.* (2017) found a significant increase in the Tegner scores of HTO patients after 24 months. However, studies by Saragaglia *et al.* (2014) and Faschingbauer *et al.* (2015) showed no significant change in pre- to post-operative Tegner scores at 69 and 22 months, respectively. A final study, by Salzmann *et al.* (2009), reported a significant decrease in Tegner scores at 36 months. The mostly consistent results in the literature regarding return to physical activity after HTO with graft materials support the findings of the present study and suggest that the use of graft materials is preferable to no graft, which has been shown to have largely varying and unpredictable results (Salzmann *et al.*, 2009; Saragaglia *et al.*, 2014; Faschingbauer *et al.*, 2015; Krych *et al.*, 2017).

6.5.1 Complications

Complication rates of patients who underwent medial opening-wedge HTO have previously been reported to be as low as 4% (Figueroa *et al.*, 2018) and as high as 44% (Spahn, 2004), with one literature review reporting a mean rate of 16% (Woodacre *et al.*, 2016). The overall complication rate observed in the present study (10%; *n*=6) was relatively low. The rate of plate-related pain (4%; *n*=2) fell within the range of previously reported rates of 1% and 11% (Noyes *et al.*, 2006; Miller *et al.*, 2009; Song *et al.*, 2010; Seo *et al.*, 2016; Woodacre *et al.*, 2016; Figueroa *et al.*, 2018; Han *et al.*, 2019). Similarly, the rates of nerve pain (2%; *n*=1), haematoma (2%; *n*=1) and pulmonary embolism (2%; *n*=1) in the present study were comparable to previously reported findings where rates of nerve pain were around 4% (Song *et al.*, 2010; Seo *et al.*, 2016), rates of haematoma ranged from 2% to 5% (Amendola *et al.*, 2004; Spahn, 2004; Floerkemeier *et al.*, 2014; Seo *et al.*, 2016) and rates of thromboembolic complications ranged from 0.2% to 4% (Amendola *et al.*, 2004; Spahn, 2004; Spahn, Kirschbaum and Kahl, 2006; Miller *et al.*, 2009; Floerkemeier *et al.*, 2014; Figueroa *et al.*, 2018). Most of the complications observed in the present study occurred in the Control group (*n*=5), which could suggest that the inclusion of a bone graft during HTO results in a lower complication rate. However, this interpretation is speculative and more research is needed to be able to draw any firm conclusions.

6.5.2 Limitations

To better contextualise the present findings, the limitations to the study must be presented. The pre-operative Tegner and UCLA scores were estimated retrospectively at the time of follow-up meaning that potential recall bias was a limitation of the present study. Additionally, some of the demographic characteristics of each group varied, which may have confounded the results presented. The Control group contained all the smokers who participated in the study, and a significant difference in pre-operative Tegner scores between smokers and non-smokers may have affected the mean score of the overall group. However, since there were only five smokers in the Control group, it is likely that this statistical comparison is not reliable. Smoking has been associated with lower physical activity levels and increased sedentary behaviour in adults (Conway and Cronan, 1992; Auer *et al.*, 2014; Lauria *et al.*, 2017). This suggests that the activity levels of the Control group may have been confounded because the only smokers in the study were contained within it.

Overall pre-operative activity levels of the Control group were higher than those of the Allograft group. Post-operative physical activity was lower in the Control group but research is equivocal regarding any negative impact that smoking has in the mid-term (Spahn, Kirschbaum and Kahl, 2006; Floerkemeier *et al.*, 2014). The controversy in the literature based on a similar follow-up time to that of the control group in the present study (37.4 months versus approximately 45 months in the aforementioned literature), combined with the small number of smokers in the Control group, makes it difficult to make firm conclusions about the potential confounding variable of smoking on the present findings.

A further limitation of this study is the difference in mean follow-up times for both groups (28 months in the Allograft group and 37 months in the Control group), which may have affected the outcome measures. However, the largest change in post-operative activity levels occurs within the first operative year, with no significant change occurring in the second year (Krych *et al.*, 2017; Nerhus *et al.*, 2017; Kim *et al.*, 2018). There is evidence to suggest that the level of activity achieved in the second post-operative year is maintained 5 years after HTO (Krych *et al.*, 2017). This indicates that time effects between groups in the present study were unlikely to have influenced the reported post-operative outcome scores because follow-up occurred in the third and fourth post-operative years, on average, where deleterious effects would not be expected. Further research would serve to confirm this.

The significant difference in gap size found between males and females is not likely to have affected the final analysis since there were similar numbers of both sexes in each group. Similarly, the significantly increased physical activity levels reported by males versus females pre-operatively are not expected to have confounded the results of the present study for the same reason.

The types of internal plate fixation that can be used during HTO have been shown to significantly differ biomechanically (Diffo Kaze *et al.*, 2019) and can impact certain clinical factors such as union, complications rates, and the incidence of lateral cortex fractures in the short-term (Amendola and Bonasia, 2010; Cotic *et al.*, 2015). Four different HTO plates were used with the patients involved in the present study but the most common implant was the standard Tomofix, which is considered to be the gold standard (Diffo Kaze *et al.*, 2015). Overall, it is unlikely that the different plate types had a significant impact on the post-operative outcome in the present study. The purpose of the plate is to support the opened osteotomy gap until union has been achieved; at which point the plate can be removed. A similar number of plate removals were conducted in each group in the present study. It is assumed that the patients whose plates remained in-situ at the point of follow-up had not experienced significant issues with the implant. It is therefore unlikely that the plates significantly impacted on the overall results of the study.

6.5.3 Clinical implications and future research

The consistent clinically important improvement observed in HTO with allograft wedges suggests that their use is preferable over HTO without grafting. The systematic review in Chapter 4 detected the inclusion of bone grafts as a potential confounding variable for post-operative physical activity levels. The results of the present study confirm this observation and further cement the traditional indication of an active patient being better suited for HTO over UKA. The fact that an active patient is one of the main differences in the indications between HTO and other surgical interventions, further supports the regular inclusion of allograft wedges during HTO since that group of patients returned to physical activity at a level that exceeded their pre-operative values. The results suggest that the use of allograft wedges alleviated pre-operative symptoms to a degree where a higher level of physical activity could be achieved, whereas in HTO without graft materials the surgery merely prevented a decrease in pre- to post-operative physical activity.

6.6 Conclusion

This study showed that HTO with allograft wedges resulted in a larger pre- to post-operative increase in physical activity levels than HTO without graft augmentation. Both operative techniques resulted in similar improvements in reported knee function, according to the KOOS score. However, the inclusion of allograft wedges during HTO was preferable to no grafting due to more consistent, clinically important improvements in post-operative KOOS scores. The use of allograft wedges during HTO is recommended; especially for physically active patients or those with a desire to become more active after surgery.

Other than the potential confounding variables mentioned above – which were deemed unlikely to have significantly impacted the results of the present study – the fact remains that the inclusion of allograft wedges during HTO only accounted for a small-medium proportion of the observed effect. In the absence of obvious measurable variables that could have accounted for a further proportion of the effect, it is possible that some confounding factors are less tangible and less objective. Such variables may not necessarily be revealed through the quantitative approaches that have thus far dominated the HTO literature.

CHAPTER 7 – MULTIPLE FACTORS INFLUENCE THE DECISION TO RETURN TO PHYSICAL ACTIVITY AFTER HIGH TIBIAL OSTEOTOMY: A QUALITATIVE APPROACH

"Every person is unique. Group membership cannot capture that variability. Period."
-Jordan B Peterson, 2018

7.1 Abstract

Background: A limited number of studies have speculated that subjective factors may explain observed changes in activity participation behaviours after HTO surgery. Such factors should be examined clinically since they may impact behaviour and, therefore, rehabilitation progress and overall outcome. Patients who have undergone other forms of knee surgery have cited numerous subjective variables that modified their post-operative physical activity behaviours such as: fear of reinjury, confidence in the knee, personal preference, lifestyle changes, expectations, and social support. Qualitative research has not yet been published pertaining to HTO patients. This study aimed to investigate which factors influence patient decisions to return to physical activity after HTO.

Methods: Semi-structured interviews were conducted and transcribed verbatim. Data were analysed thematically to realise codes, categories, and themes. Patient-reported outcome scores were completed as secondary measures. Eleven HTO patients (mean age: 52 ± 7.7 years) participated at a mean 32 ± 10.1 months post-operatively.

Results: Four themes emerged from the interviews: physical factors, psychological factors and intentions, information and experiences, and actual physical activity. Multiple factors contributed to pre- to post-operative changes in physical activity behaviours; not all of which related to the operated knee. A reduction in high-impact activities, and an increase in low-impact activities, was reported. Tegner scores showed an overall increase in activity levels post-operatively (4.4 ± 1.2) versus pre-operatively (2.8 ± 2.1). The “Sports” and “Quality of Life” KOOS subscales were the lowest (50.5 ± 21.4 and 51.7 ± 27.3, respectively).

Conclusion: Residual pain during high-impact activities, fear of reinjury, aging, subsequent injuries, reduced confidence, and a lack of guidance after the initial recovery period impacted the post-operative activity behaviour of HTO patients. A reduction of high-impact sports participation, but an overall increase in activity levels post-operatively, can be expected. Most patients changed the type of activity they performed rather than ceased to be active.

7.2 Introduction

This thesis has hitherto argued in favour of the use of bone grafts during HTO as a method of improving post-operative physical activity outcomes. Allograft wedges have been shown to provide greater stability to an osteotomy construct compared to HTO without graft materials (Chapter 5), which translated to clinically important improvements in knee function and an increase in pre- to post-operative activity levels (Chapter 6). However, the previous chapter revealed that the inclusion of an allograft wedge during the osteotomy procedure only accounted for a small-medium proportion of the observed effect. Demographic characteristics and operative variables were largely similar between groups in the previous study, and of those that were not, potential confounders were not deemed to have had a high likelihood of significantly affecting the results. Therefore, in order to uncover other possible unknown variables that may affect post-operative physical activity levels, a mixed methods approach – with a focus on qualitative measures – could offer a different perspective on the matter.

Most of the literature reporting on HTO involves quantitative approaches to assess post-operative outcomes. The Tegner activity scale and the Knee Injury and Osteoarthritis Outcome Score (KOOS) are validated, and commonly used, multiple-choice questionnaires that measure levels of physical activity and knee function (Tegner and Lysholm, 1985; Roos and Lohmander, 2003). While many studies concur that HTO achieves an increase in post-operative knee function (W-Dahl, Toksvig-Larsen and Roos, 2005; Bode *et al.*, 2013; Sischek *et al.*, 2014; Lash *et al.*, 2015), research is equivocal regarding physical activity. Some studies show that patients returned to the same, or higher level of sport (Schröter *et al.*, 2013; Krych *et al.*, 2017), while others report patients returning to lower levels compared to their pre-surgery activity (Salzmann *et al.*, 2009; Yim *et al.*, 2013). The systematic review in Chapter 4 suggested that this controversy may be explained by differing operative techniques between studies. This was confirmed in Chapter 6 where the inclusion of a bone graft during surgery resulted in significant increases in activity levels post-operatively compared to patients that underwent HTO without a graft material.

Qualitative approaches have been previously used to investigate subjective variables pertaining to post-operative physical activity in patients who underwent anterior cruciate ligament reconstruction or total knee arthroplasty (Tjong *et al.*, 2014; Harding *et al.*, 2015; Filbay, Crossley and Ackerman, 2016; Burland *et al.*, 2018; Ezzat *et al.*, 2018). Greenfield *et al.* (2007) noted that qualitative approaches in orthopaedic and sports medicine research could provide a unique insight into patients' emotional and psychological status. The authors suggested that subjective factors should be examined clinically since they may impact behaviour and therefore, rehabilitation progress and overall outcome. Thus far, qualitative research has not been published pertaining to HTO. Patients who have undergone other forms of knee surgery have cited numerous subjective variables that modified their post-operative physical activity behaviours such as: fear of reinjury, confidence in the knee, personal preference, lifestyle changes, expectations, and social support (Tjong *et al.*, 2014; Harding *et al.*, 2015; Filbay, Crossley and Ackerman, 2016; Burland *et al.*, 2018; Ezzat *et al.*, 2018). It is not unreasonable to predict that such factors may also apply to osteotomy patients, however this has not been previously investigated.

A limited number of studies have speculated that subjective factors – such as advice from clinicians for patients to avoid certain types of physical activity – may explain observed changes in activity participation behaviours (Salzmann *et al.*, 2009; Faschingbauer *et al.*, 2015; Kim *et al.*, 2018). Furthermore, Bonnin *et al.* (2013) demonstrated that 62% of patients reported participation in sporting activities was “limited” by their knee. However, this was not investigated in any further detail. Since HTO is commonly selected in active patients, developing a more thorough understanding as to why patients do or do not return to certain activities after their surgery is important. Additionally, physical activity is positively correlated with health-related quality of life (Vuillemin *et al.*, 2005; Bize, Johnson and Plotnikoff, 2007; Filbay, Crossley and Ackerman, 2016) so having a better understanding as to why there is an apparent variation in post-operative physical activity levels between patients may help to improve the outcome of HTO, and thus the quality of life for patients. No study has investigated the reasons that influence a patient’s decision to return to activity, and the level they return to, after HTO.

The research question of the present study was: which are the most common factors that influence patient decisions regarding their return to physical activity post-operatively, and how do they impact the type and frequency of activity undertaken?

7.3 Methods

7.3.1 Study Design

One-to-one interviews were scheduled with participants to take place in a private setting of their choosing (their home, the local university, or the hospital). Upon arrival, participants’ knee function was assessed through a KOOS questionnaire. Additionally, two Tegner questionnaires were completed to estimate pre-operative and current physical activity levels. Answers to these questionnaires offered an initial insight into each participant’s surgical outcome, which helped to inform some of the interview questions regarding apparent changes (or lack thereof) in physical activity and overall knee function.

Semi-structured interviews were audio-recorded and conducted face-to-face. An interview-guide containing open-ended questions was used by the interviewer to offer participants the opportunity to expand on any area of conversation and to fully communicate their meaning and experience. The question-guide was updated throughout the data collection process (Appendix F). The purpose of this was to elicit further information that may not have been previously mentioned but would provide relevant data for the purposes of the study. It allowed for more detailed information to be shared that would not otherwise be obtainable through quantitative methods. The order of the questions remained flexible to allow the conversation to move naturally and, where appropriate, the interviewer asked further probing questions to gather extra information or clarifications from patients.

7.3.2 Participants

Patients who underwent medial opening-wedge HTO with allograft bone wedges and no simultaneous procedures (other than arthroscopy) were eligible for this study. Surgery was performed by a single, experienced orthopaedic surgeon between 2014 and 2017. Patients who had subsequently undergone revision surgery or conversion to arthroplasty were not included. Forty eligible patients were identified based on these criteria and were continuously recruited for this study until the point of data saturation was reached. This was determined as the point at which new participants were not providing new information and data became repetitive (Creswell, 2007; Hennink, Hutter and Bailey, 2011; Silverman, 2017). Eleven patients participated in the study. An information sheet was provided to all patients and consent forms were signed prior to participation. This study gained ethical approval from the University of Winchester review board (Appendix F).

7.3.3 Data analysis

Personal identifiers were removed from transcripts, and pseudonyms assigned to participants during the transcription process, to preserve anonymity. Data were collected and analysed thematically. Interviews were transcribed verbatim and coded electronically using NVivo 11 Pro (QSR International) software. Coding was conducted line-by-line after having read through each transcript several times to create familiarity with the responses given to the questions. Codes were grouped into categories according to interpreted similarities found between them. These categories were then further examined and grouped according to connections they had, resulting in overarching themes being established. The created themes gave an overview of the influencing factors that contributed to patients' return to physical activity after HTO.

Trustworthiness, confirmability and credibility of the codes, categories and themes was established by having a second researcher analyse three of the transcripts. Discrepancies between the two analyses were then discussed, amended, and agreed upon by both researchers. Secondary quantitative outcome measures from the questionnaire data were analysed (mean ± SD), and a paired samples t-test was performed on the Tegner scores, using a statistical software package (IBM SPSS Statistics 24), to detect any significant pre- to post-operative changes in physical activity levels.

7.4 Results

7.4.1 Participants and patient-reported outcome measures

Demographic information for the participants can be found in Table 7.1 and a summary of the questionnaire results can be seen in Table 7.2. The Tegner scores showed that seven patients returned to a level of activity greater than their pre-operative status, two returned to an equivalent level, whilst a further two did not. Overall, there was a significant increase in activity according to the pre-operative and post-operative Tegner scores. Total KOOS scores appeared to show a good overall outcome, however a large amount of variation was observed between patients (mean 73.7 ± 17.5). When examining the subscales of the KOOS, "Sports" (mean 50.5 ± 21.4) and "Quality of Life" (mean 51.7 ± 27.3) scored the lowest on average.

Table 7.1: *Patient demographics (mean ± SD)*

Sex (male:female)	9:2
Age at surgery (years)	52 ± 7.7
Time since surgery (months)	32 ± 10.1
Operated knee (right:left)	5:6
No. of plates removed (*n*)	9

Table 7.2: *Patient-reported outcome measures (mean ± SD)*

Tegner scores	
Pre-operative	2.8 ± 2.1
At time of interview	4.4 ± 1.2
p-value	0.02
KOOS subscale scores*	
Total	73.7 ± 17.5
Symptoms	75.7 ± 18.0
Pain	75.0 ± 18.9
Activity and Daily Living	81.0 ± 18.0
Sports	50.5 ± 21.4
Quality of Life	51.7 ± 27.3

Note: *at time of interview
KOOS = Knee Injury and Osteoarthritis Outcome Score

7.4.2 Qualitative analysis

Seventy-two codes, nine categories and four overarching themes arose from the interviews. The first theme, “physical factors”, was defined as involving aspects relating to physical processes, changes or sensations that occurred before, during, and after surgery. The second theme to emerge, “psychological factors and intentions”, pertained to patient thoughts, feelings, attitudes, and outlook on their HTO experience. Theme three, “information and experiences”, comprised mentions of any person or thing (external to the patient) that may have been a source of information relating to HTO, which could have impacted their return to activity. This included elements such as family, physiotherapy, and information received pre- and post-operatively by surgeons or through research online. The final theme was termed “actual physical activity”, which consisted of the activities that patients participated in pre-symptomatically, pre-operatively, and post-operatively; and movements or activities that patients now avoided due to their knee issues.

Theme 1: Physical Factors

It was not uncommon for patients to have injuries or complaints, other than the HTO, that had negatively impacted their activity levels since their operation. Four of the patients who had their fixation plate removed reported a positive impact of its removal on their physical activity levels. One started to “walk a huge amount more” (Participant: P1), another found that “cycling [was] easier” (P11), a third felt that the removal of the plate allowed him to “up the game […] with regards to the physio, the recovery, going to the gym, and getting back to work”

(P5), and a fourth "didn't feel the confidence" (P7) in his knee while the plate was there. Conversely, two other patients reported a more negative impact in the immediate aftermath of the plate removal: one felt concerned about whether the knee would be "strong enough […] to withstand doing any form of activity" (P10), and a second recalled that "the leg felt weak" (P4). The remaining three patients who had their plates removed suggested that there was not a "huge difference in the feeling between having the plate and not having the plate" (P2).

All participants still experienced some degree of residual pain in the operated knee. However, the pain was not constant and only occurred after prolonged use of the joint or when performing twisting or "jarring" (P3) movements. As a result, some participants ceased to participate in activities involving sprinting and cutting movements such as football (P10), netball (P11), squash (P3), and tennis (P5); all of which they did participate in prior to their HTO. However, another participant (P4) had returned to playing tennis at the international level for his age category.

Muscle wasting in participants' legs as a result of the prolonged time of inactivity during the initial post-operative period was another common experience among patients. This was exemplified by P6 who observed that it had taken "a long time" for the muscle to build back up during recovery.

Theme 2: Psychological Factors and Intentions

Being able to run (P1), ski (P5), walk on uneven ground (P11), be pain free (P8), and play tennis (P1, P5) were examples of goals and expectations that patients had pre-operatively, which were not achieved by the outcome of the HTO. Some patients had an outcome that accurately reflected their pre-operative expectations of being able to do "what [they] wanted to do" (P3) regarding knee function and physical activity; not "expecting to get a fully functioning knee back"; and to get "to the stage where [they] could do something without any impact on [their] daily life" (P7). Conversely, one patient reported that they went to the gym multiple times per week and lifted weights similar to their pre-operative levels, which was "something [they] never thought [they would] be able to do" (P10).

Participants showed signs that they were very motivated during the initial post-operative period to recover from the surgery and get back to physical activity. However, there were varying degrees of satisfaction regarding the speediness of the recovery, with some suggesting they were "a bit disappointed it had taken so long" (P7), and that they would have wanted their recovery to be "quicker" (P5, P6) or "a little bit faster" (P8). Most patients remained "conscious" (P6, P9, P10) or "mindful" (P5, P7) of the knee, and had become more “cautious” (P8) in their movements and activities to “protect” (P3) the knee’s “life cycle” (P2), and reduce the risk of “doing [themselves] harm or damage” (P4). Fear was commonly cited as a reason to avoid certain movements: “the pain has induced a fear in me” (P1); “I’m scared of making it worse, I’m scared of being back in the pain I was in before” (P5).

Most participants referred to the surgery, recovery, or outcome as being difficult “from a mental health point of view” (P1). Anger was reported by one patient who did not like that he was “always conscious” of the knee (P6). Another patient expressed annoyance at the residual pain he still experienced because “[he] had all this done and [did not] particularly want to be going through all that again” (P8). Frustration toward the “inability to do something [classed] as ‘everyday’” (P3) in the first few weeks post-operatively was also apparent. A lack of confidence in the ability of the knee also seemed prevalent among patients: “it has definitely extremely knocked my confidence in wanting to do any sport” (P5); “I didn’t feel confident jogging half a road” (P7); “it was a bit of a confidence thing” (P8).

Theme 3: Information and experiences

There was agreement regarding the level of information that patients received post-operatively pertaining to the recovery process. Generally, patients found that “there was a lot of guidance in the first few weeks” (P11), which reduced as time went on, occasionally leaving them not knowing “what [their] parameters [were]” (P7) around the type and intensity of activity they could, or should, have performed. When asked about the information that the patients would like to have received post-operatively, guidelines that outlined the progression that can be generally expected during recovery was often mentioned: “information in regard to […] indicative milestones where you can be aiming […] it’ll manage each individual’s expectations” (P7); “if there was something in place that said ‘this is where you can expect to be’” (P8); “you can set your goals and your objectives based on having more information” (P9); “it’s only a very small part of it: getting that surgery right […] but actually it’s getting that pre-op information and post-op plans and actions to get you back to where you should be” (P9); “if I was in a group […] and they recommended hydrotherapy […] I probably would have done it sooner” (P10); “some kind of web group […] where people can put on their own experiences and people can ask questions” (P11).

In an effort to seek further information around the procedure itself, patients reported that they sourced guidance “online” (P6); from “YouTube videos” (P5, P10), “Google” (P5, P7); “testimonials from the clinic” (P9); and “websites suggested by the surgeon” (P7, P11). The use of YouTube videos had mixed responses from participants. P5 watched videos of previous HTO patients diarising their recovery, which he found “massively increased” his confidence to begin cycling. On the other hand, P10 viewed videos of the procedure itself and found it “pretty scary”. P9 found that patient testimonials led him to have “truly believed that after 12 weeks […he would] be good”, which was not reflected in his outcome.

Theme 4: Actual Physical Activity

This theme focused on the type and frequency of activity that patients participated in before and after HTO. Pre-symptomatically, all patients participated regularly in at least one physical activity, and reported a decrease and change in participation due to their knee issues prior to undergoing HTO: “walking was difficult, so I did a lot more cycling” (P1); “I couldn’t walk round a golf course” (P7); “when I started getting the knee pain, I stopped doing the squats” (P8); “any sport-orientated activity, I’d struggle with” (P10); “I stopped doing squash. I stopped doing things that involved pivoting prior to the osteotomy” (P11).

A summary comparison of pre-symptomatic and post-operative physical activity participation of the patients can be found in Figure 7.1. A tendency for a large pre-symptomatic to post-operative decrease in high impact activities such as running/jogging, skiing/snowboarding, racquet sports, and football (soccer) was reported alongside a similarly large increase in lower impact activities like weight-training, indoor rowing, swimming, gardening, and housework/DIY. The only sporting activity where participation was equal pre-pathology and post-operatively was cycling/spinning: a low-impact activity.

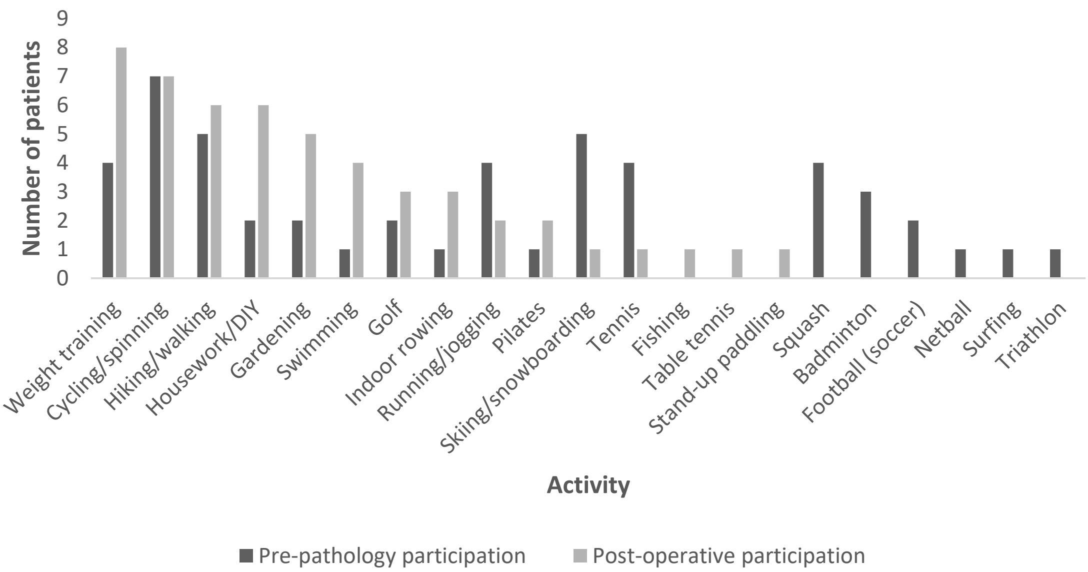

Figure 7.1: Change in activities that patients performed pre-pathology and post-operatively.

Reasons provided for patient decisions regarding participation in physical activity after HTO varied. In addition to the fear of pain, aging and work commitments were commonly attributed to changes in activity habits: "as you get older, things happen […] you're not going to be able to do things you used to be able to do" (P3); "by the time I've done a 12 hour day the last thing I want to do is get changed and go to a swimming pool or go to the gym" (P5); "as you get older, you get less active" (P6). Patients generally reported a conscious decision to avoid activities involving "impact" (P1, P5, P8, P10, P11) or pivoting movements: "all the twisting and turning, jolting and jarring […] I can't do that" (P3); "impacts. That's why I don't run" (P8); "I have no real confidence that my knee could withstand that" (P10). Gait issues were also noted: "if I wear hard-soled shoes […] I drag my foot a little bit" (P1); "my walking gait is slightly impaired […] I'm obviously not picking this leg up properly" (P6); "I have to take the weight off of this leg sooner than you normally would, so I kind of limp" (P8). One patient attributed a subsequent injury to gait changes that occurred: "probably the Achilles injury is from not quite walking correctly, not having the right balance" (P11).

7.5 Discussion

The main finding of this study is that there are several physical and psychological factors, plus the quality of information and experiences, that impacted on patient activity participation after HTO. These included: residual pain during high impact activities; a lack of confidence in the knee; a lack of longer-term guidance or information for patients; and fear of re-injury. Other variables, not necessarily related to the HTO, included: subsequent injuries, aging, and work commitments. Furthermore, reduced patient satisfaction with the outcome of the surgery seemed to be linked to an increased awareness of the knee post-operatively and inaccurate pre-operative expectations. Additionally, it was not uncommon for the removal of the fixation plate to have a positive effect on physical activity participation; though this requires further investigation. This was the first study involving HTO patients to use a primarily qualitative protocol, which allowed for research questions to be generated that might not otherwise have been realised through quantitative investigations.

There are several quantitative studies that have reported findings regarding the rate that patients return to physical activity after HTO (Salzmann *et al.*, 2009; Bonnin *et al.*, 2013; Faschingbauer *et al.*, 2015; Ekhtiari *et al.*, 2016; W-Dahl, Toksvig-Larsen and Lindstrand, 2017). These studies generally reported that patients could return to activities at a similar or greater level after HTO in comparison to their pre-operative levels; supporting the findings of the present investigation. Mean KOOS scores (Table 7.2), recorded at a mean follow-up of 32 months after surgery, were not dissimilar to other studies in the literature (W-Dahl, Toksvig-Larsen and Roos, 2005; Sischek *et al.*, 2014) with similar follow-up times (24 months). This suggests that the quantitative outcome scores presented in the present study could be representative of HTO patients in general, despite the relatively small sample size.

Bonnin *et al.* (2013) and W-Dahl *et al.* (2017) reported changes in the type of activity undertaken by patients post-HTO but did not investigate the underlying causes of these changes. No study has thoroughly investigated the contributing reasons towards patient decisions to participate in physical activities post-operatively. Saragaglia *et al.* (2014) sought to identify the cause behind the small number of patients (*n*=3) who did not resume physical activities post-operatively in their study. They found that each patient attributed it solely to pain in the operated knee. However, the line of questioning used to determine this cause was not in-depth. Faschingbauer *et al.* (2015) speculated that changes in activity may have been a result of recommendations by the surgeon to avoid impact sports, or that patients wanted to protect the knee from potential further damage.

The fear of re-injury is one of the most frequently occurring issues that sports medicine physicians encounter when talking with patient-athletes (Mann *et al.*, 2007). It is a common theme among patients who undergo forms of knee surgery other than HTO (Tjong *et al.*, 2014; Burland *et al.*, 2018; Ezzat *et al.*, 2018). Furthermore, the fear of re-injury is known to have a negative influence on quality of life (Filbay, Crossley and Ackerman, 2016), which may explain why “Quality of Life” was the second lowest scoring subset of the KOOS questionnaire (Table 7.2). A further factor that may have contributed to the low quality of life KOOS scores could be the lack of confidence reported by some of the participants. A positive correlation has previously been found between self-efficacy and activity level, quality of life, and return to sport in anterior cruciate ligament reconstruction patients (Tjong *et al.*, 2016). There is perhaps a need for more investigation into methods of identifying and supporting patients who exhibit signs of low confidence in their operated knee. This could help to encourage a return to physical activity that may otherwise have been avoided due to fear of reinjury or pain, rather than the actual existence of a high risk thereof.

The literature generally agrees that patients experience an overall reduction in pain post-HTO (Slevin *et al.*, 2016). The results of the present investigation concurred but also supported the conclusions of Bonnin *et al.* (2013), who found that residual pain during high-intensity activity was not a rare phenomenon among HTO patients. This was reflected in the comments made by the interviewed participants pertaining to the twisting movements and “impacts” that they tended to avoid. Residual pain as a modifier for physical activity behaviour is further supported by the changes in the type of activity patients participated in post-operatively compared with those they participated in pre-symptomatically. Participation in high-impact activities decreased post-operatively but an increase in low-impact activities may be indicative of patients wanting to remain physically active while avoiding movements that may induce pain. The extent to which patients experience pain during the activities they do participate in post-operatively, or the levels of pain they tolerate before ceasing a bout of exercise, is unclear.

Patient pre-operative expectations of post-operative outcome should be a primary focus for rehabilitation purposes (Oberg and Oberg, 2000) since satisfaction with the outcome is influenced by expectation (Mannion *et al.*, 2009). A recent study demonstrated that patient expectations of HTO were high regarding pain reduction, and function of the knee post-operatively (Grünwald *et al.*, 2018). The present study similarly showed that some patients voiced disappointment with their outcome at various stages of their recovery; even if they were satisfied overall at the time of interview. This disappointment seemed to be in direct connection to pre-operative expectations, which were not met post-operatively. Further research is required to help better manage patients' physical activity expectations, particularly during the recovery period. Ekhtiari *et al.* (2016) came to a similar conclusion after conducting a systematic review on return to work and sport following HTO. They suggested that the creation of a "return to sport timeline" would enable surgeons to provide more accurate information to patients, resulting in more realistic expectations, and potentially higher satisfaction with the outcome of surgery. Furthermore, a systematic review of patient education outcomes after surgery recommended that information should be given to patients constantly because certain outcomes are only relevant months after surgery (Ronco *et al.*, 2012). This recommendation is further supported by the present study, since patients claimed they would have benefitted from more information post-operatively: particularly regarding the time it takes to return to various physical activities; something that is not possible immediately after surgery.

7.5.1 Strengths and limitations

Though the present study largely supported the available literature regarding HTO patients returning to physical activity, the qualitative element was a strength which provided greater context behind the predominantly quantitative body of research. In doing so, this study can help surgeons, physiotherapists, and clinical researchers to better understand the patient experience by identifying additional aspects of recovery that require extra attention in the future. It is encouraging to confirm that patient activity behaviours were influenced by the recommendations and advice received from the medical professionals with whom the patients had contact. Nevertheless, the present study demonstrated that once contacts with medical professionals became more infrequent – such as after the initial 3-6 month rehabilitation period – it was not uncommon for patients to feel uncertain regarding the limits of their knee; and whether or when they could (or should) have returned to certain physical activities.

This study also has several limitations that should be considered when interpreting the results. Firstly, participant recruitment stopped after the point that data saturation was reached. Since a small number of patients was needed to achieve data saturation in this instance, the statistical significance of the quantitative aspects of the results may be diminished. However, the mixed methods approach of the study helps to increase its overall strength (Clark and Ivankova, 2018). The time since surgery at the point of interview ranged from 18 to 44 months, which may have resulted in recall bias particularly when patients were estimating their condition in the initial recovery period. A similar criticism can be made of the pre-operative Tegner scores as these were approximated retrospectively by the patients at the time of interview. Social desirability bias may have also been an issue leading to potential exaggerated importance of certain events, or omissions of others, by participants during the interviews. The disparity in numbers between male and female participants may have meant that the results of this study are not transferable to the entire population. However, the Tegner and KOOS scores were similar to much of the literature, suggesting that this sample may have been a reasonable representation of an average HTO cohort.

7.5.2 Recommendations for future research

It is difficult to outline any direct clinical implications from the results due to the qualitative approach of the research presented in this chapter. However, the findings served the purpose of identifying potential directions for future research. This study suggested that a combination of physical, emotional, and psychological factors contributed to the post-operative physical activity behaviours of patients. It remains important for research to continue assessing the various demographic and operative variables that impact on the post-operative outcomes of HTO. Nonetheless, there is a distinct lack of research focused on providing information about the influence of more subjective, less measurable variables, which also appear to be key influencers, particularly regarding physical activity behaviour. Based on the findings of this study, future research should examine pain tolerance during physical activity, as well as methods of improving the accuracy of patient expectations, which may improve certain psychological factors and overall patient satisfaction with the surgery.

A lack of confidence in the knee, and a perceived lack of guidance and information after the initial recovery period, were issues commonly reported by patients in the present study. These points suggest an absence of knowledge or perhaps the presence of inaccurate expectations of outcome. Self-efficacy and the accuracy of patient expectations are positively correlated with satisfaction of surgical outcome (Cross *et al.*, 2009; Mannion *et al.*, 2009). Efforts to suitably moderate patient expectations should therefore not be overlooked by clinicians (Oberg and Oberg, 2000). Grünwald *et al.* (2018) found that HTO patients had high expectations of their surgical outcome with regard to pain relief, work capacity, and post-operative knee function. They also demonstrated that many patients underestimated the eventual likelihood of a future need for additional surgery (such as conversion to arthroplasty), and highlighted the importance of surgeons ensuring that patient expectations are realistic.

7.6 Conclusion

Multiple factors influenced the post-operative activity behaviours of HTO patients: residual pain during high impact activities, fear of reinjury, aging, subsequent injuries, a lack of confidence in the knee, and a lack of guidance or information after the initial recovery period. A reduction of participation in high impact activities, but an overall increase in activity levels post-operatively, was apparent. Most patients opted to change the type of activity they performed rather than to completely cease being physically active.

There is a clear need for research to investigate how to improve expectation management for HTO patients. The actual information given to patients by surgeons, and the way that expectations are currently managed, is unknown. The next chapter seeks to provide unprecedented insight into this area and, contrary to the vast majority of HTO research, offers a unique perspective by focusing on the surgeons who perform the procedure rather than the patients on whom the procedure is performed.

CHAPTER 8 – PATIENT INFORMATION AND EXPECTED OUTCOME AFTER HIGH TIBIAL OSTEOTOMY: CONSENSUS AND CONTENTION AMONG SURGEONS

"The good news about an osteotomy is you get to keep your own knee, the bad news about an osteotomy is you get to keep your own knee" -Participant "S14" in this chapter

8.1 Abstract

Background: Patient expectations of post-operative ability after knee surgery tend to be unrealistically high and their accuracy has been shown to have a significant relationship with the surgical outcome. Returning to physical activity after knee surgery is one of the most commonly cited expectations that patients have pre-operatively. However, research has found that these expectations were achieved in only around 56% of HTO cases. Managing the expectations of HTO patients is therefore an important factor that needs to be adjusted accordingly on a patient-to-patient basis. Despite the suggested influence that a surgeon's advice has over patient behaviours post-operatively, it is not known whether differences between surgeons exist in reference to the information they give to patients. The purpose of this study was to summarise the information provided by experienced osteotomy surgeons to their HTO patients regarding the procedure, the initial post-operative recovery period, and what they consider to be a realistic outcome after surgery.

Methods: Semi-structured interviews were conducted and transcribed verbatim. Data were analysed thematically to realise codes, categories, and themes. Fourteen experienced orthopaedic surgeons from the UK, Germany, and the Netherlands patients participated in this qualitative study.

Results: Three overarching themes were found: 1) indications, procedures, and post-operative milestones; 2) patient education, expectations and personal responsibility; and 3) post-operative limitations and quality of life. Most of the information surgeons reported providing to their patients pertained to the peri-operative period rather than the longer-term outcome. The management of patient expectations of the post-operative outcome was a major focus of the information typically provided to patients. Areas of agreement largely coincided with a clear consensus in the available scientific literature.

Conclusion: Information provided to prospective patients by their surgeons was comprehensive and primarily focused on the peri-operative period, and the management of expectations for the first 3-6 months of recovery. Areas of controversy among surgeons included operative technique, the necessity for plate removal, and the average timelines for various post-operative milestones to be achieved.

8.2 Introduction

The previous chapter presented findings of the first qualitative investigation involving HTO patients, which resulted in a recommendation for a focus on the information given by surgeons pre-operatively, and the way in which patient expectations are managed. Building on the findings of the previous chapter – and having demonstrated the relevance and value of a qualitative approach to HTO research – this chapter presents a second qualitative study that draws attention away from the patient and towards the surgeon. In doing so, the following study ensured that this thesis provides a comprehensive approach to improving the outcomes of HTO.

The literature unequivocally agrees that HTO improves knee function and reduces pain (Brouwer *et al.*, 2014; Saier *et al.*, 2017) however, there is controversy concerning the degree to which patients are able to return to physical activity after surgery (Hoorntje *et al.*, 2017; Kunze *et al.*, 2019). Patient demographics, such as body mass index and age (Trieb *et al.*, 2006; Hui *et al.*, 2011; Santoso and Wu, 2017), and operative variables such as the inclusion of graft materials and the type of fixation used during HTO (Zhim *et al.*, 2005; Lash *et al.*, 2015; Slevin *et al.*, 2016; Han *et al.*, 2017), have been shown to impact post-operative outcome. Additionally, multiple studies have indicated that the advice surgeons gave to their patients may contribute to observed changes in post-operative physical activity behaviour (Noyes, Barber and Simon, 1993; Salzmann *et al.*, 2009; Faschingbauer *et al.*, 2015; Kim *et al.*, 2018).

Patient expectations of post-operative ability after knee surgery tend to be unrealistically high (Feucht *et al.*, 2016; Grünwald *et al.*, 2018) and their accuracy has been shown to have a significant relationship with the surgical outcome (Saragaglia *et al.*, 2014; Rossi *et al.*, 2015). Returning to physical activity after knee surgery is one of the most commonly cited expectations that patients have pre-operatively (Mancuso *et al.*, 2001). However, research has found that these expectations were achieved in only around 56% of HTO cases (Bonnin *et al.*, 2013; Feucht *et al.*, 2016). Managing the expectations of patients is therefore an important factor that needs to be investigated, and adjusted accordingly on a patient-to-patient basis (Oberg and Oberg, 2000; Aalderink, Shaffer and Amendola, 2010). Despite the suggested influence that a surgeon's advice has over patient behaviours post-operatively (Noyes, Barber and Simon, 1993; Salzmann *et al.*, 2009; Faschingbauer *et al.*, 2015; Kim *et al.*, 2018) – and therefore on the reported outcome after HTO – it is not known whether differences between surgeons exist in reference to the information they give to patients. Identifying such differences, and understanding the reasons for them, would highlight areas of practice that require further scrutiny to ensure that appropriate information is given to patients. This would lead to an improvement in patient expectations and post-operative satisfaction and functional outcome.

The purpose of the present study was to summarise the range of information provided by experienced osteotomy surgeons to their prospective patients regarding the HTO procedure, the initial post-operative recovery period, and what they consider to be a realistic outcome after surgery.

8.3 Methods

8.3.1 Study Design

One-to-one interviews were scheduled with 14 experienced orthopaedic surgeons from the United Kingdom (*n*=8), Germany (*n*=5), and the Netherlands (*n*=1) who regularly perform high tibial osteotomies. Semi-structured interviews were conducted between June and October 2019 at the respective hospitals of the surgeons (*n*=10) or over the course of two days during a scientific congress in Germany (*n*=4). All interviews were conducted in English. Purposive and snowball sampling was used to identify participants, who were recruited based on the relative high frequency of osteotomies they performed annually in their respective countries. Recruitment occurred continuously for the study until the point that data saturation was reached: when new participants did not provide new information and were repeating ideas and themes already identified (Creswell, 2007; Hennink, Hutter and Bailey, 2011; Silverman, 2017). All surgeons provided written informed consent to participate, and ethical approval for the study was granted by the University of Winchester ethics review panel (Appendix G).

Interviews were audio-recorded and conducted face-to-face by a single interviewer, who used an interview guide consisting of open-ended questions to focus the direction of the dialogue (Appendix G). Open-ended questions were used to allow opportunities for participants to expand upon any points and to ensure they were able to fully communicate their meaning. The interview guide was continuously updated through the data collection process to reveal further information that had not previously arisen, but which was relevant for the purposes of the study. The order in which questions were asked remained flexible to allow the conversation to flow naturally. The interviewer asked probing questions where necessary to clarify the meaning of what was said or to elicit further information from participants. Using this approach meant that greater context and more detailed information could be conveyed, which otherwise may not have been possible to gather using quantitative methods or closed questions.

8.3.2 Data analysis

Personal identifiers were removed from transcripts, and pseudonyms assigned to participants during the transcription process to preserve anonymity. Data were collected and analysed thematically. Interviews were transcribed verbatim and coded electronically using NVivo 11 Pro (QSR International) software. Coding was conducted line-by-line after having read through each transcript several times to create familiarity with the responses given to the questions. Codes were grouped into categories according to interpreted similarities found between them. These categories were then further examined and grouped according to connections they had, resulting in overarching themes being established. The created themes gave an overview of the information given to prospective HTO patients as well as points of agreement and differences of opinion between surgeons regarding their approach to patient management. Where interviews yielded quantitative findings – such as suggested average timelines for patients to achieve post-operative milestones – numbers were aggregated to offer additional insight into areas of apparent consensus and contention among participants. Finally, the number of HTO's performed by each surgeon annually was also recorded to demonstrate the experience of the included participants.

8.4 Results

The number of HTO's performed annually by each participant varied widely (mean 90 ± 69; range 10-200). There were differences in the number of HTO's performed by participants from different countries where the German participants reported performing more HTO's per year (*n*=5; mean 131 ± 64; range 65-200) than the UK participants (*n*=8; mean 45 ± 31; range 10-96). The single Dutch surgeon reported performing around 200 HTO's per year.

After thematic analysis of the interviews 67 codes and 8 categories arose, from which 3 overarching themes were realised (Table 8.1). These themes were: 1) indications, procedures, and post-operative milestones; 2) patient education, expectations and personal responsibility; and 3) post-operative limitations and quality of life.

Table 8.1: *Themes, categories and example representative codes generated from interviews with surgeons*

Theme	**Categories**	**Example representative codes**
1) Indications, procedures, and post-operative milestones	Post-operative milestones	Time in hospital; plate removal; return to manual work
	Startpoint and endpoint	Patient demographics; survivorship; criteria for surgery
2) Patient education, expectations, and personal responsibility	Nuanced information given to patients	Information dependent on osteoarthritis severity; information based on experience; information based on science
	Patient education	Managing expectations; explaining aim of procedure; sources of information
	Responsibility of patient	Pain management; risks associated with pushing too hard; fitness
3) Post-operative limitations and quality of life	Post-operative limitations and quality of life	Limitations of physical activity; post-operative pain; interaction between pain and activity

8.4.1 Theme 1: indications, procedures, and post-operative milestones

Participants were largely in agreement regarding pre-operative factors such as the indications for surgery and their associated risks and complications. However, differences between surgeons were noticed when discussing post-operative milestones such as returning to various activities after surgery. In relation to the indications for medial opening-wedge HTO, participants agreed that patients should have a “medial compartment that has failed” (participant S3) or is “failing” (S2), with varus malalignment (S1, S3, S5, S9, S14). Patients tend to be “fairly active” (S3) and aged 40-60 years old (S5, S14), although an age outside of these limits did not automatically preclude a patient from an HTO as one surgeon reported performing some osteotomies “in over 70 year-olds” (S5).

Multiple participants commented that they were aware of differences between their practice and that of other surgeons on the matter of HTO patient management: “our management of knee osteoarthritis is very different from the rest of the UK” (S4); “unlike others, I don’t routinely remove the plate” (S5). Consequently, approaches towards variables – primarily relating to operative technique – differed between surgeons: “I do [HTO] without a tourniquet” (S2); “I tend to do an oblique [incision]. It just works for me” (S5); “I generally don’t [use graft materials] but if it’s a really big [osteotomy], then I do” (S13). In addition to the preference differences between surgeons, UK-based participants also reported sometimes having difficulties with patients and other medical professionals in terms of spending “a lot of time mainly steering people a little bit away from a knee replacement and trying to offer them the alternative of osteotomy. None of them were really aware of it in [the UK]” (S14): “I don’t think there’s an easy way of making people understand. It’s difficult for surgeons to understand so why would you expect a patient to understand?” (S6); “There’s still a conception amongst GPs and other professionals that ‘you’re too young for a knee replacement: keep going, keep going’” (S13). Knee replacements were commonly referenced by participants as something that regularly featured in conversations with prospective HTO patients: “there are more people that end up with 0/10 pain with osteotomies than knee replacements” (S1); “the biggest cause of failure for knee replacement is implantation at an early age. You want to do everything you can to avoid your first joint replacement” (S3);

> “I tell [patients] that even though a half knee replacement or a full knee replacement might give them quicker pain relief and quicker ability to do certain things, [osteotomy] has different outcomes: higher achievement levels that are sometimes way beyond those that you get with a joint replacement” (S6).

Post-operative milestones were discussed by participants in reference to their experience of the progress of the "average" patient undergoing solely a unilateral medial opening-wedge HTO. Table 8.2 details the various post-operative milestones identified during the interviews along with the suggested timeframe within which a patient is expected to achieve them. The number of participants who suggested each timeframe was also noted to begin to identify areas of consensus and contention between surgeons. Some participants suggested they would be reluctant to offer an expected timeframe for some post-operative milestones due to a variety of factors that vary from patient-to-patient: "it depends on the shape and size of the patient. It depends on the size of the osteotomy" (S4); "it's a great operation but it's variable how quickly people get [to a full recovery]" (S1); "I try not to commit to a timeframe [for an expected full recovery] because I find it difficult to decipher and it often boils down to the personality of the patient" (S14).

Frequency of contact between the patient and the surgeon after surgery varied between participants. All participants would see patients 6 weeks following HTO for a follow-up appointment, eleven participants saw patients again 12 weeks after HTO, and seven participants saw patients after a year. A minority of participants reported normally seeing patients more frequently with additional meetings 2 weeks and 6 months post-operatively. Five participants added that they make clear to patients the possibility of contacting them via email or telephone in case of any problems or issues that may arise between appointments: "if there's a problem they have direct access and they know they can come back to me" (S5); "I'd be available on the telephone if they needed it" (S14).

Practice pertaining to the removal of the fixation plate was variable between participants. Some surgeons (S4, S9, S12) routinely tell patients "the plate is coming out" (S4), whereas others only remove plates if necessary due to related symptoms such as irritation (S1, S5, S6, S7, S10, S11, S13, S14): "I tell them the plate's a present from me for the rest of their life. If it bothers them, they can have it out." (S5). Issues requiring plates to be removed reportedly occur in a significant number of cases ranging from 40% (S7) to 98% (S11) of patients. For plates that get removed, participants reported varying times at which this occurs, on average, after the initial HTO surgery. One participant (S6) removes plates 9 months after surgery whereas most other participants conduct the removal 12-18 months after HTO (S4, S7, S10, S12, S13, S14).

Most surgeons agreed that a return to driving a car was possible 4-6 weeks after HTO, which was deemed to be the time at which patients "need to be capable with their crutches –

which they usually are at that stage” (S13). However, multiple participants mentioned that this timeframe was variable dependent on which leg received the osteotomy or whether the patient drives a car with automatic transmission. If the operated knee is on the left leg, or if patients drives an automatic car, a return to driving was expected to be sooner after surgery. This was due to the weightbearing status of the patient whereby “the first three weeks is going to be complicated by a lot of pain and bruising so when [patients] put their weight down, it’ll hurt a lot” (S2). Regarding a return to activity after HTO, “normal” physical activity was defined as: the time at which patients would be expected to resume the activities they had performed prior to surgery. Participants differentiated between the type of physical activity performed and the time needed after surgery before a return to that activity was possible. “Low-impact activities” referred to those which put low amounts of sudden force through the knee and included activities such as cycling and swimming. “High-impact activities” were those which involve exerting higher forces through the joint, including tennis, jogging, and contact sports such as football (soccer).

The overall estimated length of the recovery period from HTO varied between participants. All surgeons highlighted that recovery often depends on the individual due to demographic and operative variables such as body mass and osteotomy gap size. Most surgeons referred to 6 months post-HTO as a major milestone where patients first “really start to see the benefit of the operation” (S2), but that they then continue to gradually improve until 12 months after surgery. However, two participants suggested that 3 months after surgery is the point at which patients are “basically at the level at which they can expect to remain” (S10) and have made a “full recovery” (S11). Some referred to a point at which patients “turn the corner” (S1, S2, S13) during their recovery, which varies among patients, but there was an general consensus that “pretty universally, when [patients] get to 12 months, everybody is doing well” (S4). Although the emergent trend between participants was that a full recovery was to be expected within the first post-operative year, three surgeons mentioned that their patients tended to experience further improvements into the second year (S2, S5, S6).

Table 8.2: *Post-HTO milestones and agreement among surgeons on the time to reach them*

Milestones/events	Average time to reach milestone post-HTO	No. of surgeons in agreement
Time in hospital (nights)	1-2	4
	3-4	3
Time on crutches (weeks)	2-4	3
	6	9
	8-12	2
Osteotomy healing time (months)	2	1
	3-6	2
	9	1
	12-15	3
Largest reduction in pain (months)	1.5	1
	3	5
	6	3
Plate removal (where necessary) (months)	9	1
	12-18	6
Return to driving a car (weeks)	4-6	9
	8-10	2
Return to work (sedentary job) (weeks)	2-3	6
	4-6	7
Return to work (manual job) (weeks)	8-12	13
	20	1
Return to normal physical activity (months)	4-6	5
	8-12	3
	18	1
Return to low-impact activities (months)	1-2	5
	3-6	3
Return to high-impact activities (months)	6	2
	8-9	3
	18	1

8.4.2 Theme 2: patient education, expectations, and personal responsibility

Patient education was a factor that participants reported as a major focus of the pre-operative period: "they can't get enough information" (S3). Participants reported that "the first thing [one needs] to do is explain what the pathology is and explain the weightbearing axis" (S13) to patients. An explanation of the aim of the osteotomy procedure to the patient in simple terms was common among participants:

> "what [surgeons are] trying to do is offload the damaged area onto the better area of the knee so that [the patient's] pain is significantly improved [which buys] their knee time. [Surgeons aim to] either stop, or massively slow down, the progression of arthritis so that hopefully [patients will] be able to get back to what they want to do; and put off needing some form of knee replacement for a lot longer" (S5).

It was normal for the HTO procedure to be explained to patients in detail along with the related risks. This was undertaken in a variety of ways, which changed from surgeon-to-surgeon: "I draw them a couple of pictures and explain the general principle of the operation using sawbones" (S2); "I go through a powerpoint presentation and I show them the physical steps of the operation" (S3); "we usually show the patients an example of the surgery. We go through the pictures of an example patient and step-by-step we show them how it's done" (S8); "We tell them especially about the risks" (S10); "I often demonstrate anonymised x-rays of an osteotomy being performed" (S14). Most information that referred to the pre- and intra-operative period was passive, meaning that it was intended to educate the patient without requiring any follow-up action. There were some exceptions to this trend as some surgeons also direct patients to sources of further information that can be accessed by the patient independently to increase their understanding of the procedure and recovery process: "I point them to my own website where a patient's left a blog; a kind of warts-and-all account of life after an osteotomy" (S2); "I explain that there's a video online that I made a few years back that's been viewed nearly 90,000 times that they might want to watch" (S3); "They all get an osteotomy information leaflet" (S4);

> "I often invite them to talk to previous patients, previous patients who've written blogs, previous patients who are GP's. There's quite a network of individuals who are happy to contribute and strike up a dialogue" (S6).

Additionally, surgeons inform the patients about the various potential treatments and techniques available to them. This is to include the patient in the decision-making process and to ensure that they are able to provide informed consent for the surgery:

"I talk to them about their options… you can live with what you've got… you can try a brace… I talk about injections, arthroscopic surgery, distraction, osteotomy, partial knee replacement and total knee replacement" (S3);

"patients quite like the idea of those options being available to them and that's often the first time they've heard of the concept of choices that they're allowed to make" (S14).

Much of the information shared regarding the post-operative period – ranging from immediately after the surgery until the point of full recovery – was focused on managing the expectations, fears, and confidence of the patient: "it's not going to be an overnight cure to the pain… typically it's going to take 6 months to get better, and a year to get the full benefit" (S1); "the first 3 months is a question of restricting [the patient's] activity and giving them realistic goals. But then 6 months onwards you have to flip it over and allay their anxiety" (S2); "[patients] have a damaged joint and we say that we are wanting to decrease the level of pain but we do not tell them that they are going to be pain-free" (S8);

"I can't tell [patients] 'you will be doing sports', I can only tell [them] 'yes we have a chance to unload your joint and postpone arthroplasty' and whatever else comes is a bonus" (S9).

Patients were viewed as having a significant impact on their own recovery, outcome, and longevity of their operated knee. Therefore, information given about the post-operative period was often intended to instil a sense of personal responsibility in patients:

"The best thing you can do is: leg up, take your painkillers, control the swelling. The better job you do at controlling your swelling, with icing machines and elevating the limb, the more it's going to pay dividends" (S1);

"If you're comfortable: if you want to kick a ball around with your children, fine. If you want to play 5-a-side [football], 3 times per week, the chances are it's going to break down sooner rather than later" (S3);

"[patients] are actually psychologically in charge of their situation" (S6).

The justification for the information given to patients tended to be based on a combination of the available scientific literature and personal experience: “we’ve been going for 14 years with the surgery, many [patients] are beyond 10 years now and I’ve only done a handful of revisions” (S3); “I’m learning now, because of the research, to talk more about activity levels. It’s very important to [patients], and I didn’t realise that before” (S7); “experience shows us that [patients] do not need that much anaesthesia so you can tell [them] that it’s not the most painful procedure” (S8);

> “I think anecdotally [using a bone graft during HTO] reduces pain levels in the immediate post-operative period but I haven’t seen a randomised controlled trial to prove that yet […] I’ve read quite a lot about radiostereometric analysis and found that things generally don’t move [with the Tomofix plate]. And the message that’s come through from European surgeons is often that you can weight-bear fairly early” (S14).

Participants were also cautious about giving firm recommendations for certain issues where there is only limited scientific evidence available from which to draw conclusions:

> “I wouldn’t be comfortable at promising a return to elite levels of sport although there is some research that indicates that [patients] probably can get back. But [those studies are] only small numbers so it’s hard to guarantee that” (S2);

> “I think [using a bone wedge during HTO] is like plugging the medullary canal so it stops it bleeding so much. I’m waiting for evidence to show that it’s better. I don’t think it’s out there yet” (S13);

> “[osteotomy] is an operation that’s coming back into vogue because of the enthusiasts who see a role for it […] I think we need to study it further and we need to conduct a lot more of it and understand it better […] We have an opportunity in the next decade or two to change the way in which we conduct knee surgery. It’s probably going to come from educating younger surgeons, and patients, to the possibilities so they’re aware of [osteotomy] as an option” (S14).

8.4.3 Theme 3: post-operative limitations and quality of life

In the first 2-4 weeks after HTO, most participants talked about pain being a major limiting factor for patients, requiring the use of painkillers and crutches to manage symptoms. After 6 weeks, participants reported that pain has usually reduced to the extent where patients no longer need to use crutches. The presence of the fixation plate was cited as a potential source of continued irritation and pain beyond the initial recovery from surgery, once the osteotomy has healed radiologically: "Reserve judgement, if you've got residual pain, until after the plate comes out" (S1). The consensus among participants was that HTO is "a pain-relieving operation" (S3) wherein patients experience a significant reduction in pain once recovered from surgery compared to their pre-operative levels. It was apparent that some patients report having a completely pain-free knee after HTO but that is not necessarily the norm. Therefore, surgeons "wouldn't promise zero pain levels" (S6). In further support of this point, four participants referred to the pre-operative and post-recovery pain levels in terms of scores on a 10-point Visual Analogue Scale. They suggested that patients tended to experience relatively high pain levels equal to 8-9 out of 10 pre-operatively compared to 0-2 out of 10 after recovering from HTO surgery.

Pain during physical activity was a source of some variation in information provided by participants. There was a trend of agreement that pain could be affected by physical activity levels and "if [patients] put more burden through the joint then they are going to have a higher level of pain" (S8). Upon reaching a point where the osteotomy has radiologically healed, some participants reported that they did not impose limitations or restrictions on patients with regard to physical activities that they should or should not perform: "once the osteotomy has healed, [patients] should expect to return to any level of physical activity that they aspire to" (S2); "we don't limit or rule out any specific kind of sporting activity" (S10); "I don't place restrictions on them. I think they find their own restrictions" (S14). Other participants were more reserved, depending on the patient: "if they are between grade 3 or grade 4 [Kellgren-Lawrence] I tell them 'no jumping activities anymore, in any sports'" (S7). Whereas other participants were generally more restrictive with the advice they give to patients concerning physical activity potential: "they should not play squash or badminton, running, or hiking. No extreme impact sports but they should return to a normal range of motion and a normal activity level" (S8).

8.5 Discussion

The primary finding of this study was that most of the information surgeons reported providing to their patients pertained to the peri-operative period rather than the longer-term outcome. Once patients were beyond 3 months after surgery, information and contact between surgeons and patients became less specific and more infrequent. All surgeons reported spending a lot of time with the patient pre-operatively to educate them fully as to the purpose, procedure, recovery, and expected outcome of the HTO. Educating the patient regarding their own post-operative responsibility, and the extent to which their actions may directly influence their outcome, was a common theme among participants. The management of patient expectations of the post-operative outcome was a major focus of the information typically provided to patients. However, differences in the information given and procedures followed by the surgeons were apparent, which could result in differing levels of expectations among their respective patients.

8.5.1 Indications and surgical options

Indications for surgery were identified to include medial compartmental osteoarthritis in a patient that is active and, typically, under the age of 60 years. This is largely in agreement with the surgical indications borne out in the literature (Amendola and Bonasia, 2010; Dettoni *et al.*, 2010). The present study showed that alternative procedures to HTO, particularly arthroplasty, are normally also discussed with patients as part of the pre-operative process. This may be related to recent research, which demonstrated that unicompartmental knee arthroplasty can result in similar, or superior, clinical outcomes to HTO in patients where surgical indications overlap (Fu *et al.*, 2013; Santoso and Wu, 2017; Cao *et al.*, 2018). Another factor may be due to the higher profile and incidence of arthroplasty over osteotomy internationally (Koskinen *et al.*, 2007; Niinimaki *et al.*, 2012; Hunt *et al.*, 2014; Nwachukwu *et al.*, 2014; Elson *et al.*, 2015; Kley, 2020), meaning that patients may be more familiar with the principle of a knee replacement compared to knee realignment. This speculation is supported by the few participants in the present study who spoke in terms of being presented with patients who “expected to be offered a knee replacement” (S14) and therefore needing patients to “buy-in” (S6) to the prospect of an HTO.

Differences emerged between participants in relation to the technique used for HTO. The most referenced operative difference related to the inclusion of graft materials during surgery, and whether it was subsequently necessary to remove the internal fixation plate. Participants mostly reported performing HTO with either no graft, or with auto- or allogenous materials, which mirrors the controversy among the myriad literature on the subject (Han *et al.*, 2015; Lash *et al.*, 2015; Slevin *et al.*, 2016; van Heerwaarden *et al.*, 2018). Multiple studies have demonstrated significantly improved clinical outcomes after HTO both with and without graft materials (Salzmann *et al.*, 2009; Zorzi *et al.*, 2011; Han *et al.*, 2015), leading to no clear consensus on one option being preferable to another. However, there is some evidence to suggest that the inclusion of graft materials leads to a biomechanically stronger construct than HTO without grafting, which may be favourable during the initial recovery period (Takeuchi *et al.*, 2010; Belsey *et al.*, 2019a; Belsey *et al.*, 2019b). Regarding types of graft material, recent systematic reviews tend to agree that synthetic graft materials are less favourable than auto- and allografts, which may explain the prevalent use of the latter two over the former among surgeons in the present study (Lash *et al.*, 2015; Slevin *et al.*, 2016).

8.5.2 Post-operative milestones

With the exceptions of time spent on crutches (6 weeks), return to driving a car (4-6 weeks), return to laborious jobs (8-12 weeks), and time of plate removal (12-18 months), there was little agreement between participants pertaining to the times at which they expected patients to achieve various post-operative recovery milestones. Firstly, concerning the areas of agreement between participants, a recent systematic review and meta-analysis showed that full weightbearing after HTO was safe and possible 2-8 weeks after surgery (Lee, Ahn and Lee, 2017). The literature tends to show that plate removal is appropriate 12-18 months after surgery (Brinkman *et al.*, 2008; Goshima *et al.*, 2019), which is largely in line with the information given by participants in the present study. Research is lacking regarding a return to driving a car after HTO. Multiple studies have reported that return to work that requires heavy labour varies from 13-22 weeks after HTO (Schröter *et al.*, 2013; Faschingbauer *et al.*, 2015; Agarwalla *et al.*, 2019). This is longer than the 8-12 weeks range offered by almost all participants (n=13) in the present study; perhaps suggesting an underestimation being provided to patients of more labour-intensive jobs. Regarding sedentary jobs, opinion was evenly split among participants with 5 suggesting a return to work after 2 weeks, and 7 participants suggesting 4-6 weeks. Previous research demonstrated that a return to low-intensity jobs ranged widely from 4-12 weeks after HTO (Schröter *et al.*, 2013; Faschingbauer *et al.*, 2015; Agarwalla *et al.*, 2019), which was more in line with the latter group of participants in the present study.

Time until a return to physical activity was a source of controversy among participants in the present study. Two surgeons suggested 4 months were needed before patients can return to normal activity; three suggested this typically occurred after 6 months; a further three referred to 8-12 months; and a final participant suggested a normal return to activity could be expected after 18 months. A limited number of studies have reported on return to physical activity within the first 6 months after HTO, which makes comparison to the present study somewhat difficult. However, studies have shown that activity levels (according to the Tegner activity scale) had returned to pre-operative levels 6 months after surgery (Nerhus *et al.*, 2017; Kim *et al.*, 2018). Two studies observed a decrease in activity levels versus pre-operative Tegner scores at 3 months post-HTO (Krych *et al.*, 2017; Nerhus *et al.*, 2017) but Kim *et al.* (2018) observed a slight increase. Many studies have demonstrated that patients tended to have achieved an activity level at least equal to their pre-operative status 12 months after surgery (Bastard *et al.*, 2017; Krych *et al.*, 2017; Nerhus *et al.*, 2017). This suggests that a return to normal activity after HTO is possible within 3 months but should not necessarily be expected until at least 6 months post-operatively. The present study showed that most surgeons expected their patients to have fully recovered from the osteotomy within 6-12 months after surgery. Considering that previous research demonstrated that bony union typically occurred 3-9 months post-operatively (Han *et al.*, 2015; Lash *et al.*, 2015), and a return to pre-operative activity levels was likely from 6 months onwards (Bastard *et al.*, 2017; Krych *et al.*, 2017; Nerhus *et al.*, 2017), the findings of the present study around recovery times were broadly in line with the literature.

An emergent trend was that surgeons largely viewed HTO as a pain-reducing procedure rather one that allows patients to be normally pain-free once recovered. This is supported by the literature, in which the overwhelming consensus is that HTO significantly reduces the symptoms of painful knee osteoarthritis (Brouwer *et al.*, 2014; Slevin *et al.*, 2016; Webb, Dewan and Elson, 2018; Kunze *et al.*, 2019). The present study also showed agreement that an increase in pain may be experienced by patients during participation in high-impact physical activities. Studies tend to show a pre- to post-HTO change in the type of activity performed by patients with a propensity for a shift from high- to low-impact activities being common (Faschingbauer *et al.*, 2015; Hoorntje *et al.*, 2017). It could, therefore, be concluded that the change in participation from high- to low-intensity activities post-operatively may be a consequence of an increased risk of knee pain during higher-impact activities. However, Bonnin *et al.* (2013) found motivation to significantly influence post-operative participation in high-impact sports where 66% of motivated patients participated in high-impact sports after HTO compared to 28% of unmotivated patients. Furthermore, several studies have speculated that advice from surgeons to patients not to participate in high-impact activities after HTO is likely to be a contributing factor to the observed post-operative change in activity participation (Salzmann *et al.*, 2009; Faschingbauer *et al.*, 2015; Kim *et al.*, 2018). Consequently, in order to determine the accuracy of surgeons warning patients about increased pain during high-impact activity, further research is needed to ascertain the extent to which pain contributes to the observed change in activity participation compared with other variables such as motivation and the surgeon's own advice. This is particularly relevant considering the results of a recent study, which demonstrated no difference in the progression of osteoarthritic symptoms between runners and non-runners who were over the age of 50 years (Lo *et al.*, 2018). In fact, running was associated with improved knee pain and was recommended as an activity not to be discouraged in people with knee osteoarthritis.

The results of the present study showed that follow-up appointments between the surgeons and their patients usually occurred at 6 weeks, 3 months, and 12 months after surgery, with the option of a 6 month consultation if required. The frequency of surgeon-patient contact appears to coincide with numerous significant recovery milestones as noted in the literature. As discussed, 6 weeks is consistent with the time that patients can often begin to transition to full weightbearing without crutches (Lee, Ahn and Lee, 2017). It also allows an opportunity for radiographs to be taken to monitor the progress of the healing osteotomy and the maintenance of the correction (Spahn, Kirschbaum and Kahl, 2006; Weil *et al.*, 2014; Schröter *et al.*, 2017). 3 months is often the minimum time for bony union to have occurred, and is therefore an appropriate time to evaluate the progress of the healing (Han *et al.*, 2015; Lash *et al.*, 2015). As will be discussed in the next section, 12 months is generally the minimum time post-operatively that the removal of the plate should be considered (Lind-Hansen *et al.*, 2016; Goshima *et al.*, 2019). Hence, it fits that the present study showed that most participants reported meeting with patients at this timepoint.

8.5.3 Plate removal

All participants agreed that the removal of the internal plate fixator was required in cases where patients experienced irritation or pain caused by the plate. Otherwise, opposing practices were reported with some surgeons routinely removing plates – often citing anecdotal experience of patients noticing a further "incremental gain" (S1) afterwards – and other surgeons intending for the plate to remain in-situ with removal only occurring if necessary due to pain, as mentioned above.

A possible link between plate removal and a further improvement in clinical outcomes has been proposed in previous research, although is mostly speculative and supported by a very limited number of available studies (Niemeyer *et al.*, 2010; Bode *et al.*, 2015; Goshima *et al.*, 2019). Previously reported studies that investigated the impact or necessity of plate removal after HTO are lacking, which may explain the lack of consensus observed among participants in the present study. Where plate removal has been noted in the literature, it was normally cited as having been a response to irritation or plate-related pain (Aryee *et al.*, 2008; Niemeyer *et al.*, 2010; Ghinelli *et al.*, 2016). However, there are also some reports that cite plate removal as a routinely performed procedure, irrespective of plate-related complications (Lind-Hansen *et al.*, 2016; Pagkalos *et al.*, 2018; Kanto *et al.*, 2020). It has been suggested that plate removal should not be performed until at least 18 months after osteotomy to avoid loss of correction (Aryee *et al.*, 2008; Brinkman *et al.*, 2008). Conversely, more recent research showed that plates can be safely removed sooner (12-16 months after HTO) without loss of correction provided that at least 50% of the posterior cortex of the osteotomy gap has achieved bony union (Lind-Hansen *et al.*, 2016; Goshima *et al.*, 2019). A further recent study found that 69% of patients expected an additional improvement in outcome after plate removal and that 82% of patients opted to have the plate removed as soon as possible after surgery (Grünwald *et al.*, 2018). Given that patients aspire to have the plate eventually removed due to an assumed subsequent improvement in outcome, and that attitudes greatly varied among surgeons in the present study in reference to plate removal – possibly compounded by the lack of research focus in this area – further investigation into the effects of plate removal after HTO is needed.

8.5.4 Patient education

The present study showed that pre-operative patient education about the pre-, intra-, and post-operative procedures related to HTO and the subsequent recovery were a prominent trend among surgeons. The attention given towards patient education prior to surgery is deemed essential (for ethical purposes) since it is necessary to ensure that patients are capable of providing informed consent to undergo a procedure (McDonald *et al.*, 2014). The present study demonstrated that another purpose of pre-operative patient education is to highlight the personal responsibility that patients have regarding factors such as post-operative pain management. This has been noted as something that is more prevalent in modern times due to less time spent in hospital and a possible lack of nursing or therapeutic resources (Johansson *et al.*, 2005). There is also some evidence that patient education itself reduces the length of time spent in hospital after surgery and decreases anxiety both pre- and post-operatively (Johansson *et al.*, 2005; Louw *et al.*, 2013; McDonald *et al.*, 2014).

Some findings have shown that anxiety levels may be positively correlated with post-operative pain, although this remains controversial (Louw *et al.*, 2013; McDonald *et al.*, 2014). A comprehensive systematic review of patient education protocols for knee and hip arthroplasty patients reported that protocols comprised a combination of 21 different factors (Table 8.3) as found in previously published literature (Louw *et al.*, 2013). All 21 factors featured regularly in the interviews conducted for the present study, suggesting that patient education for osteotomy patients was at least as comprehensive as that for more commonly performed procedures such as joint arthroplasties. Previous publications have suggested that patient education should take multiple forms because a single format (for example a written booklet) does not account for the varied and preferred learning styles of individual patients (Johansson *et al.*, 2005; Kruzik, 2009; De Achaval *et al.*, 2012). In addition to the transfer of information orally between surgeons and patients, references to information booklets, pictures, videos, and websites were frequent in the present study, suggesting that surgeons were taking a multi-dimensional approach to patient education.

Table 8.3: *List of topics (n=21) covered during pre-operative patient education sessions (Louw et al., 2013)**

Activity of daily living
Advice from past patients
Anaesthesia and medication
Anatomy of normal joints
Complications
Discussion of stressful scenarios associated with surgery (pain, mobility, noises)
Frequently asked questions
Hospital stay
Medical and support staff (and their roles)
Milestones
Mobility (time on crutches, bed mobility, transfers)
Movements to avoid
Pain education (pain overview, pain management, pain communication)
Pathoanatomy of arthritic joints
Post-operative procedures
Posture
Preadmission procedures
Preparation procedures for surgery
Range of motion
Reassurance
Surgical procedure

*systematic review of hip and knee arthroplasty patients

8.5.5 Managing expectations

The accuracy of patients' pre-operative expectations of their post-operative outcome is positively correlated with quality of life and satisfaction with the procedure (Mancuso *et al.*, 2001; Noble *et al.*, 2006; Zhou *et al.*, 2017). Therefore, the large focus on patient education related to managing expectations that was found in the present study was unsurprising. Initial patient expectations vary depending on factors such as diagnosis, patient characteristics, and functional status (Mancuso *et al.*, 2001; Feucht *et al.*, 2016; Grünwald *et al.*, 2018). In general, patients have been found to have high expectations of their surgical outcome and tend to underestimate the time for a full recovery, and overestimate the reduction in pain and physical activity ability they eventually experience (Cross *et al.*, 2009; Mannion *et al.*, 2009; Rossi *et al.*, 2015).

Surgeons have been shown to be better predictors of post-operative outcomes than patients but they still underestimate post-operative knee pain and overestimate post-operative function (Rosenberger *et al.*, 2005). This highlights the importance of effective patient education to accurately moderate expectations to improve overall patient satisfaction with the outcome (Noble *et al.*, 2006). With the exception of one osteotomy study (Grünwald *et al.*, 2018), most research into patient expectations for knee surgery was conducted with patients who underwent arthroplasty, cruciate ligament reconstruction, or meniscal surgery. Similar research involving osteotomy patients is limited and therefore warranted. Regarding the results of the present study, participants largely reported sharing information with patients that was in line with the literature, as discussed above. However, certain areas of disagreement that arose between participants appeared to be associated with a lack of available literature, or a lack of consensus within the literature, on a given subject. This suggests that further research into the highlighted areas of disagreement among surgeons could provide greater clarity, which would then increase the level to which physicians are able to accurately manage patient expectations and improve overall satisfaction with HTO.

8.5.6 Strengths and limitations

A strength of this study is that it included participants who perform a large volume of HTO relative to their respective countries, meaning the information shared during interviews was based on highly experienced practitioners. Furthermore, participants originated from 3 different countries with practices spanning 3 European countries and 1 Asian country, suggesting that the results of the study were not necessarily only representative of a single population. Another strength of this study was that it was the first to present qualitative findings from the perspective of osteotomy surgeons. It provided an opportunity to identify areas of controversy concerning patient management and has uniquely highlighted areas of required future research, which may not have been as readily apparent through more typical quantitative studies.

This study also had several limitations. The number of participants was limited by the point of data saturation. This point was reached after 14 interviews; however the small sample size may be somewhat offset by the inclusion of the highly experienced, high volume osteotomy surgeons that participated. Results may have been affected by recall bias since information pertaining to patient management and general practice was collected through interviews rather than being observed during consultations with patients. Social desirability bias may also have been a factor that perhaps led to potential exaggeration or omission of certain events or experiences during interviews.

8.5.7 Recommendations for future research

Generally, areas of controversy among surgeons corresponded with either a lack of consensus in the published literature or limited-to-no related publications from which to draw firm conclusions. This study showed that the use of allograft wedges varies between institutions and individuals, and is contingent on the potential costs – both surgical and financial – of the harvesting and acquiring of bone grafts, as well as whether a bone bank is readily available to a surgeon or hospital (Amendola and Panarella, 2005; Jung *et al.*, 2010; Hung and Noi, 2012). Therefore, in addition to providing further insight into the use of graft materials during HTO, future research needs to investigate methods on how to optimise and improve outcomes for patients in whom the osteotomy gap is left unfilled. Meanwhile, research on how to increase the availability of access to, and reduce the cost of, graft materials must be conducted.

Research is also required into the types of physical activities patients can return to after surgery – particularly within the first 6 months after surgery – as well as potential factors other than the surgery that may impact post-operative activity participation. Understanding these areas would likely increase agreement among surgeons and enhance the consistency of information being provided to patients, thereby further improving the accuracy of their expectations. This would lead to improvements in patient satisfaction and the overall clinical outcome of osteotomy surgery.

8.6 Conclusion

Information provided to prospective patients by their surgeons is comprehensive and primarily focused on the peri-operative period and the management of patient expectations for the first 3-6 months of recovery. After this point, contact between the patient and surgeon – and the amount of information provided to patients – is reduced. There were many areas of agreement among surgeons regarding the importance of patient education and expectation management. Areas of agreement such as the pain-reducing effect of HTO and indications for surgery largely coincided with a clear consensus in the available scientific literature. However, timelines for a return to work (for high- and low-intensity jobs) appeared to be underestimated compared to the published literature. Areas of controversy among surgeons included operative technique, the necessity for plate removal, and the average timelines for various post-operative milestones to be achieved. This thesis will now seek to address these issues in the next chapter.

CHAPTER 9 – PAIN AND PHYSICAL ACTIVITY IN THE FIRST 12 MONTHS AFTER HIGH TIBIAL OSTEOTOMY

9.1 Abstract

Background: HTO is a procedure that is normally appropriate for active individuals. The largest improvement in physical activity after surgery appears to occur by the end of the first post-operative year. However, little is known about the specific rate and time at which patients return to different activities within that recovery period. The purpose of this study was to investigate changes in pain and physical activity within the first 12 months after surgery.

Methods: 29 patients (mean age at surgery 49.7 ± 6.7 years; 17 males) participated in this retrospective multicentre, multi-surgeon study. Participants completed questionnaires (VAS pain, Tegner, and a non-validated activity participation questionnaire) pertaining to their status pre-operatively and 1 week, 1 month, 3 months, 6 months, and 12 months post-operatively, at a mean 52.3 ± 29.2 months after surgery.

Results: Pain was significantly reduced compared to pre-operative levels (median 7.0; IQR 4.0-8.3) at 3 months (median 2.5; IQR 1.0-6.3), 6 months (median 2.0; IQR 0.8-3.8), and 12 months (median 0.5; IQR 0.0-1.5) after surgery. Physical activity was significantly reduced 1 week (median 0.0; IQR 0.0-1.0) and 1 month (median 1.0; IQR 1.0-2.5) after surgery compared to pre-operative levels (median 4.0; IQR 2.0-4.0). A return to baseline activity levels was observed at 3 and 6 months, and a significant increase in activity was observed at 12 months (4.0; IQR 3.0-4.5). Most activities at 3 months, and all activities at 12 months, had increased participation rates compared to pre-operative levels. The highest participation rates were seen in "activities of daily living" and "low-impact activities".

Conclusion: 3 months after HTO was the point at which the first significant reduction in pain, and a return to pre-operative activity levels, was observed. This was also the point at which participation rates for most activities, including return to work, was possible at an equal or greater level than pre-operatively. Participation in high-impact activities was possible within 6 months after surgery.

9.2 Introduction

This thesis has stated many times that HTO is traditionally indicated in patients who are under the age of 65 years and physically active (Amendola and Bonasia, 2010; Wolcott, Traub and Efird, 2010; Kunze *et al.*, 2019). A number of recent systematic reviews and meta-analyses, each with a mean follow-up of around 5 years, have shown that approximately 80% of patients treated with HTO were able to return to a level of physical activity at least equal to their pre-operative status (Ekhtiari *et al.*, 2016; Hoorntje *et al.*, 2017; Kunze *et al.*, 2019). Similar positive results regarding return to physical activity after surgery have been demonstrated with a follow-up of 2 years (Faschingbauer *et al.*, 2015; Cotic *et al.*, 2015; Krych *et al.*, 2017; Nerhus *et al.*, 2017; Kim *et al.*, 2018), 1 year (Brinkman *et al.*, 2010; Schröter *et al.*, 2011; Bastard *et al.*, 2017; Krych *et al.*, 2017; Nerhus *et al.*, 2017; Kim *et al.*, 2018), 6 months (Brinkman *et al.*, 2010; Nerhus *et al.*, 2017; Kim *et al.*, 2018), and 3 months after surgery (Kim *et al.*, 2018).

Using the validated Tegner scale as a measure of physical activity levels (Tegner and Lysholm, 1985), several studies have demonstrated that activity tended to increase over the first 12 months after HTO, compared to pre-operative levels, but did not significantly change in the second post-operative year (Krych *et al.*, 2017; Nerhus *et al.*, 2017; Kim *et al.*, 2018). Krych *et al.* (2017) also followed up their cohort 5 years after HTO and showed no further significant change in activity levels from the 1 and 2 year Tegner scores. This suggests that the largest improvements in patient physical activity levels can be expected within the first year after surgery and that it is maintained for at least a further 4 years.

The use of the Tegner score as a method of assessing return to physical activity after HTO does not provide an insight into any changes in the number or type of physical activities performed that may occur during the post-operative recovery period. Some findings demonstrate a tendency towards participation in low-impact activities (e.g. swimming, cycling, etc) and fewer overall sessions of physical activity per week after HTO (Noyes, Barber and Simon, 1993; Bonnin *et al.*, 2013; Faschingbauer *et al.*, 2015; Hoorntje *et al.*, 2017; Kim *et al.*, 2018). Conversely, other research has found that patients equalled (Salzmann *et al.*, 2009; Saragaglia *et al.*, 2014) or increased the number of post-operative weekly sessions of activity (Cotic *et al.*, 2015), and demonstrated an increase in high-impact activity participation compared to pre-operative levels (Bastard *et al.*, 2017).

The literature supports the notion that patients are able to return to physical activity after HTO (Ekhtiari *et al.*, 2016; Hoorntje *et al.*, 2017; Kunze *et al.*, 2019), but it is not clear how long it takes patients to return to different types of activity. One study based at a single institution anecdotally described that the authors observed patients returning to low-impact activities after 3-4 months but that it took at least 6 months to return to high-impact activities such as running (Aalderink, Shaffer and Amendola, 2010). Since those claims were anecdotal, further research would confirm them, but no study has yet attempted to do so. Somewhat in support of the abovementioned observations by Aalderink *et al.* (2010), the previous chapter of this thesis found that the first 6 post-operative months appeared to be the most significant in terms of the amount of progress made in improvement of knee pain and function. It concluded that a research focus particularly on that first 6 month period, regarding timelines to achieve post-operative milestones, would be beneficial to improve the accuracy of the information given to patients by surgeons, thereby helping to manage patient expectations.

Similar to the reported findings regarding return to activity after HTO, reported pain is significantly reduced in the short- (Takeuchi *et al.*, 2008; Pongsoipetch and Tantikul, 2009; Hernigou *et al.*, 2013; Faschingbauer *et al.*, 2015; Cotic *et al.*, 2015; Ghinelli *et al.*, 2016; Saier *et al.*, 2017) and mid-term after surgery (Dowd, Somayaji and Uthukuri 2006; Kohn *et al.*, 2013; Bonasia *et al.*, 2014; Bode *et al.*, 2015; Hohloch *et al.*, 2017). Although not explicitly examined, much of the literature suggests a negative correlation between pain and physical activity after HTO (Brinkman *et al.*, 2010; Cotic *et al.*, 2015; Nerhus *et al.*, 2017; Kim *et al.*, 2018). However, other studies have reported a significant reduction in pain after surgery but no increase in physical activity (Salzmann *et al.*, 2009; Kunze *et al.*, 2019), which implies that one factor does not necessarily equal the other, only that they are associated. The suggestion that knee pain and physical activity may be negatively correlated in HTO patients is supported by studies that reported a similar phenomenon in patients who underwent anterior cruciate ligament reconstruction (Bigouette *et al.*, 2019; Hart *et al.*, 2020).

HTO is a procedure that is normally appropriate for active individuals (Kunze *et al.*, 2019) and the largest improvement in return to physical activity after surgery appears to occur by the end of the first post-operative year (Krych *et al.*, 2017; Nerhus *et al.*, 2017; Kim *et al.*, 2018). However, little is known about the specific rate and time at which patients return to different physical activities within that recovery period. Therefore, the creation of a timeline demonstrating the normal progression of activity participation rates, including the type of activity performed, would be useful. This would help clinicians to more accurately manage the expectations of patients, which have previously been shown to vary greatly pertaining to post-operative physical activity ability and expected pain during different activities (Ekhtiari *et al.*, 2016; Grünwald *et al.*, 2018).

The purpose of the present study was to investigate the changes in pain and physical activity levels, as well as in the type of activity performed, at regular intervals within the first

12 months after surgery. Additionally, this study aimed to create a return-to-activity timeline that would highlight key milestones during the first 12 months after HTO, which can be used to help improve the management of patient expectations in the future.

9.3 Methods

9.3.1 Participants and study design

29 patients (mean age at surgery 49.7 ± 6.7 years; 17 males) who underwent medial opening-wedge HTO between 2011 and 2018 volunteered to participate in this retrospective multicentre, multi-surgeon study. Patients were eligible to participate if they underwent HTO for varus osteoarthritis of the knee with no simultaneous procedure conducted (except arthroscopy, which was performed in 14 patients [48%]). Eligible patients were identified from a prospectively maintained database of osteotomy patients, which is stored at a single institution. Participants were contacted through the post at a mean 52.3 ± 29.2 months after surgery and were asked to complete a series of questionnaires to estimate their pain and activity levels 1 week pre-operatively as well as 1 week, 1 month, 3 months, 6 months, and 12 months post-operatively. Ethical approval for this study was granted by the University of Winchester institutional review board (Appendix H).

9.3.2 Operative technique

Medial opening-wedge HTO was performed under general anaesthesia by one of three experienced orthopaedic surgeons following a previously described standard protocol (Staubli *et al.*, 2003). Femoral head allograft bone wedges were inserted into 13 osteotomies (45%) and no augmentation was used in the remaining 16 patients. The osteotomy was fixed with a standard Tomofix plate (*n*=21), a size 2 ActivMotion plate (*n*=6), or a PEEKpower plate (*n*=2). 22 patients (76%) had their fixation plates removed at the time of survey. Of these patients, 8 (36%) had their plate removed within the first 12 months after surgery.

9.3.3 Outcome measures

Pain, activity levels, and activity type performed at each time period were recorded retrospectively through the use of a Visual Analogue Scale (VAS) for pain, a Tegner activity score, and a non-validated activity participation questionnaire (APQ; Appendix H). Participants completed a new, blank version of each questionnaire to report their pain, activity levels, and activity type at each time period (pre-op, and 1 week, 1 month, 3 months, 6 months, 12 months post-op). The VAS is a valid and commonly used measure to report the pain experienced after HTO (Brouwer *et al.*, 2007). Patients were asked to draw a horizontal line that intersected with the scale – a 10 cm vertical line where the bottom equalled “No pain” and the top equalled “The worst imaginable pain” – to indicate the amount of pain (out of 10) experienced at each time period.

The Tegner activity score has been validated for clinical use (Tegner and Lysholm, 1985; Zahiri *et al.*, 1998) and a recent systematic review and meta-analysis of return to sport after HTO found it to be the most commonly used method of reporting changes in physical activity (Kunze *et al.*, 2019). It consists of a 10-point scale where 0 indicates that the user is on sick leave because of their knee issue, while 10 indicates that the user plays competitive football or rugby at the national or international level. Numbers 1-9 on the Tegner score are similarly accompanied by indicative activities, and activity intensities, which increase with the numbers according to the stresses they would exert on the knee and body.

The APQ was created for the purposes of the present study to track the participation of patients in individual activities and to allow for a more detailed report of the return to specific daily and sporting activities. The questionnaire consisted of a list of activities with a single checkbox next to each one. The list was created from, and ordered according to, those that appear on the Tegner scale. Patients were asked to indicate as many of the activities that they participated in at each time period by marking the corresponding checkbox. There was also an option at the bottom of the APQ for the user to add any “Other” activities that they performed but did not otherwise appear in the activity list. Activities were categorised according to whether they were “Activities of daily living”, “Low-impact activities”, or “High-impact activities”. High- and low-impact activities were determined following the precedent borne out in the literature of similar activities being categorised in the same way (Bonnin *et al.*, 2013; Faschingbauer *et al.*, 2015).

9.3.4 Data analysis

Histograms were first used to determine whether data were normally distributed. Analysis of variance with repeated measures was performed to detect significant differences in the mean number of activities performed at each measurement period. A post-hoc Bonferroni correction was performed to allow for pairwise comparisons between the individual measurement periods. The most performed activities were noted at each measurement period were recorded.

A Friedman test was performed to detect differences in VAS and Tegner scores between each time point. Where significant differences were detected, Wilcoxon tests were performed post-hoc. A Mann-Whitney *U* test was performed to check for differences in the VAS and Tegner scores at each time point between males and females; the use of a bone graft during surgery; and those patients who underwent simultaneous arthroscopy versus those that did not.

A Spearman corrleation (r_s) was calculated to determine any significant associations between the VAS and Tegner scores as well as between the demographic variables and surgical outcome. Statistical significance was set at $p < 0.05$ and all statistical analyses were conducted using IBM SPSS Statistics 25 (IBM Corporation, Armok, New York, USA).

9.4 Results

9.4.1 VAS and Tegner scores

The operative and demographic information of the participants at the time of surgery can be found in Table 9.1 and the mean VAS and Tegner scores for each measurement period can be found in Table 9.2. Pain was increased during the first week after surgery (Z = -1.60; $p = 0.11$) but had decreased by 1 month (Z = -1.46; $p = 0.14$), although neither change was significant compared to pre-operative levels. Pain was significantly reduced compared to pre-operative levels at 3 months (Z = -3.56; $p < 0.01$), 6 months (Z = -4.26; $p < 0.01$), and 12 months (Z = -4.51; $p < 0.01$; Table 9.2). Over time, pain was significantly reduced at each measurement period ($p < 0.01$) apart from the difference between reported pain pre-operatively and 1 week after surgery where no significant change was detected.

Physical activity was significantly reduced 1 week (Z = -4.50; $p < 0.01$) and 1 month (Z = -3.49; $p < 0.01$) after surgery compared to pre-operative levels but a return to baseline activity levels was observed at 3 months (Z = -0.50; $p = 0.62$) and 6 months (Z = -1.11; $p = 0.27$; Table 9.2). Physical activity levels significantly decreased ($p < 0.01$) over time at 1 week and 1 month (Z = -4.01; $p < 0.01$) post-operatively but then significantly increased by 3 months (Z = -4.47; $p < 0.01$). Significant increases in physical activity then continued at 6 months (Z = -2.20; $p = 0.03$) and 12 months (Z = -2.88; $p < 0.01$). Tegner scores at 3 and 6 months (median 3.0, IQR 2.0-4.0; and 4.0, IQR 2.5-4.0, respectively) were not significantly different than the pre-operative value (median 4.0, IQR 2.0-4.0), but the difference at 12 months was significant according to the Wilcoxon signed rank test (median 4.0, IQR 3.0-4.5; Z = -2.66; $p = 0.008$). Pain and physical activity levels showed a moderate to strong negative correlation at each measurement period, according to Spearman's correlation. All VAS-Tegner correlations were statistically significant (Table 9.2).

Table 9.1: *Baseline demographics and operative information*

Characteristic	**Total (mean ± SD)**
Participants (*n*)	29
Age (y)	49.7 ± 6.7
Sex (male:female)	17:12
Body Mass Index (kg/m^2)	29.1 ± 6.6
Smoker? (yes:no)	1:28
Follow-up (months)	52.3 ± 29.2
Operated knee (right:left)	14:15
Gap size (mm)	8.6 ± 3.5
Allograft bone wedge (yes:no)	13:16
No. of plates removed (*n*)	22
Time of plate removal (months)	15.2 ± 5.9

Table 9.2: *Pain and physical activity scores*

Measurement period	**VAS (median [IQR])**	**Tegner (median [IQR])**	**VAS-Tegner correlation (Spearman's r_s; p-value)**
1 day pre-op	7.0 [4.0-8.3]	4.0 [2.0-4.0]	-0.44; 0.018
1 week post-op	7.5 [5.0-9.0]	0.0 [0.0-1.0]*†	-0.49; 0.007
1 month post-op	5.0 [2.3-8.0]†	1.0 [1.0-2.5]*†	-0.59; 0.001
3 months post-op	2.5 [1.0-6.3]*†	3.0 [2.0-4.0]†	-0.56; 0.001
6 months post-op	2.0 [0.8-3.8]*†	4.0 [2.5-4.0]†	-0.56; 0.002
12 months post-op	0.5 [0.0-1.5]*†	4.0 [3.0-4.5]*†	-0.38; 0.044

Note: *significant difference versus pre-op value ($p < 0.05$)
†significant difference versus preceding measurement period ($p < 0.05$)
VAS = Visual Analogue Scale for Pain; IQR = Interquartile Range

The demographic variable of sex; the inclusion of a graft during surgery; and a simultaneous arthroscopy did not result in any significant between-subject effects ($p > 0.05$), however other trends were observed. Males had significantly higher median pre-operative Tegner scores (4.0, IQR 3.0-4.0; $U = 39.5$; $p < 0.01$) and significantly lower pre-operative VAS scores (6.0. IQR 3.0-8.0; $U = 57.0$; $p = 0.048$) compared to females (2.0, IQR 1.0-3.8 and 8.3, IQR 5.5-8.9, respectively; Figures 9.1 and 9.2). No significant post-operative differences between sexes were detected although males tended to remain more physically active than females at each measurement period ($p > 0.05$). No significant differences were detected between patients who underwent HTO with and without bone grafting (Figures 9.3 and 9.4) or between patients who underwent simultaneous arthroscopy versus those who did not.

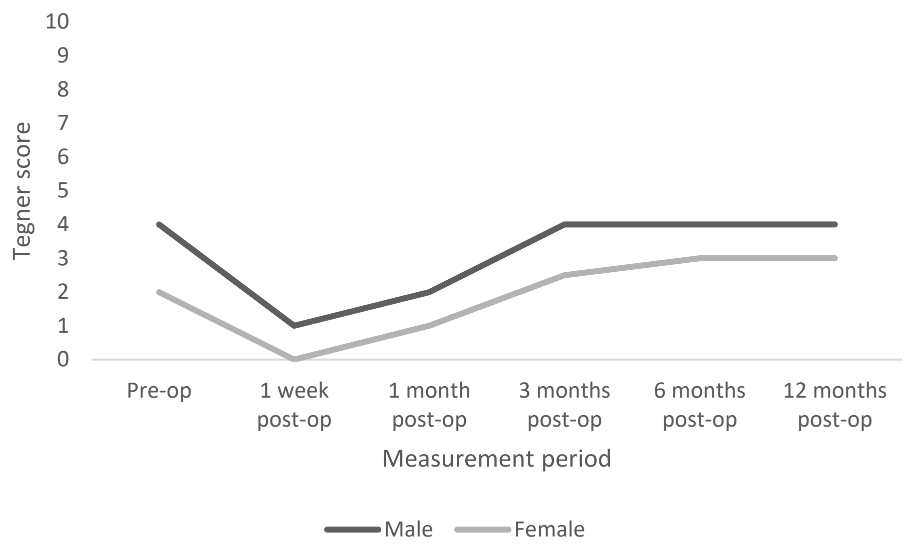

Figure 9.1: Median Tegner scores over time between sexes

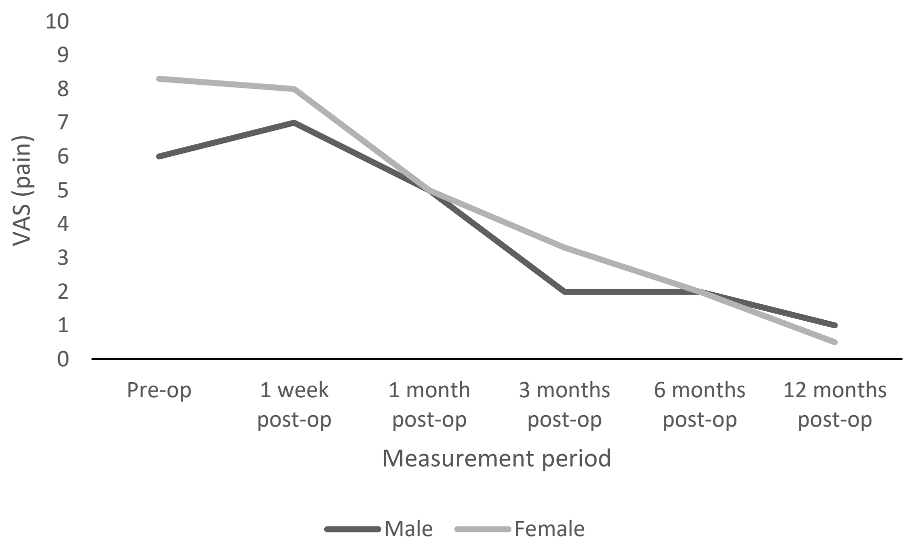

Figure 9.2: Median VAS scores over time between the sexes

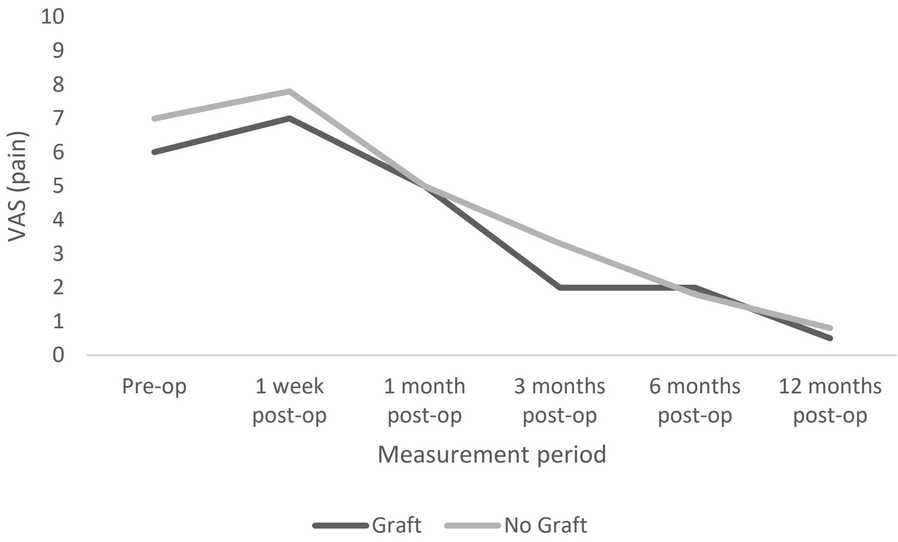

Figure 9.3: Median VAS scores over time between HTO with and without grafting

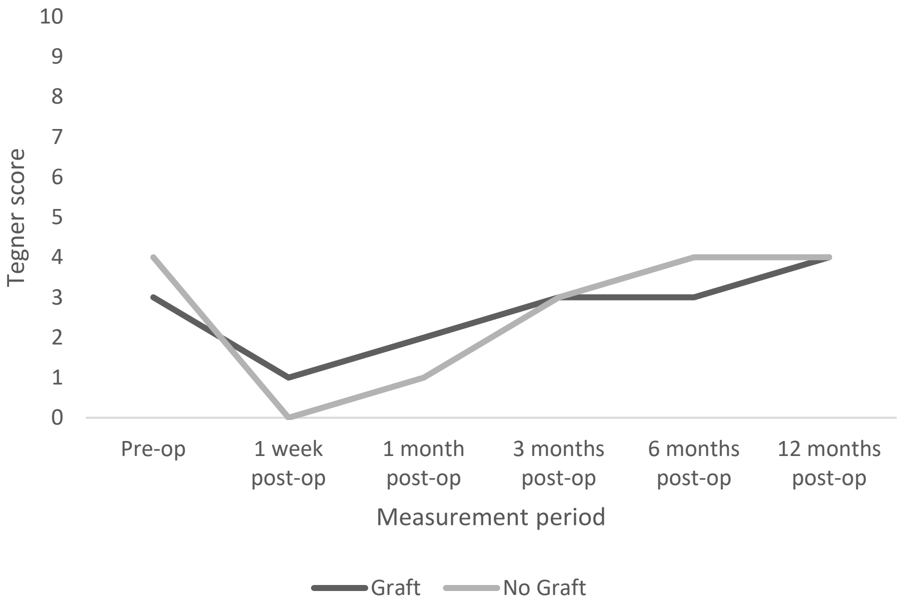

Figure 9.4: Median Tegner scores over time between HTO with and without grafting

9.4.2 Activity Participation Questionnaire

Pre-operatively, patients participated in a total of 15 different activities but this had increased to 20 activities by 12 months post-operatively (Table 9.3). The same number of "Activities of daily living" (*n*=9) and "Low-impact activities" (*n*=4) were performed pre-operatively and at 12 months after surgery. The number of “High-impact activities” performed increased from $n=3$ pre-operatively to $n=8$ post-operatively. Of the 5 activities that were not participated in pre-operatively, 2 patients were able to jog on uneven ground and 1 patient performed cross-country running 3 months after surgery. Participation in these two activities was further increased at 12 months ($n=4$ and $n=2$, respectively). No ball sports or racquet sports were performed pre-operatively, but two patients participated in each at 12 months post-HTO. The mean number of activities performed by each patient had surpassed pre-operative levels (6.0 ± 2.6) by 3 months post-operatively (6.9 ± 2.3) and continued to significantly increase ($p < 0.01$) at 6 months (8.6 ± 2.2) and 12 months (9.9 ± 2.4; Figure 9.5).

Table 9.5 shows the overall rate of participation in all activities pre-operatively versus each post-operative measurement period. One week after surgery 62.1% of patients were able to walk on even ground and approximately one third were able to climb stairs. One month after surgery, all participants who could walk on even ground pre-operatively were able to do so again. 100% of patients were able to walk on even ground within 3 months regardless of pre-operative ability. At 3 months after surgery, the participation rate of all “Activities of daily living” equalled or exceeded pre-operative levels. Similarly, all “low-impact activities” except for golf, and all “high-impact activities” except for downhill skiing, that were performed pre-operatively had participation rates that equalled or exceeded baseline levels by 3 months. A small number of patients reported being able to jog on uneven ground ($n=2$; 6.9%) and go cross country running ($n=1$; 3.5%), which were activities not performed by any patient pre-operatively. 6 months after surgery, the participation rate of all activities that were performed pre-operatively was equal to or greater than baseline levels; and had increased compared to 3 months after surgery. Regardless of pre-operative ability, all 29 patients were able to walk on even ground within 3 months, climb stairs within 6 months, and walk on uneven ground within 12 months post-operatively (Table 9.5). One patient was retired from work prior to undergoing HTO and therefore had no job to return to post-operatively. Excluding the retired patient, participants’ rate of work pre-operatively was 82.1%. Post-operatively, return to work was 10.7% after 1 week, 35.7% after 1 month, 82.1% after 3 months, 92.9% after 6 months, and 96.4% after 12 months.

Table 9.3: Type of activity and number of patients participating at each measurement period

Activity (*n*=20)	Pre-op	1 week post-op	1 month post-op	3 months post-op	6 months post-op	12 months post-op
Activities of daily living (n=8)						
Walking on even ground	26	18	**26**	29	29	29
Driving a car	26	0	9	**27**	28	28
Stair climbing	24	10	18	**26**	29	29
Work	23	3	10	**23**	26	27
Light domestic work	18	2	15	**24**	25	26
Walking on uneven ground	14	1	11	**22**	28	29
Kneeling	8	0	1	**8**	15	17
Heavy domestic work	7	0	1	**9**	18	23
Low impact activities (n=4)						
Cycling	11	1	5	**12**	16	17
Swimming	5	0	3	**6**	12	16
Golf	3	0	0	2	**4**	5
Yoga/Pilates	2	0	0	**2**	5	6
High impact activities (n=8)						
Jogging on even ground	2	0	1	**2**	4	11
Jumping	1	0	0	**2**	5	10
Downhill skiing	1	0	0	0	**1**	3
Jogging on uneven ground	0	0	0	**2**	1	4
Cross country running	0	0	0	**1**	1	2
Cross country skiing	0	0	0	0	**1**	1
Football/rugby	0	0	0	0	0	**2**
Tennis/badminton	0	0	0	0	0	**2**

Bold = point at which post-operative participation equalled or exceeded pre-operative participation

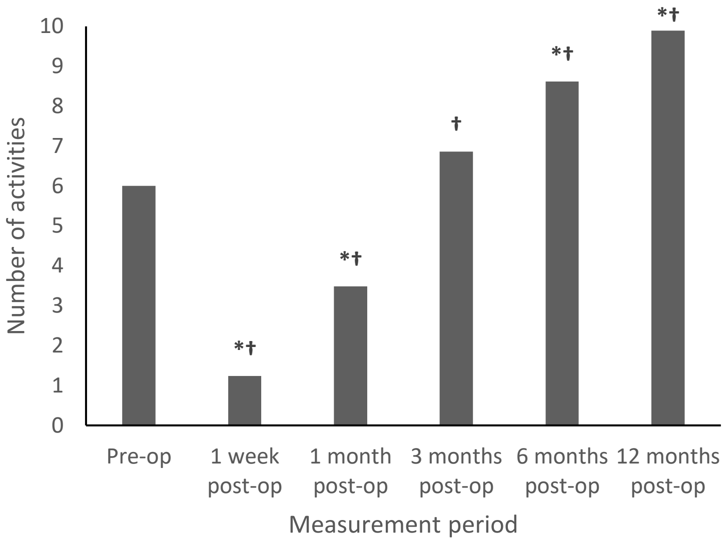

Figure 9.5: Mean number of activities performed by each patient.

**significant change vs. pre-op value (p < 0.01).*

†significant change vs. previous measurement period (p < 0.01).

Table 9.4: *Change in post-op activity participation versus pre-operatively (%)*

Activity (*n*=15)	**1 week**	**1 month**	**3 months**	**6 months**	**12 months**
Activities of daily living (n=8)					
Walking on even ground	-30.8	**0.0**	11.5	11.5	11.5
Stair climbing	-58.3	-25.0	**8.3**	20.8	20.8
Work	-87.0	-56.5	**0.0**	13.0	17.4
Light domestic work	-88.9	-16.7	**33.3**	38.9	44.4
Walking on uneven ground	-92.9	-21.4	**57.1**	100.0	107.1
Driving a car	-100.0	-65.4	**3.9**	7.7	7.7
Kneeling	-100.0	-87.5	**0.0**	87.5	112.5
Heavy domestic work	-100.0	-85.7	**28.6**	157.1	228.6
Low impact activities (n=4)					
Cycling	-90.9	-54.6	**9.1**	45.5	54.6
Swimming	-100.0	-40.0	**20.0**	140.0	220.0
Yoga/Pilates	-100.0	-100.0	**0.0**	150.0	200.0
Golf	-100.0	-100.0	-33.3	**33.3**	66.7
High impact activities (n=3)					
Jogging on even ground	-100.0	-50.0	**0.0**	100.0	450.0
Jumping	-100.0	-100.0	**100.0**	400.0	900.0
Downhill skiing	-100.0	-100.0	-100.0	**0.0**	200.0

Bold = point at which change in participation equalled or exceeded pre-operative levels

Table 9.5: *Overall rate of participation in physical activities before and after HTO (%)*

Activity (*n*=20)	**Pre-op**	**1 week**	**1 month**	**3 months**	**6 months**	**12 months**
Activities of daily living (n=8)						
Walking on even ground	89.7	62.1	**89.7**	100	100	100
Driving a car	89.7	0	31.0	**93.1**	96.6	96.6
Stair climbing	82.8	34.5	62.1	**89.7**	100	100
Work	79.3	10.3	34.5	**79.3**	89.7	93.1
Light domestic work	62.1	6.9	51.7	**82.8**	86.2	89.7
Walking on uneven ground	48.3	3.5	37.9	**75.9**	96.6	100
Kneeling	27.6	0	3.5	**27.6**	51.7	58.6
Heavy domestic work	24.1	0	3.5	**31.0**	62.1	79.3
Low impact activities (n=4)						
Cycling	37.9	3.5	17.2	**41.4**	55.2	58.6
Swimming	17.2	0	10.3	**20.7**	41.4	55.2
Golf	10.3	0	0	6.9	**13.8**	17.2
Yoga/Pilates	6.9	0	0	**6.9**	17.2	20.7
High impact activities (n=8)						
Jogging on even ground	6.9	0	3.5	**6.9**	13.8	37.9
Jumping	3.5	0	0	**6.9**	17.2	34.5
Downhill skiing	3.5	0	0	0	**3.5**	10.3
Jogging on uneven ground	0	0	0	**6.9**	3.5	13.8
Cross country running	0	0	0	**3.5**	3.5	6.9
Cross country skiing	0	0	0	0	**3.5**	3.5
Football/rugby	0	0	0	0	0	**6.9**
Tennis/badminton	0	0	0	0	0	**6.9**

Bold = the point at which activity participation equalled or exceeded pre-operative levels

9.5 Discussion

The present study showed that patients who underwent medial opening-wedge HTO experienced a significant reduction in pain and a return to pre-operative physical activity levels within 3 months of surgery. Pain continued to decrease significantly after 6 and 12 months, while activity levels and the number of activities performed increased. An increase in the number of high-impact activities such as jogging, skiing, racquet sports, and ball sports was observed at 12 months. Most activities at 3 months, and all activities at 12 months, had increased participation rates compared to pre-operative levels. A high participation rate (79-100%) 12 months after surgery in all "Activities of daily living" except for kneeling (58.6%) suggested that patients were largely able to perform activities that at least satisfied their daily needs after HTO. Regarding sporting activities, "Low-impact activities" tended to have higher participation rates (17-59%) than "High-impact activities" (3-38%). However, both categories had increased participation across all disciplines within 12 months after surgery compared to pre-operatively (increases of 7-38% and 0-7%, respectively). To my knowledge, this was the first study to investigate the interaction between pain and physical activity after HTO, and to observe the rate and time at which patients were able to return to different activities after surgery.

9.5.1 Pain and activity levels

One of the main aims of HTO is to relieve the symptoms of painful osteoarthritis. The present study showed that patients experienced a significant reduction in pain within 3 months of surgery, which continued to decline up to 12 months post-operatively. Similar patterns have previously been reported by Cotic *et al.* (2015), Saier *et al.* (2017) and Kim *et al.* (2018). Saier *et al.* (2017) reported a significantly lower VAS score at 6 weeks after HTO compared to pre-operative levels. A significant improvement in pain was observed between 1 and 3 months in the present study, which suggests a similar trend in findings. The reduction in pain at 6 weeks observed by Saier *et al.* (2017) was maintained after 3 months and then further reduced at 6 and 12 months after HTO, which was consistent with the results of the present study. Similar findings were presented by Kim *et al.* (2018) who reported a significant reduction in pain compared to pre-operative levels 3 months after surgery, followed by non-significant but consistently decreasing pain levels after 6 months and 12 months. The present study found a similar trend but with the addition of significant reductions in pain over time after 6 months and 12 months.

The literature tends to show that patients can return to pre-operative physical activity levels 12 months after HTO. Kim *et al.* (2018) found a gradual increase in Tegner scores at 3 months, 6 months, and 12 months compared to pre-operative levels: the difference was not deemed clinically important until 6 months after surgery. The authors defined a clinically important difference in Tegner score to be a change in 0.85 points. The present study similarly reported a gradual increase in Tegner scores from 3 months onwards but a clinically important difference, according to the parameters of Kim *et al.* (2018), was not observed. Contrary to the results of the present study, Bastard *et al.* (2017) reported identical mean Tegner scores pre-operatively and 12 months after HTO suggesting no increase in activity, only a return to pre-operative levels. Pre-operative Tegner scores in the Bastard *et al.* (2017) study referred to activity performed prior to the onset of pain that necessitated the need for the HTO. In comparison, pre-operative scores in the present study referred to the day before surgery, which may explain the difference in results. Krych *et al.* (2017) and Nerhus *et al.* (2017) both reported decreased Tegner scores 3 months after surgery but significantly increased scores after 12 months. Pre-operative Tegner scores were achieved 6 months after surgery in the Nerhus *et al.* (2017) study. Patients in both studies took longer to return to pre-operative levels of activity than in the present study, however this difference had disappeared by 12 months.

Overall, the general VAS and Tegner results of the present study largely agreed with the literature: pain was significantly reduced by HTO and a return to pre-operative activity levels within 12 months was observed. However, results varied regarding how early within the first post-operative year this occurred. A moderate negative correlation, which was statistically significant, was observed between VAS and Tegner scores. This confirmed the general trend in the literature where studies have reported, but not specifically examined the relationship between, the measured decrease in pain and increase in activity within the first year after surgery (Brinkman *et al.*, 2010; Cotic *et al.*, 2015; Nerhus *et al.*, 2017; Kim *et al.*, 2018).

9.5.2 Rates of participation

Activity participation was equal to, or greater than, pre-operative levels within 6 months after surgery. A study by Kim *et al.* (2018) reported a mean return to sport time of 8.4 months after HTO. The present study showed that more time was needed before patients participated in “high-impact activities” (6 months) compared to “low-impact activities” and “activities of daily living” (3 months). A previous paper similarly suggested that 3-4 months was needed for a return to low-impact activities, whereas ≥6 months was needed for a return to high-impact activities (Aalderink, Shaffer and Amendola, 2010). This was further supported by Kanto *et al.* (2020) who found that patients returned to high-impact activities at a mean 8.7 ± 2.7 months after surgery, which is similar to the findings in the present study. The type of activity performed was not taken into consideration by Kim *et al.* (2018) when reporting time to return to physical activity, which may explain the difference between their findings and those in the present study.

A significant increase in the mean number of activities performed per patient compared to pre-operative levels was observed from 6 months onwards. A wide range of post-operative rates of activity participation (65-97%) have previously been described (Noyes, Barber and Simon, 1993; Salzmann *et al.*, 2009; Bonnin *et al.*, 2013; Saragaglia *et al.*, 2014; Faschingbauer *et al.*, 2015; Cotic *et al.*, 2015; Bastard *et al.*, 2017; Kim *et al.*, 2018; Kunze *et al.*, 2019). An explanation for the large variance in the literature of post-operative activity participation was offered in the systematic review and meta-analysis by Hoorntje *et al.* (2017). They found that the pre-operative reference point – whether baseline scores represented pre-surgical or pre-symptomatic status – impacted the return to activity rates. A larger rate was reported among studies that used pre-surgical status (111%) versus pre-symptomatic status (85%) as a baseline (Hoorntje *et al*., 2017). This should be taken into consideration when comparing the results of the present study with other publications.

Contrary to the present study, some research has shown no significant change in the mean number of activities performed post-operatively (Salzmann *et al.*, 2009; Cotic *et al.*, 2015; Hoorntje *et al.*, 2017; Kim *et al.*, 2018), or has reported a significant decrease in the mean number of activities performed (Faschingbauer *et al.*, 2015). Bonnin *et al.* (2013) reported a 65.4% return to activity at a level equal to, or greater than, pre-operative levels. However, none of the aforementioned studies included activities of daily living (except walking and kneeling) in their analysis, and focused predominantly on sporting activities. This may have accounted for the difference in results compared to the present study. Furthermore, Kim *et al.* (2018) and Bonnin *et al.* (2013) reported rates of return to sport at 24 months and 50 months post-operatively, respectively, versus 12 months in the present study. It could be interpreted that activity participation is therefore not maintained over time. On the contrary, recent systematic reviews and meta-analyses –each with a mean follow-up of approximately 5 years – reported rates of return to activity of 76% (Kunze *et al.*, 2019), 91% (Ekhtiari *et al.*, 2016), and 94% (Hoorntje *et al.*, 2017). This implies that activity participation beyond 12 months after HTO is variable but, in fact, remains high in most cases.

The mean rate of participation at final follow-up in "high-impact activities" (15.1%) fell within the range of those (9-43%) that have been previously reported in the literature (Noyes, Barber and Simon, 1993; Bonnin *et al.*, 2013; Bastard *et al.*, 2017; Hoorntje *et al.*, 2017). The mean participation rate in "low-impact activities" (37.9%) was slightly lower than the range of rates (44-71%) that have previously been reported (Noyes, Barber and Simon, 1993; Bonnin *et al.*, 2013; Hoorntje *et al.*, 2017). The present study was the first to record rates of participation in various "activities of daily living". All activities within this category (except for kneeling) reported a participation rate at final follow-up of >79%. The low participation rate for kneeling (58.6%) may have been due to higher levels of discomfort compared with the other activities from within the same category (Bonnin *et al.*, 2013).

Studies tend to show that activity participation after HTO shifts from higher impact to lower impact activities (Noyes, Barber and Simon, 1993; Faschingbauer *et al.*, 2015; Hoorntje *et al.*, 2017; Kim *et al.*, 2018). Participation rates in the present study increased over time for all activities, regardless of impact, but the rates for "high-impact activities" were generally lower than for "low-impact activities, which in turn tended to be lower than those for "activities for daily living" (Cotic *et al.*, 2015). Similar to the present study, Bastard *et al.* (2017) found a higher participation rate in high-impact activities 12 months post-operatively (43%) compared to pre-operatively (37%). One other study observed no significant pre- to post-operative change in participation in high-impact activities at a mean 36 months after HTO (Salzmann *et al.*, 2009).

The abovementioned findings, paired with the general trend of a shift towards lower impact activities after surgery, suggest that HTO does not necessarily limit the ability for patients to be able to participate in high-impact activities post-operatively; rather that more patients choose to perform lower impact activities. This is supported by Bonnin *et al.* (2013) who showed that 28% of patients performed strenuous activities at a mean 4.2 years after HTO, which rose to 66% among patients who were motivated to perform such activities. The same study found that the operated knee was commonly the reason for a lack of participation in higher impact activities (except running and downhill skiing), although it did not state what the other reasons were (Bonnin *et al.*, 2013). Furthermore, it is thought that advice from surgeons not to participate in high-impact activities after HTO is another reason that explains the observed shift towards lower impact activities post-operatively (Noyes, Barber and Simon, 1993; Salzmann *et al.*, 2009; Faschingbauer *et al.*, 2015; Kim *et al.*, 2018). Again, this supports the notion that the trend in the literature towards a post-operative decrease in high-impact activities is not solely due to the osteotomy as a limiting factor.

9.5.3 Return to work

The rate at which participants were able to work pre-operatively was achieved within 3 months of HTO (82.1%). This further increased at 6 and 12 months where 96.4% of patients had returned to work. These findings are supported by recent systematic reviews and meta-analyses, which found similar rates of return to work (80.8% and 85%) at a mean 4.1 and 3.5 months after surgery, respectively (Hoorntje *et al.*, 2017; Kunze *et al.*, 2019). Ekhtiari *et al.* (2016) conducted another systematic review to assess return to work after HTO and found a similar post-operative rate (81.8%) but noted that only 62.8% of patients were able to return to work at an equal or greater level of physical demand. This is perhaps indicative of a similar pattern to the trends around return to physical activity, wherein post-operative participation remained high but a shift towards lower impact activities was observed (Hoorntje *et al.*, 2017). If this was the case then it is possible that factors other than the operated knee, such as motivation and surgeon's advice (Faschingbauer *et al.*, 2015; Kim *et al.*, 2018), may be confounding influences regarding return to work after HTO. Further research is needed to confirm this.

In the present study, over one third of patients had returned to work within one month of surgery. This rate continued to increase within the first post-operative year. The difference in time taken to return to work may be explained by previous studies, which found that more labour intensive jobs took longer to return to (around 4 months) than those with a lower work load (around 3 months) after HTO (Aalderink, Shaffer and Amendola, 2010; Faschingbauer *et al.*, 2015; Ekhtiari *et al.*, 2016; Hoorntje *et al.*, 2017). It was inferred from this that patients in the present study who returned to work 1 month after surgery were involved in jobs that were not as physically demanding as those who did not work until 3, 6, or 12 months post-operatively. The type of job that participants did was not recorded in the present study, so this is speculative.

9.5.4 Limitations

This study had several limitations. Firstly, it was a retrospective investigation which required patients to determine varying pain and activity levels within short intervals of time over the first post-operative year, which may have resulted in recall bias (Hassan, 2005; Mannion *et al.*, 2009). Secondly, sampling bias may have been an issue since a self-selecting convenience sample was used rather than a consecutive series of patients. Finally, a non-validated activity participation questionnaire was used to determine rates of participation in various activities.

However, activities listed on the questionnaire were not chosen randomly; they were taken from the validated Tegner activity scale (Tegner and Lysholm, 1985). This allowed the study to be the first to provide an insight as to the timeline of participation in a wide range of physical activities within the first post-operative year after HTO.

9.5.5 Clinical implications and future research

The present study was the first to provide a detailed insight into the progression of pain and physical activity at regular intervals within the first 12 months after surgery. The results can be used by surgeons to help better manage and improve patient expectations of the length of recovery after HTO as well as the likelihood and time at which different types of activity may be performed. However, further prospective investigations with larger sample sizes are required to confirm these findings.

The results support those presented in Chapter 8, which found that surgeons believe the first 6 post-operative months to be where the largest improvements in pain and physical function occur. This study explains and provides support for the large focus of patient information and education by surgeons on the initial post-operative period. However, as outlined in Chapter 7, patients reported a desire for more information from medical professionals regarding expected knee function and activity levels later in the first post-operative year. The present study showed that a further significant reduction in pain and increase in physical activity levels occurred between 6 and 12 months post-operatively. Therefore, more guidance to establish realistic expectations within this time period is recommended to reduce feelings of confusion or uncertainty during a time where the knee is still significantly improving.

9.6 Conclusion

3 months after HTO was the point at which the first significant reduction in pain, and a return to pre-operative activity levels, was observed. This was also the point at which participation in most activities, including return to work, was possible at an equal or greater rate than pre-operatively. Participation in high-impact activities (such as jogging and jumping) was possible within 6 months after surgery. Some patients played ball sports and racquet sports after 12 months, although the highest participation rates were seen in “activities of daily living” and “low-impact activities”. Overall, physical activity was significantly negatively correlated with pain. Patients first started to benefit from HTO 3 months after surgery, with improvements in pain and activity levels continuing for the duration of the first post-operative year.

As discussed in Chapter 7, variables such as residual pain, fear of pain, changing personal interests, and injuries unrelated to the HTO were all reported to be potential confounding variables that impacted participation in certain high-impact activities such as jogging or team sports. Recommendations for future research could be made to investigate each of these confounding variables. However, only two of them fit within the scope of this thesis: the fear of pain and the existence of residual pain during high-impact activities. It is apparent from the present study that HTO successfully and significantly reduces, but does not eliminate, knee pain. The degree to which pain is experienced during high-impact activities is unknown. Understanding the way in which the intensity of an activity affects pain levels would help to determine whether the commonly reported fear of pain is justified, or if it is something that should be addressed and allayed as part of patient expectation management by surgeons.

CHAPTER 10 – PAIN AND GAIT AT DIFFERENT EXERCISE INTENSITIES ARE NO DIFFERENT AFTER MEDIAL OPENING-WEDGE HIGH TIBIAL OSTEOTOMY COMPARED TO AGE-MATCHED CONTROLS

10.1 Abstract

Background: HTO successfully reduces medial knee pain and improves knee function. However, residual pain during strenuous activities, such as running, is not unusual. HTO normalises walking gait somewhat but pain can cause an individual to alter their gait. The degree to which pain is tolerated during exercise after surgery, and the impact that exercise intensity has on pain levels and gait, is unknown. The purpose of this study was to compare changes in pain levels and gait during walking and jogging at different intensities between HTO patients and healthy, age-matched controls.

Methods: Eleven HTO patients (mean age 55.7 ± 8.6 years; mean BMI 28.5 ± 4.1 kg/m^2; 7 males) and eleven age-matched healthy control subjects (mean BMI 24.8 ± 4.1 kg/m^2; 5 males) completed the exercise protocol in this study. Knee function and pain was assessed prior to testing using a KOOS questionnaire, a VAS pain score, and a pain intensity score (PIS). Eight bouts of 3 minutes of exercise were performed on a flat treadmill by each participant: 4 bouts walking (performed at RPE 9, 11, 13, and 15) and 4 bouts jogging (performed at RPE 9, 11, 13, 15). Spatiotemporal gait parameters and knee pain were measured during each bout of exercise.

Results: Knee function prior to testing was significantly worse in the HTO group compared to the Control group. Pain according to the VAS and PIS was not significantly different between groups prior to exercise. No significant differences in gait parameters were detected between groups for all bouts of exercise. The HTO group always reported higher absolute VAS and PIS values compared to the Control group during each exercise test, however for bouts 1, 2, and 3 (walking RPE 9, 11, and 13, respectively) median differences were not statistically significant. Median VAS and PIS scores for bout 4 (walking RPE 15), and all jogging bouts, were significantly higher in the HTO group versus the Control group, but never exceeded 0.5/10 (IQR 0-3).

Conclusion: HTO patients demonstrated a normalised gait with very low pain levels in the mid-term after surgery during short bouts of exercise, regardless of the exercise intensity and despite having worse knee function than the control group. HTO patients can expect a post-operative return to physical activity, including high-intensity jogging, without a compromised gait and with minimal residual pain.

10.2 Introduction

The previous chapter demonstrated an inverse relationship between physical activity levels and pain within the first 12 months after HTO. When examining the breakdown in activities performed by patients, rates of participation in daily activities (e.g. stair climbing) and low-impact recreational activities (e.g. cycling) were generally higher than those for high-impact activities (e.g. jogging). To infer from these data that HTO patients are therefore less likely to be able to participate in high-impact activities after surgery would, however, not necessarily be accurate. The findings in Chapter 7 found that multiple variables including pain – either a fear of pain or actual residual pain – were contributing factors to the apparent reluctance of patients to participate in high-impact activities post-operatively. This chapter seeks to address the potential issue around pain during activity to provide further context to the findings of the results previously presented in this thesis.

Many studies show that HTO successfully reduces medial knee pain and improves knee function (Brouwer *et al.*, 2007; Bonasia *et al.*, 2014). However, residual pain during strenuous activities such as running is not unusual (Bonnin *et al.*, 2013; Saragaglia *et al.*, 2014). The degree to which pain is tolerated during exercise after surgery, and the impact that exercise intensity has on pain levels, is unknown. Patients can be deterred from returning to physical activity after surgery due to various psychosocial factors including a fear of pain, motivation, perceived importance of exercise, pre-operative education, advice from a surgeon, and confidence in the knee (Tjong *et al.*, 2014, 2016; Faschingbauer *et al.*, 2015; Ramanathan *et al.*, 2015; Burland *et al.*, 2018; Grünwald *et al.*, 2018). Understanding the degree to which pain and exercise intensity are limiting factors in HTO post-operatively will provide an evidence base to allow medical professionals to improve the accuracy with which they manage patient expectations of post-operative physical activity ability.

Pain is associated with adjustments in gait in individuals with knee osteoarthritis (Turcot *et al.*, 2013). A study that investigated pain at a self-determined "free" walking speed showed that HTO patients were, on average, pain-free at one and five years after surgery (Borjesson *et al.*, 2005). Patients commonly exhibit a pre- to post-operative change in gait due to the nature of the bone realignment, and adjustment of the weightbearing line, that occurs during HTO (Liu *et al.*, 2019). A recent systematic review and meta-analysis found that gait speed and stride length increased after HTO, while knee adduction moments and lateral thrust decreased (Lee *et al.*, 2017). A number of studies have compared the gait of HTO patients post-operatively against healthy control subjects (Lind *et al.*, 2013; van Egmond *et al.*, 2017; da Silva *et al.*, 2018; Whatling *et al.*, 2019). Results vary between studies and between different gait parameters regarding the normalisation of gait after surgery. This means that there is a certain level of controversy over whether HTO reliably normalises gait, however the literature tends to show an inclination towards a pre- to post-operative improvement of gait in HTO patients (Lee *et al.*, 2017; Santoso and Wu, 2017).

The gait of HTO patients compared to healthy controls has only been investigated during walking at a self-selected speed (Lind *et al.*, 2013; van Egmond *et al.*, 2017; da Silva *et al.*, 2018; Whatling *et al.*, 2019). Since knee pain and an altered gait are positively associated, the possible trend that HTO tends to normalise post-operative gait parameters is to be expected. However, each of the abovementioned studies were only conducted during walking. Residual pain during strenuous activities has been previously been reported (Bonnin *et al.*, 2013). The gait of HTO patients during high-impact activities is not known. It is possible that residual pain may result in a compensatory altered gait pattern in HTO patients, which may result in an increase in the progression of osteoarthritis. If this were the case, participation in high-impact activities should not be recommended, despite the results of Chapter 9 and the literature showing that it is sometimes possible for patients to do so (Bonnin *et al.*, 2013; Nakamura *et al.*, 2020). This would simultaneously serve to resolve the apparent variability among surgeons regarding advising the avoidance of high-impact activities post-operatively (Chapter 8).

The purpose of this study was to compare changes in pain levels and gait during walking and jogging at different intensities between HTO patients and healthy, age-matched controls. It was hypothesised that: 1) reported pain would be higher in the HTO patients in each condition, and 2) the gait of the HTO patients would significantly differ from the controls during jogging and fast walking, but not during slow walking.

10.3 Methods

10.3.1 Participants

Twelve patients (mean age at surgery 51.4 ± 8.8 years; 7 males) who had previously undergone medial opening-wedge HTO performed by one of three experienced consultant surgeons were recruited to participate. Patients were considered eligible to participate if they were over the age of 18 years, had not undergone another procedure concurrent to the osteotomy (other than arthroscopy), and had since had their internal fixation plate removed. All plates were removed at a mean 14.3 ± 5.6 months after HTO. Eleven age-matched control participants were recruited from university staff and the local community using advertisements. Control participants had never undergone any lower limb surgery.

All participants provided written informed consent and completed a physical activity readiness questionnaire (PAR-Q) prior to their participation in the study (Appendix I). The PAR-Q included a blood pressure measurement and disclosure of any medical or physical issues that would have precluded participation in the test protocol. Resting heart rate, height, and mass of each participant were also measured as part of the PAR-Q, the latter two of which were used to calculate body mass index (BMI). Ethical approval for this study was granted by the University of Winchester ethics review board (Appendix I).

10.3.2 Operative details

Biplanar medial opening-wedge high tibial osteotomies were performed under general anaesthesia according to a previously described standard protocol (Staubli *et al.*, 2003). Four patients underwent HTO with an allograft bone wedge, and no filler was used in the remaining eight knees. One patient was implanted with a small Tomofix plate; seven with a standard Tomofix plate; two with an ActivMotion plate; and two with a PEEKpower plate.

10.3.3 Gait analysis

Spatiotemporal gait parameters were measured using a wireless centre-of-mass triaxial accelerometer sensor (G-Walk, BTS Bioengineering S.p.A., Milan, Italy), which has previously been validated for clinical use (Park and Woo, 2015). The sensor was attached to the waist of participants using an elasticated belt and was positioned centrally in the L5 area of the lower spine. A dedicated software program (G-Studio, BTS Bioengineering S.p.A., Milan, Italy) was used to record and analyse the following parameters transmitted wirelessly via Bluetooth by the sensor: number of strides, cadence (steps/minute), speed (m/s), stride length (m), gait cycle duration (s), stance phase duration (%), and swing phase duration (%). The gait sensor was attached to each participant prior to the warm-up and remained in place for the duration of the exercise testing.

10.3.4 Knee Injury and Osteoarthritis Outcome Score (KOOS)

The knee function of all participants was assessed prior to activity testing using a KOOS questionnaire, which has been validated for clinical use and the follow-up of osteoarthritis patients who have undergone surgical procedures (Roos and Lohmander, 2003). The KOOS consists of a series of 42 questions that are divided into 5 categories: symptoms, pain, activities of daily living, sport and recreation, and quality of life. Each question has a Likert-scale-style set of 5 answers, which are then scored from 0 to 4, with the sum for each category being calculated separately. Scores are then standardised to fall on a 0-100 scale where 0 equals severe issues with knee, and 100 representing no issues (Roos *et al.*, 1998). Recording a KOOS score for all participants prior to testing allowed for a baseline assessment of any differences in knee function between HTO and control groups.

10.3.5 Pain scales

A Visual Analogue Scale for pain (VAS) and a second Pain Intensity Scale (PIS) were used to record participant-reported pain levels in the knee prior to, during, and after bouts of exercise during the test protocol. The VAS has been commonly cited in the literature to report upon pre- and post-operative pain in HTO patients (Brouwer *et al.*, 2007). It consists of a 10 cm vertical line with markers at each extreme labelled “No pain” and “The worst imaginable pain”. Participants were asked to draw a horizontal line across the VAS to represent their current knee pain level. The distance from the “No pain” marker to the intersecting horizontal line was then measured using a ruler to provide a numerical score out of 10: where 1 cm is equal to 1 unit of reported pain. The PIS has been shown to be a reliable and valid measure for lower limb pain during exercise (Cook *et al.*, 1997). It is a 0-10 numerical scale where 0 = “No pain at all”, 3 = “Moderate pain”, 5 = “Strong pain”, 7 = “Very strong pain”, and 10 = “Extremely intense pain”. The VAS and PIS were both included in this study because the VAS would allow for comparison to other HTO studies in the literature; and the PIS would allow for comparison and validation of the VAS for measuring pain during exercise. All participants completed a VAS and PIS prior to the exercise testing to establish pain levels at rest.

10.3.6 Rating of perceived exertion

All exercise testing was performed at a self-directed intensity, which was guided by a Rating of Perceived Exertion (RPE) scale (Borg, 1998). The RPE scale is one of the most frequently utilised tools to record perceived physical strain during exercise and is commonly used clinically and during laboratory research (Faulkner and Eston, 2007). It has been shown to have high reliability and validity (Borg, 1998), and has acceptable inter-trial agreement within trials of varying exercise intensities (Buckley and Eston, 2007). RPE can also be used as a predictor of exercise intensity, heart rate, and oxygen uptake (Table 10.1) (Buckley and Eston, 2007; Faulkner and Eston, 2007). The scale ranges from 6-20 where 6 equals “No exertion at all” and 20 represents “Maximal exertion” (Borg, 1998). Other written cues are included on the scale alongside the numbers to guide users as to the level of exertion that they represent (Figure 10.1). Participants were verbally anchored to the scale prior to testing and an opportunity for familiarisation with the scale occurred during the warm-up (Green, Michael and Solomon, 1999; Faulkner, Parfitt and Eston, 2007). The RPE scale was used to determine the exertion a participant should aim to achieve in each bout of exercise, which therefore determined the intensity at which they worked.

Table 10.1: *The relationship between RPE and % of maximal aerobic power (%VO_{2max}) and % of maximal heart rate (HR_{max}).*

RPE	<10	10-11	12-13	14-16	17-19	19-20
%VO_{2max}	<20	20-39	40-59	60-84	≥85	100
%HR_{max}	<35	35-54	55-69	70-89	≥90	100

Source: adapted from Buckley and Eston (2007), *in Winter et al.* (p. 121).

6	**No exertion at all**
7	**Extremely light**
8	
9	**Very light**
10	
11	**Light**
12	
13	**Somewhat hard**
14	
15	**Hard (heavy)**
16	
17	**Very hard**
18	
19	**Extremely hard**
20	**Maximal exertion**

Figure 10.1: The Borg scale for the Rating of Perceived Exertion (RPE) (Borg, 1998).

10.3.7 Test protocol

Participants were first asked to perform a warm-up on a cycle ergometer for two consecutive bouts of 2.5 minutes: the first 2.5 minutes cycling at a speed equivalent to an RPE 11 and the second at a speed equivalent to RPE 13 (Lim *et al.*, 2016). The warm-up was conducted on a cycle ergometer – as opposed to the treadmill upon which the exercise testing took place – to minimise the likelihood of exercise-induced knee pain occurring in the HTO patients prior to testing. A VAS and PIS was completed by all participants immediately following the five minutes on the cycle ergometer to assess whether higher pain levels were experienced during the warm-up protocol.

All participants then performed eight bouts of 3 minutes of exercise on a flat treadmill (Woodway, Waukesha, Wisconsin, USA). Four bouts were performed while walking and the remaining four were performed while jogging. Bouts were undertaken at an RPE 9, 11, 13, or 15, which provided sufficient variation in exercise intensity between bouts (Table 10.1). The order in which bouts 1-8 were performed was randomised prior to testing. The bout length of 3 minutes was chosen since this is the minimum time needed for heart rate to increase to a level relative to intensity during steady state exercise on a treadmill (McArdle, Katch and Katch, 2010; Fletcher *et al.*, 2013). Pain levels pertaining to the operated knee were recorded using the VAS and PIS half-way through each bout (90 seconds) and at the end of each bout (180 seconds). The knee, about which the control subjects reported their pain levels, was assigned randomly prior to testing. In between bouts, participants returned to a seated position until their heart rate returned to within 15 bpm of resting levels before being asked to begin the next bout. It normally took 3-5 minutes for a participant's heart rate to return to within this range. Participants could abandon a bout of exercise or withdraw from the study at any time if pain levels became intolerable and they did not wish to continue.

10.3.8 Statistical analysis

A power analysis to calculate the sample size needed for the present study was conducted based upon a previous research paper that investigated differences in gait between healthy controls and patients who underwent total knee arthroplasty (Biggs *et al.*, 2019). A minimum of 12 participants (6 per group) was required to achieve a power of 0.95 with an alpha error of 0.05 and a large effect size (d=2.13).

All data were first examined using histograms to detect whether they were normally distributed. Two -way analysis of variance (ANOVA) with repeated measures was performed to detect differences in gait parameters between each individual bout of exercise. All scores during walking (bouts 1-4) were also aggregated to create a grand mean for each gait parameter, which was then compared against the grand mean for jogging (bouts 5-8) using a further ANOVA with repeated measures. This allowed for an overall comparison between the two types of exercise (walking versus jogging) to be conducted. Data for the subjective pain scores between each individual bout of exercise were analysed using a Friedman test. Where significant differences between bouts were detected, post-hoc analyses using a Wilcoxon signed rank test were performed. `

Independent samples t-tests were conducted to compare differences between the demographic data of both groups. KOOS scores and all pain scores were analysed using a

Mann-Whitney *U* test. Paired samples t-tests compared the heart rate and reported pain of participants before and after the five-minute cycling protocol to determine whether it was an effective warm-up that simultaneously did not exacerbate any underlying or residual knee pain. Finally, a Spearman correlation (r_s) was calculated to find any significant relationships between demographic data and the KOOS, VAS, and PIS.

Mean ± SD was calculated for all parametric data and median values for all non-parametric data were presented with a corresponding interquartile range (IQR). Statistical significance for all tests was determined as $p < 0.05$. All statistical tests were performed using IBM SPSS Statistics 26 (IBM Corporation, Armok, New York).

10.4 Results

10.4.1 Demographics

23 participants participated in the present study (12 HTO patients; 11 healthy controls). One HTO patient withdrew from the study prior to completion of the exercise bouts due to pain in a severely osteoarthritic ankle, which was a consequence of a motorcycle accident they had been involved in as a teenager. As a result, it was not possible to collect a complete dataset of gait and pain scores for this patient, so they were excluded from the final analysis. Equipment failure on two occasions during testing meant that the gait data from one participant in each group were not able to be included in the final analysis. Pain scores for both of those participants were included in the final analysis. Therefore, the gait data presented were based on 10 participants in each group, and the subjective outcome scores were based on 11 participants in each group. The demographic characteristics of the participants can be found in Table 10.2. Participants in the HTO group had a significantly higher BMI than those in the Control group ($p = 0.046$). There were no other differences in demographic characteristics between groups.

Table 10.2: *Demographic information*

Characteristic	HTO (Mean ± SD)	Control (Mean ± SD)	Total (Mean ± SD)
No. of patients	11	11	22
Age at test (y)	55.7 ± 8.6	56.3 ± 5.6	56.0 ± 7.1
Sex (male:female)	7:4	5:6	12:10
Height (m)	1.72 ± 0.1	1.68 ± 0.1	1.70 ± 0.1
Mass (kg)	84.2 ± 14.5*	70.2 ± 12.6	77.2 ± 15.1
BMI (kg/m^2)	28.5 ± 4.1*	24.8 ± 4.1	26.6 ± 4.4
Resting heart rate (bpm)	71 ± 12	77 ± 12	74 ± 12
Operated knee (right:left)	8:3	7:4	15:7
Time since HTO (months)	48.6 ± 22.0	n/a	n/a

Note: *sig. diff. versus Control group ($p < 0.05$); SD = Standard Deviation
BMI = Body Mass Index; HTO = High Tibial Osteotomy

10.4.2 Subjective outcome scores

Baseline KOOS, VAS and PIS scores for each group can be found in Table 10.3. Each of the subcategories of the KOOS were significantly lower in the HTO group compared to the Control group ($p < 0.01$). Pain according to the VAS and PIS was not significantly different between groups prior to exercise ($p > 0.05$). Significant negative correlations were found between BMI and the "Symptoms" ($r_s[20] = -0.69$, $p < 0.001$); "Pain" ($r_s[20] = -0.56$, $p = 0.007$); "Activities of Daily Living" ($r_s[20] = -0.48$, $p = 0.023$); "Sport" ($r_s[20] = -0.44$, $p = 0.042$); and "Total" ($r_s[20] = -0.62$, $p = 0.002$) subcategories of the KOOS scores. Significant negative correlations were also found between body mass and all six subcategories of the KOOS ("Symptoms" $r_s[20] = -0.67$, $p = 0.001$); "Pain" $r_s[20] = -0.54$, $p = 0.01$); "Activity and Daily Living" $r_s[20] = -0.55$, $p = 0.008$); "Sport" $r_s[20] = -0.44$, $p = 0.041$); "Quality of Life" $r_s[20] = -0.49$;, $p = 0.021$); and "Total" $r_s[20] = -0.63$, $p = 0.002$). The warm-up on the cycle ergometer did not significantly increase reported pain levels in either group but did significantly increase heart rate ($p < 0.01$), suggesting that it was fit for purpose.

Table 10.3: *Baseline subjective outcome scores*

Score	HTO (Median [IQR])	Control (Median [IQR])	Mann-Whitney *U* value	p-value
KOOS Symptoms	85.7 [71.4-92.9]*	100 [96.4-100]	13.5	0.002
KOOS Pain	86.1 [66.7-97.2]*	100 [97.2-100]	17.5	0.003
KOOS ADL	86.8 [79.4-100]*	100 [98.5-100]	21.0	0.006
KOOS Sport	55.0 [40.0-75.0]*	100 [95.0-100]	8.5	<0.001
KOOS QoL	62.5 [56.0-93.8]*	100 [100-100]	17.0	0.002
KOOS Total	81.3 [69.9-90.5]*	99.4 [96.4-100]	12.0	0.001
VAS (pain)	0.0 [0.0-0.5]	0.0 [0.0-0.0]	44.0	0.070
PIS	0.0 [0.0-0.5]	0.0 [0.0-0.0]	44.0	0.069

Note: *significant difference versus Control group ($p < 0.05$)
IQR = Interquartile Range; HTO = High Tibial Osteotomy
KOOS = Knee injury and Osteoarthritis Outcomes Score
ADL = Activity and Daily Living; QoL = Quality of Life
VAS = Visual Analogue Scale; PIS = Pain Intensity Scale

Median VAS and PIS scores never exceeded 0.5/10 (IQR 0-3) in the HTO group and 0/10 (IQR 0-0) in the Control group during exercise. The HTO group always reported higher absolute VAS and PIS values compared to the Control group for each exercise test, however during and after bouts 1, 2, and 3 (walking RPE 9, 11, and 13, respectively) median differences were not statistically significant ($p > 0.05$). Median VAS and PIS scores during and after bout 4 (walking RPE 15), and all jogging bouts, were significantly higher in the HTO group versus the Control group ($p < 0.05$) but never exceeded 0.5 (IQR 0-3). Scores from the VAS were strongly correlated with scores from the PIS ($r_s[372] = 0.91$; $p < 0.001$).

Within the HTO group, pain was significantly lower during bout 1 (walking RPE 9) than during bouts 6, 7, and 8 (jogging RPE 11, 13, 15, respectively; $p < 0.05$). Similarly, pain during bout 2 (walking RPE 11) was significantly lower than all jogging bouts ($p < 0.05$). After exercise, bout 4 (walking RPE 15) caused significantly higher pain than bouts 1, 2, 5, and 6 (walking RPE 9 and 11, and jogging RPE 9 and 11, respectively; $p < 0.05$). Additionally, pain after bouts 6 and 7 (jogging RPE 11 and 13, respectively) was significantly higher than after bout 2 (walking RPE 11; $p < 0.05$). Within the Control group, no significant differences in pain were detected between bouts.

10.4.3 Gait analysis outcomes

Table 10.4 shows the mean values for all of the gait parameters measured. No group-by-condition interaction was observed for any of the gait parameters ($p > 0.05$). Time main effects were observed for all gait parameters. Number of strides, cadence, speed, and stride length tended to increase between bouts within each group, though mostly without statistical significance. Gait cycle duration tended to decrease non-significantly between bouts within each group. Stance phase percentage within groups was similar between walking bouts and was significantly lower than the jogging bouts. Swing phase percentage within groups was similar between walking bouts and was significantly higher than the jogging bouts.

Table 10.4: *Mean ± SD gait parameter values for the HTO group and Control group*

Exercise	Bout	Group	Number of strides	Cadence (steps/minute)	Speed (m/s)	Stride length (m)	Gait cycle (s)	Stance phase (%)	Swing phase (%)
Walk	1 (RPE 9)	HTO	291.7 ± 48.2	97.0 ± 13.9	0.9 ± 0.2	1.1 ± 0.2	1.3 ± 0.3	62.5 ± 3.8	37.5 ± 3.8
		Control	285.4 ± 54.7	95.7 ± 19.3	1.0 ± 0.3	1.2 ± 0.2	1.3 ± 0.5	61.4 ± 2.9	38.6 ± 2.9
	2 (RPE 11)	HTO	319.3 ± 42.8	104.5 ± 17.0	1.2 ± 0.3*	1.4 ± 0.2**	1.2 ± 0.3	62.0 ± 2.9	38.1 ± 2.9
		Control	335.7 ± 26.0††	110.8 ± 7.7††	1.2 ± 0.2†	1.3 ± 0.2†	1.1 ± 0.1††	60.5 ± 1.7	39.5 ± 1.7
	3 (RPE 13)	HTO	368.6 ± 43.1*	121.6 ± 16.9	1.5 ± 0.4	1.5 ± 0.2	1.0 ± 0.3	61.7 ± 2.9	38.3 ± 2.9
		Control	376.5 ± 38.0†	123.9 ± 12.9†	1.6 ± 0.3	1.5 ± 0.3	1.0 ± 0.1†	60.7 ± 2.2	39.3 ± 2.2
	4 (RPE 15)	HTO	400.6 ± 40.3**	133.6 ± 13.4**	1.7 ±0.2	1.5 ± 0.2	0.9 ± 0.1*	61.7 ± 2.8	38.3 ± 2.8
		Control	397.2 ± 29.2††	129.8 ± 8.5††	1.8 ± 0.2†	1.7 ± 0.2†	0.9 ± 0.1††	60.1 ± 1.5	39.9 ± 1.5
Jog	5 (RPE 9)	HTO	460.0 ± 18.0**	149.9 ± 8.6*	2.3 ± 0.3**	1.8 ± 0.2*	0.8 ± 0.1**	66.7 ± 7.1	33.3 ± 7.1
		Control	449.3 ± 68.4	146.5 ± 18.2	2.3 ± 0.3††	1.8 ± 0.2††	0.8 ± 0.2	69.0 ± 7.7††	31.0 ± 7.7††
	6 (RPE 11)	HTO	459.0 ± 37.6	153.0 ± 11.5*	2.4 ± 0.3	1.9 ± 0.2	0.8 ± 0.1*	66.5 ± 5.9	33.5 ± 5.9
		Control	441.8 ± 79.5	147.2 ± 26.9	2.5 ± 0.5	1.9 ± 0.3†	0.9 ± 0.3	68.8 ± 7.4	31.2 ± 7.4
	7 (RPE 13)	HTO	469.6 ± 66.6	157.3 ± 23.5	2.5 ± 0.5	1.9 ± 0.2	0.8 ± 0.1	67.5 ± 7.1	32.5 ± 7.1
		Control	489.6 ± 29.5	159.9 ± 7.9	2.7 ± 0.4	2.0 ± 0.3	0.8 ± 0.0	68.1 ± 7.0	31.9 ± 7.0
	8 (RPE 15)	HTO	502.3 ± 22.3	169.9 ± 9.7	2.6 ± 0.3	1.9 ± 0.2	0.7 ± 0.0	68.8 ± 7.2	31.2 ± 7.2
		Control	489.8 ± 63.2	161.5 ± 12.0	2.7 ± 0.4	1.9 ± 0.3	0.6 ± 0.1	68.8 ± 6.8	31.2 ± 6.8

Note: †sig. diff. versus preceding bout within Control group ($p < 0.05$); ††sig. diff. versus preceding bout within Control group ($p < 0.01$)
*sig. diff. versus preceding bout within HTO group ($p < 0.05$); **sig. diff. versus preceding bout within HTO group ($p < 0.01$)
RPE = Rating of Perceived Exertion

When comparing aggregated results from the walking bouts against those from the jogging bouts (Table 10.5), main effects of condition were observed for all gait parameters ($p < 0.01$). When comparing the aggregated walking-versus-jogging gait parameters between groups, no significant differences were observed.

Table 10.5: *Mean ± SD gait parameters and pain scores during walking and jogging.*

	HTO group		**Control group**	
	Walking	**Jogging**	**Walking**	**Jogging**
Number of strides	345.0 ± 59.3*	472.7 ± 43.3	348.7 ± 57.0†	457.7 ± 83.5
Cadence (steps/minute)	114.1 ± 20.6*	157.6 ± 16.0	115.0 ± 18.2†	150.5 ± 25.5
Speed (m/s)	1.3 ± 0.4*	2.4 ± 0.4	1.4 ± 0.4†	2.5 ± 0.5
Stride length (m)	1.4 ± 0.2*	1.9 ± 0.2	1.4 ± 0.3†	1.9 ± 0.3
Gait cycle duration (s)	1.1 ± 0.3*	0.8 ± 0.1	1.1 ± 0.3†	0.9 ± 0.3
Stance phase (%)	61.9 ± 3.0*	67.4 ± 6.6	60.7 ± 2.1†	68.7 ± 6.9
Swing phase (%)	38.1 ± 3.0*	32.6 ± 6.6	39.3 ± 2.1†	31.3 ± 6.9
VAS pain	0.5 ± 1.1	0.9 ± 1.6	0.0 ± 0.0	0.0 ± 0.0
PIS	0.6 ± 1.3	0.9 ± 1.2	0.0 ± 0.0	0.0 ± 0.0

Note: *signifcant difference ($p < 0.01$) walking versus jogging (HTO group)
†significant difference ($p < 0.01$) walking versus jogging (Control group)
VAS = Visual Analogue Scale; PIS = Pain Intensity Scale

Table 10.6 shows the comparison in stride duration, stance phase percentage, and swing phase percentage of each bout between the operated knee and non-operated knee of the HTO group. There were no significant differences between knees.

Table 10.6: *Mean ± SD gait parameters of the operated knee vs. non-operated knee in the HTO group.*

Exercise	Bout	Knee	Stride duration (s)	Stance phase (%)	Swing phase (%)
Walk	1 (RPE 9)	Operated knee	1.3 ± 0.3	61.2 ± 2.6	38.8 ± 2.6
		Non-operated knee	1.3 ± 0.3	63.6 ± 5.2	36.4 ± 5.2
	2 (RPE 11)	Operated knee	1.2 ± 0.3	61.8 ± 3.6	38.2 ± 3.6
		Non-operated knee	1.2 ± 0.2	62.0 ± 3.6	38.0 ± 3.6
	3 (RPE 13)	Operated knee	1.0 ± 0.1	60.6 ± 3.2	39.4 ± 3.2
		Non-operated knee	1.0 ± 0.1	62.7 ± 3.1	37.3 ± 3.1
	4 (RPE 15)	Operated knee	0.9 ± 0.1	61.6 ± 3.3	38.4 ± 3.3
		Non-operated knee	0.9 ± 0.1	61.8 ± 2.9	38.2 ± 3.0
Jog	5 (RPE 9)	Operated knee	0.8 ± 0.1	67.1 ± 8.2	32.9 ± 8.2
		Non-operated knee	0.8 ± 0.1	66.7 ± 7.1	33.3 ± 7.1
	6 (RPE 11)	Operated knee	0.8 ± 0.0	67.6 ± 5.5	33.4 ± 6.3
		Non-operated knee	0.8 ± 0.0	65.4 ± 6.4	33.6 ± 5.9
	7 (RPE 13)	Operated knee	0.8 ± 0.1	68.0 ± 8.5	32.0 ± 8.5
		Non-operated knee	0.8 ± 0.2	67.1 ± 6.1	32.9 ± 6.1
	8 (RPE 15)	Operated knee	0.7 ± 0.0	68.4 ± 6.2	31.6 ± 6.2
		Non-operated knee	0.7 ± 0.0	69.4 ± 8.8	30.6 ± 8.8

10.5 Discussion

The present study demonstrated that post-operative HTO patients exhibited normalised spatiotemporal gait parameters as compared to age-matched control subjects, regardless of exercise intensity. There were no significant differences between groups for cadence, speed, stride length, and stance phase duration, irrespective of exercise intensity. Within the HTO group, there were no significant differences in stride duration and stance phase duration between the operated knee and the non-operated knee. Reported pain during walking and jogging remained very low within both groups although significantly higher pain was detected in the HTO group during “hard” walking (RPE 15) and all jogging intensities compared with the Control group. The results presented indicate that HTO was successful at appropriately realigning the limb, and relieving the symptoms of medial osteoarthritis, to a degree where patients were able to perform high impact exercise while maintaining low levels of pain and a gait similar to that of age-matched healthy controls. Consequently, the null hypotheses cannot be rejected. This is the first study that has conducted a gait analysis of HTO patients while jogging.

10.5.1 Subjective KOOS and pain scores

Despite the similar gait characteristics between groups, baseline KOOS scores were found to be significantly lower in the HTO group suggesting the condition of patients’ operated knee was not normal, but that this did not significantly impact on their ability to walk or jog. This finding supported previous research, which similarly showed that HTO patients had worse functional outcome scores post-operatively compared to healthy controls (Ramsey *et al.*, 2007). Furthermore, reported pain is significantly associated with self-reported functional difficulty but not with observed physical performance in knee osteoarthritis patients (Harrison, 2004; Adegoke, Babatunde and Oyeyemi, 2012). This perhaps explains the lower reported knee function of the HTO patients according to the KOOS, but the lack of differences in gait detected during the exercise testing between groups in the present study. The observed discrepancy between self-reported knee function and objectively measured function during the treadmill test may suggest that the regular clinical use of gait analysis would be beneficial. Combining an objective measure of function with the commonly used subjective self-reported questionnaires would provide clinicians with greater insight into the surgical outcome of a patient. However, the practicality and cost-effectiveness of such testing would need to be considered and may be a barrier to its implementation.

BMI was negatively correlated with KOOS scores but no significant correlation between BMI and pain was detected. The HTO group had a significantly higher mean BMI than the Control group, which may partially explain the lower reported knee function among the HTO patients. Negative relationships have previously been found between post-operative BMI and factors including cartilage regeneration (Kumagai *et al.*, 2017) and knee function (Spahn, Kirschbaum and Kahl, 2006; Floerkemeier *et al.*, 2014), which may have confounded the lower KOOS score observed in the HTO group.

The KOOS subcategory of "Sports & recreation" demonstrated the largest median difference between groups, although this did not translate to differences in gait during the walking and jogging bouts. In addition to asking about difficulty while running, the remaining four questions of the "Sports & recreation" subcategory also enquired about difficulty experienced by patients during activities involving higher impacts (jumping), rotational movements (twisting/pivoting), and extreme ranges of motion (kneeling). Faschingbauer *et al.* (2015) observed a generally lower participation rate in strenuous activities after HTO with an 81.8% reduction in pre- to post-operative participation in ball games and a 50% reduction in jogging after HTO. Salzmann *et al.* (2009) also observed a large reduction in participation in similar activities, with pre- to post-operative participation in football decreasing 50% and participation in jogging decreased 44%. The large pre- to post-operative reduction in participation in strenuous activities in both studies appear to be associated with activities that involved movements like those that feature in the "Sports & recreation" subscale of the KOOS. This suggests that it is not unusual for patients to avoid such activities post-operatively and may be reflective of the low KOOS score for the subcategory of "Sports & recreation" observed in the present study. Jogging is often categorised as a "high-impact" activity within the literature (Salzmann *et al.*, 2009; Faschingbauer *et al.*, 2015; Bastard *et al.*, 2017) but it does not involve twisting of the knee, or impacts to the same degree as ball games and racquet sports. This could explain the apparent inconsistency observed regarding the limited ability to perform sporting movements – as evidenced by the results of the low KOOS subcategory of "Sports & recreation" – but the lack of pain experienced during the exercise protocol in the present study.

It is well established that medial opening-wedge HTO is successful at significantly reducing experienced pain in the affected knee (Coventry, Ilstrup and Wallrichs, 1993; Gaasbeek *et al.*, 2010; Santoso and Wu, 2017; Kim *et al.*, 2018). However, HTO tends not to offer complete pain relief and a certain level of post-operative residual pain is common (Takeuchi *et al.*, 2008; Bonnin *et al.*, 2013; Bonasia *et al.*, 2014; Petersen and Metzlaff, 2016). The results in the present study suggest that patients did experience residual pain after HTO, but that this only occurred during bouts of jogging or "hard" walking (RPE 15). Median pain scores at baseline and during lower-intensity walking were 0/10; identical to the Control group. These results indicate that the surgery was successful at offloading the osteoarthritic compartment of the knee to a degree where symptoms were not present during low-impact exercise, and only began to resurface during higher-impact movements. Although pain was present during jogging and "hard" walking for the HTO group, it was at a very low and tolerable level.

The VAS is commonly used to assess general reported knee pain in HTO patients (Brouwer *et al.*, 2007) though its reliability and validity has been criticised (Carlsson, 1983; Boonstra *et al.*, 2008). The significant positive correlation between the VAS and PIS scores indicated that the VAS can be recommended for clinical use when assessing experienced pain during exercise in HTO patients.

10.5.2 Gait speed

The measurement of spatiotemporal gait parameters has previously been recommended as a simple and reliable method of assessing the outcome of patients surgically treated for knee osteoarthritis (Ivarsson and Larsson, 1989; Amis, 2013; Santoso and Wu, 2017). The results of the present study demonstrated no significant differences in spatiotemporal gait parameters (speed, cadence, stride length, gait cycle duration, stance phase duration) between HTO patients and age-matched healthy controls, regardless of the intensity of the exercise undertaken.

Most studies in the literature were conducted with a short-term follow-up of approximately 12 months, whereas the present study was conducted in the mid-term at a mean 48.6 ± 22 months after HTO. This made it somewhat difficult to make direct comparisons between the present findings and those of other studies. However, two articles exist that present results of a gait analysis protocol between HTO patients and age-matched healthy controls in the mid-term (Wada *et al.*, 1998; Birmingham *et al.*, 2017). Birmingham *et al.* conducted gait analysis at a mean 78.7 ± 19.9 months post-HTO and found that the controls exhibited a mean gait speed of 1.2 ± 0.8 m/s, which was faster than the HTO patients (1.1 ± 0.2 m/s) although it is not reported whether this difference was statistically significant. These speeds were most similar to those from "bout 2" in the present study (RPE 11, "Light"), wherein the controls walked at a mean 1.2 ± 0.2 m/s versus the HTO patients (1.2 ± 0.3 m/s). Wada *et al.* (1998) conducted a gait analysis 72 months after surgery and found that control participants walked at a mean speed of 0.8 ± 0.1 m/s, which was not significantly different from the HTO patients (the precise figures for the mean walking speed of the patients were not reported. These walking speeds were slower than those in the present study wherein "bout 1" (RPE 9, "Very light") resulted in a mean 1.0 ± 0.3 m/s in the control group, and 0.9 ± 0.2 m/s in the HTO group. However, in the Wada *et al.* (1998), despite being asked to walk at a “natural” walking speed, participants were required to do so with their arms crossed in front of their chests, which may have influenced their normal gait speed.

Notwithstanding the difference in the post-operative follow-up time of patients in the present study and those in many similar studies, the literature is equivocal regarding the post-operative walking speed of HTO patients compared to healthy controls. Some studies reported no significant differences between groups, which support the results of the present study (Wada *et al.*, 1998; Lind *et al.*, 2013; Lee *et al.*, 2017; Whatling *et al.*, 2019), but others observed significantly different gait characteristics between groups (Weidenhielm, Svensson and Brostrom, 1992; van Egmond *et al.*, 2017; da Silva *et al.*, 2018; Morin *et al.*, 2018). Regardless of whether statistical significance was found between patients and control subjects, the walking speeds reported in the literature of HTO patients (ranging from 0.75 m/s to 1.43 m/s) was always slower than that of their respective control subjects (0.8 m/s to 1.54 m/s). The findings of the present study were consistent with the literature in terms of the mean walking speed of HTO patients (1.3 ± 0.4 m/s; 95% CI 1.2-1.5) tending to be slower than healthy controls (1.4 ± 0.4 m/s; 95% CI 1.3-1.5), although not statistically significantly.

Another factor that made it difficult to directly compare results from the present study to the literature is that most protocols either required their participants to walk at a single subjectively-defined self-determined speed (Weidenhielm, Svensson and Brostrom, 1992; Wada *et al.*, 1998; Lind *et al.*, 2013; van Egmond *et al.*, 2017; da Silva *et al.*, 2018; Morin *et al.*, 2018; Whatling *et al.*, 2019), or did not define how participants were asked to walk (Birmingham *et al.*, 2017). One study exists that investigated the walking ability at different speeds of patients who underwent HTO or unicompartmental knee arthroplasty 12 months previously (Börjesson *et al.*, 2007). Börjesson *et al.* (2007) focused on the significant pre- to post-operative increase in “slow”, “normal”, and “fast” walking speeds and therefore only reported precise figures for the mean difference (0.1 ± 0.2 m/s for each speed). However, graphic evidence showed that mean post-operative slow, normal, and fast walking speeds were approximately 0.9, 1.1, and 1.6 m/s, respectively. Comparable walking speeds within the HTO group in the present study were found during “bout 1” (0.9 ± 0.2 m/s), “bout 2” (1.2 ± 0.3 m/s), and “bout 4” (1.7 ± 0.4 m/s), which represented an RPE 9 (“very light”), RPE 11 (“light”), RPE 15 (“hard”), respectively. The speed at which participants walked in the study by Borjesson *et al.* (2007) was subjective and self-determined. Although the same was true in the present study, the treadmill protocol had comparatively increased reliability and repeatability since it was framed around the use of the well-defined and established RPE scale (Stamford, 1976; Borg, 1998). It is known that HTO generally improves the spatiotemporal parameters of gait in the short-term (Lee *et al.*, 2017; Liu *et al.*, 2019) but the results of the present study, combined with the results of Börjesson *et al.* (2007)*,* suggest that this is maintained in the mid-term after surgery. Further research is needed to confirm this since the present study did not include any pre-operative gait analysis.

10.5.3 Stride length

The findings of the present study showed that the stride length of HTO patients was not significantly different to healthy controls while walking and jogging. Morin *et al.* (2018) presented results to the contrary with patients exhibiting a significantly shorter mean stride length 12 months after HTO (0.6 ± 0.1 m) compared to control subjects (0.7 + 0.1 m). These findings were unusual, especially considering that pain is a significant influencing factor in the reduction of stride length compared to healthy controls (Turcot *et al.*, 2013) but that reported pain in the Morin *et al.* (2018) study, according to the VAS, was effectively non-existent 12 months after surgery (0 ± 1). The authors suggested that HTO cannot be successful at changing all gait parameters within 12 months, and that bony deformity is normally present for several years post-operatively, although this statement appears anecdotal.

Regardless, the findings of Morin *et al.* (2018) were in contrast to much of the literature, which found that stride length tended to be normalised within 12 months after HTO (Wada *et al.*, 1998; Lind *et al.*, 2013; van Egmond *et al.*, 2017; da Silva *et al.*, 2018). A recent systematic review and meta-analysis of the literature surrounding change in gait after HTO showed that many parameters, including stride length, improved after HTO (Lee *et al.*, 2017). Most studies reported that pre-operative stride length, ranging from 0.8 m to 1.4 m, was generally shorter than that of healthy controls (0.9 m to 1.5 m) but that it increased – as a result of the corrective surgery – and normalised post-operatively (Wada *et al.*, 1998; Lind *et al.*, 2013; van Egmond *et al.*, 2017; da Silva *et al.*, 2018). Overall, the literature tends to support the findings of the present study regarding stride length.

Morin *et al.* (2018) found that stride length was significantly shorter than that of control subjects, however there were no significant pre- to post-operative (12 months) changes in any of the measured gait parameters. This meant that the gait of patients remained significantly different to control subjects after surgery. Despite the lack of change in gait in the Morin *et al.* (2018) study, patients reported a significant improvement in clinical and functional outcomes. This suggests that a lack of normalisation of gait parameters does not necessarily equal a negative outcome for a patient in the short-term. However, it is possible that a normalised gait pattern is desirable in the long-term since an adjusted gait changes the distribution of forces around the knee joint (Turcot *et al.*, 2013) and any abnormal increase in force has been found to be a factor for the progression of osteoarthritis and associated knee pain (Baliunas *et al.*, 2002).

10.5.4 Other gait parameters

Findings within groups for the present study were generally as expected: jogging bouts resulted in an increased number of strides, cadence, speed, stride length, and decreased gait cycle duration compared to walking bouts. Similarly, the higher the intensity of a walking or jogging bout (i.e. the greater the RPE-controlled speed) the higher the number of strides, cadence, speed, stride length, and lower gait cycle duration was observed; which would also be expected (Veilleux *et al.*, 2016).

The mean stance phase percentage in the HTO group (61.9 ± 3.0; 95% CI 61.0-63.0) and Control group (60.7 ± 2.1; 95% CI 60.1-61.4) during walking was similar to previously approximated norms of around 62% (Pink *et al.*, 1994; Lohman, Balan Sackiriyas and Swen, 2011; da Silva *et al.*, 2018). During jogging, the mean stance phase percentage was increased in the HTO group (67.4 ± 6.6; 95% CI 65.4-69.6) and the Control group (68.7 ± 6.9; 95% CI 66.5-71.0). Research suggests that the inverse normally occurs during running, resulting in a reduced stance phase percentage of around 35% (Pink *et al.*, 1994; Lohman, Balan Sackiriyas and Swen, 2011). One of the differences between jogging and running is that jogging results in a stance phase greater than the swing phase (Lohman, Balan Sackiriyas and Swen, 2011). During data collection for the present study, participants were specifically asked to “jog” and the word “run” was not used in an attempt to standardise the instructions given. The increased stance phase observed during bouts 5-8 in the present study reflect the fact that participants jogged instead of ran, therefore the results around the stance phase percentages can be considered normal in both groups.

Two studies compared the percentage of the gait cycle spent in the stance phase in HTO patients versus healthy controls (Morin *et al.*, 2018; Whatling *et al.*, 2019). Both studies observed a significant difference between control subjects and patients around 1 year after HTO, which was contrary to the results of the present study. As explained above regarding stride length, the findings from the Morin *et al.* (2018) study were unusual since they did not observe a significant pre- to post-operative difference in gait parameters, contrary to much of the literature with a similar follow-up period (Weidenhielm, Svensson and Brostrom, 1992; Oberg and Oberg, 2000; Borjesson *et al.*, 2005; Kean *et al.*, 2009; Bhatnagar and Jenkyn, 2010; Deie *et al.*, 2014; Leitch *et al.*, 2015). The same was also true for some of the findings in the study by Whatling *et al.* (2019). They found that a significantly higher stance percentage of patients pre-operatively versus the controls subjects did not significantly decrease as a result of the osteotomy surgery, contrary to previously published research (Kean *et al.*, 2009; Bhatnagar and Jenkyn, 2010). Therefore, the reported significant difference between patients post-operatively and control subjects – contrary to the results of the present study – was not unexpected.

A recently published review claimed that spatiotemporal gait parameters were not altered by HTO 12 months after surgery (Liu *et al.*, 2019). While this would support the findings of Whatling *et al.* (2019) regarding stance phase percentages, the claim is referenced as being based on the findings of the Morin *et al.* (2018) study. As previously discussed, the lack of pre- to post-operative changes in gait observed by Morin *et al.* (2018) were contrary to the overall trend in the literature, which generally demonstrates a significant pre- to post-operative improvement in spatiotemporal gait parameters 12 months after HTO (Weidenhielm, Svensson and Brostrom, 1992; Oberg and Oberg, 2000; Borjesson *et al.*, 2005; Kean *et al.*, 2009; Bhatnagar and Jenkyn, 2010; Deie *et al.*, 2014; Leitch *et al.*, 2015).

One study reported cadence during walking between HTO patients and healthy controls (Morin *et al.*, 2018). It found, in contrast to the present study, a significant difference in mean walking cadence between HTO patients post-operatively (109.5 ± 11.2 steps/min) and healthy controls (113.2 ± 7.3 steps/min). However, the overall trend that HTO patients had a mean cadence lower than that of controls during walking was in agreement with our results (Table 10.5).

The present study was the first to compare the overall post-operative gait cycle duration of HTO patients against healthy controls. During each bout of exercise, patients exhibited an almost-equal gait cycle duration compared to the control subjects. Considering this finding along with those pertaining to stance phase percentages, the results indicated that patients exhibited a normalised overall gait cycle duration post-operatively. Regardless of whether patients were walking or jogging – or exercising at a low or high intensity (RPE 9 or RPE 15) – the operated knee behaved in a similar way to the non-operated knee. Stride duration remained similar between knees and was inversely related to exercise intensity when walking and jogging (Table 10.6). The stance and swing phase percentages were similar between knees, which is in line with previously reported results (Borjesson *et al.*, 2005; Morin *et al.*, 2018). The similarities found between knees lend further support to the conclusion that HTO allowed for a normalisation in gait post-operatively, since measured parameters were not only similar between patients and healthy controls, but also between the operated and non-operated knee within subjects.

10.5.5 Strengths and limitations

The inclusion of age-matched controls in the present study was one of its biggest strengths. Due to the number of operative variables that exist during HTO (including the type of plate used, the size of correction, and the possible use of graft materials) it can often be difficult to discount the confounding effect they might have on patient outcomes after surgery. The eligibility criteria for participation in this study attempted to mitigate these confounding variables by only including patients who had radiographically reached union and had subsequently had their plate removed, which strengthened the reliability of the findings.

The use of the RPE scale to determine the intensity of the exercise bouts could be seen as a limitation of this study due to its inherent subjectivity (Garcin, Vandewalle and Monod, 1999). However, it is known that RPE is strongly related to heart rate (Buckley and Eston, 2007). In the present study, heart rate was recorded directly after the warm-up. The latter half of the warm-up was conducted at an RPE 13, which would be expected to elicit a heart rate 55-69% of the participant's maximum (Table 10.1). The overall mean age in the study was 56.0 ± 7.1 years and the overall mean heart rate after the warm-up was 102.0 ± 25.3 bpm. The maximum heart rate of a 56 year old is around 165 bpm (McArdle, Katch and Katch, 2010), meaning that the mean heart rate achieved after the warm-up was 61.8% of the maximum, which is well within the expected range for exercise at RPE 13.

Furthermore, a previous meta-analysis showed that the mean normal gait speed of healthy people aged 50-59 is approximately 1.4 m/s (Bohannon and Williams Andrews, 2011). This was equal to the aggregated walking gait speed observed in the control group and similar to that of the HTO group (1.3 m/s). The mean age of both groups was 56 years. The 95% confidence interval of the sample in the meta-analysis by Bohannon and Williams Andrews (2011) suggested that "normal" walking is between 1.1 and 1.6 m/s. Comparing this to the results of the present study: bout 1 (RPE 9 "Very light") and bout 4 (RPE 15 "Hard") fell just outside of this range, while bout 2 (RPE 11 "Light") and bout 3 (RPE 13 "Somewhat hard") fell within these parameters. It is unlikely that walking at an RPE 9 or RPE 15 would constitute "normal" walking so it is unsurprising that they fell outside of the confidence interval presented by Bohannon and Williams Andrews (2011). However, this lends support to the notion that participants were successfully able to use the RPE scale to adjust the intensity of their walking for the purposes of the test.

All jogging bouts can categorically be claimed to have been different to the walking bouts for a number of reasons. Firstly, bout 5 (RPE 9 "Very light"), the slowest jogging speed, was significantly higher than the walking speeds observed in the present study and in the meta-analysis of Bohannon and Williams Andrews (2011). Secondly, the speed at which healthy subjects typically transition from a walk to a jog is around 2.2 m/s (Segers *et al.*, 2007) and each of the mean values for gait speed during jogging (bouts 5-8) were above this threshold. Lastly, jogging – as opposed to running or sprinting – has been defined as traveling at a velocity between 2.2 m/s and 4.5 m/s (Dugan and Bhat, 2005). Each bout of jogging fell between this range for both groups. Therefore, the use of the subjective RPE scale to determine the walking and jogging speed at which participants exercised was suitable for the purposes of this investigation. In fact, it was one of the strengths of the study.

This study was limited by the convenience sample of HTO patients and control subjects that volunteered to participate. Control subjects were age-matched to the HTO group but there was a significant difference in BMI between groups. BMI was a confounding variable for the differences in knee function, according to the KOOS results between groups. However, the lack of differences in gait between groups during the test protocol, suggests that BMI was not a confounder during exercise. Although this is perhaps counterintuitive, this finding is supported in the literature where BMI was found not to influence the performance of physical tasks in people with knee osteoarthritis (Sharma *et al.*, 2003; Adegoke, Babatunde and Oyeyemi, 2012). The absence of pre-operative KOOS, pain scores, and gait parameters, limited this study and is recommended for inclusion in future research to allow for a more detailed analysis of the influence of HTO surgery. Finally, the presented results were based on short bouts of exercise only. Research to investigate the effects of prolonged exercise on the gait and pain levels of HTO patients after surgery would be beneficial.

10.6 Conclusion

This study aimed to investigate the effect that exercise intensity had on gait and reported pain in patients who had previously undergone medial opening-wedge HTO compared to age-matched healthy controls. Low levels of pain were experienced by patients during jogging and "hard" walking (RPE 15), but no pain was experienced during lower-intensity walking. No differences in spatiotemporal gait parameters between patients and controls were observed. HTO patients demonstrated a normalised gait with very low pain levels in the mid-term after surgery during short bouts of exercise, regardless of the exercise intensity and despite having lower KOOS scores than control group. HTO patients can expect a post-operative return to physical activity, including high-intensity jogging, without a compromised gait and with minimal residual pain.

CHAPTER 11 – GENERAL DISCUSSION

11.1 Main findings

This PhD project broadly sought to provide a greater understanding of physical activity in HTO patients with a view to improving related post-operative outcomes. The evidence presented in this thesis supports the continued use of HTO for physically active patients. The procedure was showed to significantly reduce pain within 3 months of surgery, which continued to improve for at least the first 12 post-operative months, before reaching a level comparable to that of healthy controls. A return to pre-operative physical activity levels was typically possible within 3 months of surgery, which also continued to improve throughout the first post-operative year. Patients who underwent HTO with allograft wedges exhibited larger improvements in knee function and higher levels of post-operative physical activity, partly due to the increased biomechanical strength that the bone wedges provided to the osteotomy construct. Despite the development and progression of the operative technique to improve outcomes, it is clear that a combination of social, psychological, and behavioural factors also contribute to the decisions patients make around post-operative physical activity habits. Surgeons dedicate a lot of time towards managing the expectations of patients, however areas of controversy in the literature coincide with disagreement among surgeons, which limits the degree to which realistic expectations can be instilled upon patients.

This thesis first provided justification for the continued surgical indication of a highly active patient as more suited to HTO than other surgical interventions such as UKA (Chapter 4). It then demonstrated that the use of allograft bone wedges during surgery resulted in clinically important improvements in knee function and a return to higher levels of activity post-operatively compared with HTO without a gap filler (Chapters 5 and 6). The qualitative study presented in Chapter 7 revealed a number of psychosocial factors – most prominently a fear of pain, a lack of confidence in the knee, and a perception of insufficient guidance regarding the knee’s expected ability after the first 6 post-operative months – which patients commonly reported as having influenced their physical activity habits. The qualitative study in Chapter 8 supported patient claims of post-operative guidance being reduced after the first few months post-HTO. Surgeons reported that most of the information typically given to patients revolved around the purpose of the procedure, how the procedure is performed, and care of the knee immediately after surgery. Areas of consensus and contention between surgeons tended to coincide with areas of agreement and controversy within the scientific literature. An exception to this trend related to return-to-work after surgery. Surgeons tended to overstate the speed at which patients could expect to return to either high or low intensity jobs compared to reports in the literature. The main areas of controversy among surgeons were around operative technique, the necessity and timing of plate removal, and the timing of various post-operative milestones.

Chapter 9 showed a negative correlation between pain and physical activity levels after HTO in the short-term. It found that pre-operative pain was significantly reduced within 3 months of surgery, which coincided with the point where patients returned to their pre-operative activity levels. Pain continued to reduce, and activity levels continued to increase, at 6 and 12 months post-operatively. Participation rates were highest in activities of daily living and in low-impact recreational activities. Of those patients who did participate in high-impact activities, they could do so 6 months after surgery. Chapter 10 demonstrated that reduced pain and the ability to participate in high-impact activities was maintained in the mid-term after surgery. It showed that exercise intensity did not have an impact on pain levels and that the underlying residual pain in the knee was not significantly higher than age-matched control subjects who had never undergone any form of lower limb surgery. Furthermore, the gait of the HTO patients did not significantly differ from that of the age-matched control subjects irrespective of exercise intensity.

11.2 The use of graft materials during HTO

The first area of focus for this thesis – working towards the primary aim of improving physical activity outcomes after HTO – was on the use of graft materials during surgery. Where bone grafts are used in HTO, they are usually either autografts, allografts, or synthetic grafts (Amendola and Bonasia, 2010; Parkar, Pastides and Khakha, 2020). Each type of bone graft is known to have various advantages and disadvantages, which explains the continued use of all three graft types since no consensus has been reached in the literature regarding which one is best overall.

Stability of the osteotomy construct depends on the size of the osteotomy gap; whether the lateral cortex remains intact; and whether rigid internal fixation is used (Han *et al.*, 2015). A large osteotomy gap, a fractured lateral cortex, and non-locking fixation plates are all negatively associated with union of the osteotomy, correction loss, and construct failure (Han *et al.*, 2015). These consequences are more likely to occur in smokers, patients with a high BMI, or a large osteotomy gap size. In non-smokers with a BMI less than 30 kg/m^2, and with a planned osteotomy gap size of <10 mm, some studies recommend that HTO should be conducted without filling the gap due to the satisfactory union rates, without the risks associated with graft use (Han *et al.*, 2015; Slevin *et al.*, 2016). However, this does not account for the stabilising effects of bone graft use.

Prior to the study in Chapter 5 there was only one other publication that had tested the biomechanical properties of HTO with grafts versus HTO without grafts (Takeuchi *et al.*, 2010). The authors of that study specifically compared synthetic grafts versus no graft in-vitro and found that the synthetic graft group resulted in higher vertical and rotational stability than the no-graft group. The study in Chapter 5 was conducted to build upon this research by comparing a synthetic graft group and no-graft group with an allograft group. Allograft wedges have clinically similar outcomes compared to no grafts but are clinically preferable to synthetic grafts (Lash *et al.*, 2015; Slevin *et al.*, 2016). Synthetic grafts are biomechanically preferable to no graft (Takeuchi *et al.*, 2010). Therefore, it stood to reason that if allograft wedges were also biomechanically superior to no graft then their use may be preferable when faced with an active patient. The analysis showed that HTO with allograft wedges was biomechanically stronger and more stable than HTO without grafting; performed more predictably than HTO without grafting; and perhaps better protected the lateral hinge compared to HTO with synthetic grafts.

The strength and stability provided by allograft wedges to an osteotomy construct may be valuable where early or immediate post-operative weightbearing protocols are used. The study in Chapter 5 replicated the biomechanical behaviour of an osteotomy where no healing had taken place, equivalent to immediate weightbearing after surgery. Early weightbearing protocols after surgery were recommended over the more conservative approaches taken by many surgeons in a recent meta-analysis (Lee, Ahn and Lee, 2017). Lee *et al.* (2017) found that clinical outcomes after HTO were similar – and the incidence of correction loss and thrombophlebitis lower – in patients where an early weightbearing protocol was used compared to those who remained on crutches for the first 6-10 weeks post-operatively. Positive results with early weightbearing protocols have been demonstrated both in patients who underwent HTO with (Takeuchi *et al.*, 2009; Brinkman *et al.*, 2010) and without graft materials (Brosset *et al.*, 2011; Schröter *et al.*, 2015; 2017). No comparative research between the two surgical techniques regarding early post-operative weightbearing has so far been conducted. The increased biomechanical strength of HTO with bone grafts, as evidenced by the results in Chapter 5, suggests that full weightbearing may be possible sooner after HTO with graft materials compared to HTO without grafting.

The results of Chapter 5 provided support to the observed trend of the systematic review in Chapter 4, which showed a difference in pre- to post-operative physical activity levels between patients who underwent HTO with and without grafting. However, this needed to be confirmed before firmer conclusions and recommendations could be made around the use of allograft wedges during HTO for active patients. Chapter 6 contained a study that confirmed the observed trend in Chapter 4. Patients who underwent HTO with allograft wedges significantly increased their pre- to post-operative activity levels compared to those who underwent HTO without grafting, where no significant change in pre-operative activity levels was observed. Both groups exhibited statistically significant improvements in knee function according to all six sub-categories of the KOOS score (Symptoms, Pain, Activities of daily living, Sports and recreation, Quality of life, and Total score). However, upon closer inspection the pre- to post-operative increase in each KOOS sub-category was more likely to be deemed clinically important in the allograft group compared to the control group (Jacquet *et al.*, 2020). In general, the argument presented in this thesis in favour of the use of allograft wedges during HTO, as opposed to HTO without grafting, has been an argument for the difference between the good outcomes of the latter technique and the better, more consistent, and clinically important outcomes of the former technique.

There is a high likelihood that HTO patients aspire to participate in physical activity after surgery, since being active is one of the key indications for the procedure (Ekhtiari *et al.*, 2016; Hoorntje *et al.*, 2019). In addition to determining operative techniques and procedures that are superior radiologically (Smith *et al.*, 2011; Han *et al.*, 2015; Wu *et al.*, 2017), clinically (Lash *et al.*, 2015; Slevin *et al.*, 2016; Wu *et al.*, 2017), and biomechanically (Lee *et al.*, 2017; Liu *et al.*, 2019), it follows that research should also focus on maximising the extent to which patients can be physically active after HTO. Recent systematic reviews and meta-analyses showed that patients were successfully able to return to their pre-operative activity levels after surgery but only a relatively small number improved compared to their pre-operative status; and a general shift from high- to low-impact activities has been observed (Ekhtiari *et al.*, 2016; Hoorntje *et al.*, 2017; Kunze *et al.*, 2019). Chapters 4 to 6 demonstrated that HTO with allograft wedges resulted in a biomechanically stronger construct, which translated to increased pre- to post-operative physical activity levels and a greater probability of achieving clinically important improvements in knee function, compared to HTO with an unfilled gap.

The literature is unequivocal regarding the advantages and disadvantages of the three main types of graft material but is in less agreement as to which is superior since positive outcomes have been achieved with each (Han *et al.*, 2015; Lash *et al.*, 2015; Slevin *et al.*, 2016). Furthermore, some studies recommend against the use of graft materials in HTO – except in cases where the risk of complications is higher – since similar outcomes have been reported in HTO with no grafting and the disadvantages associated with graft materials are inherently avoided (Zorzi *et al.*, 2011; Ferner *et al.*, 2016; Slevin *et al.*, 2016). However, this thesis has pushed back and argued that allograft wedges are preferable over the other graft types due to the relatively low-risk disadvantages associated with them compared to the more commonly occurring disadvantages associated with autografts and synthetic wedges (Hung and Noi, 2012; Smith, Wilson and Thomas, 2013; Lash *et al.*, 2015; Slevin *et al.*, 2016; Sarman *et al.*, 2019). Furthermore, this thesis has demonstrated that HTO with allograft wedges are biomechanically and clinically superior to HTO without bone grafting regarding construct stability, pre- to post-operative knee function, and pre- to post-operative physical activity levels. Where possible, the routine use of allograft wedges during HTO can therefore be recommended for patients wanting to be physically active after surgery. Their use results in a more predictable outcome that is more likely to be clinically important, while simultaneously allowing patients to increase their physical activity levels after surgery compared to their pre-operative status.

11.2.1 Confounding variables

The first few empirical chapters of this thesis placed emphasis on the use of graft materials during HTO and their beneficial impact on the degree to which patients were able to return to physical activity after surgery. However, Chapter 6 also found that the operative variable of the use of allograft wedges only accounted for a medium amount of the observed effect. This suggested that other factors also contributed to post-operative physical activity levels. Potential factors within the study in Chapter 6 that may have contributed to the observed effect – namely differences in the follow-up time and fixation plates between groups – were identified but not deemed likely to have had any significant impact on the overall results. The follow-up times of each group (28.4 ± 14.3 months in the allograft group; 37.4 ± 12.9 months in the control group) were both outside of the first post-operative year, where the most significant changes in activity levels occur (Krych *et al.*, 2017; Nerhus *et al.*, 2017; Kim *et al.*, 2018). Activity levels have been shown not to significantly change within the second post-operative year (Krych *et al.*, 2017; Nerhus *et al.*, 2017; Kim *et al.*, 2018).; a trend which is maintained at 5 years after surgery (Krych *et al.*, 2017). The follow-up times of each group in Chapter 6 fell between the 2-5 year range and it can therefore be inferred that the significant difference between the follow-up times of each group was unlikely to have confounded the results.

Similarly, the differences between groups regarding the type of fixation plate used were again unlikely to have confounded the results in Chapter 6 because of the timing of the post-operative follow-up. The purpose of the plate is to maintain the newly aligned tibia and to provide stability to the osteotomy construct while the bone heals; at which point it can be removed. The two most commonly used plates in Chapter 6 (Tomofix and ActivMotion) perform differently with regard to biomechanical strength and stability (Diffo Kaze *et al.*, 2017), which could have confounded results if follow-up occurred prior to union of the osteotomy. No comparative studies exist that investigate the clinical outcomes of the ActivMotion plate against plates like the Tomofix. It is not known whether the incidence of longer-term plate-related complications such as irritation differs between plate types.

Plate removal is optional and can either be done routinely – depending on the preference of the surgeon (Chapter 8) – or as a result of plate-related complications (Bode *et al.*, 2015; Pagkalos *et al.*, 2018; Goshima *et al.*, 2019). The point at which the plate is safe to be removed is after bony union has reached the centre of the osteotomy gap (Goshima *et al.*, 2019). The timing of this is variable but most likely to occur within 12-18 months of surgery (Brinkman *et al.*, 2008; Lind-Hansen *et al.*, 2016; Goshima *et al.*, 2019). The follow-up times of the groups in Chapter 6 were well beyond this 12-18 month period, suggesting that for those patients whose plates remained in situ, the plate did not cause them any significant issues and was therefore unlikely to have confounded the findings. It has been speculated that the removal of plates results in further incremental improvement in post-operative outcomes after HTO (Niemeyer *et al.*, 2010; Bode *et al.*, 2015; Goshima *et al.*, 2019), however a similar number of plates were removed in each group in Chapter 6 (56% in the allograft group; 62% in the control group), eliminating this as another possible confounding variable.

11.3 Pain

Once it was deemed likely that the abovementioned variables were unlikely to have contributed to the effect observed in Chapter 6, attention needed to be turned to discovering which other factors may have added to the medium effect detected for the use of allograft wedges during surgery. Residual pain and motivation have both been found to be associated with post-HTO activity levels as well as with the type of activity performed (Bonnin *et al.*, 2013; Bastard *et al.*, 2017). Studies into other forms of knee surgery additionally identified a fear of pain or reinjury as a common contributor to patient decisions around post-operative activity (Czuppon *et al.*, 2014; Tjong *et al.*, 2014; Filbay, Crossley and Ackerman, 2016). The qualitative study in Chapter 7 identified the fear of pain or reinjury as also relevant to HTO patients, and confirmed the prevalence of residual pain as a clear influencing factor for post-operative physical activity behaviours. HTO reduces pain rather than eliminates pain, therefore a certain level of residual pain in the operated knee is logically predictable (Brouwer *et al.*, 2014; Saier *et al.*, 2017). Although it is known that residual pain is likely, and patients have reported being limited by their operated knee after surgery (Bonnin *et al.*, 2013), post-operative pain levels and the degree to which they interact with physical activity are not well understood. Therefore, understanding pain as it pertains to post-operative physical activity in HTO patients became the next major focus for this thesis.

Chapter 9 showed that pain and physical activity were negatively correlated and that the first significant reduction in pain (at 3 months post-HTO) coincided with the point at which activity returned to pre-operative levels. The trend of improvement continued to 12 months after surgery with significant reductions in pain being associated with increases in physical activity. Few studies have investigated either pain or physical activity at multiple time periods within the first post-operative year. Of those that have, similar trends have been observed although not explicitly compared or stated. Kim *et al.* (2018) showed a significant reduction in pre-operative pain 3 months after HTO, as well as non-significant but increased activity levels; a trend that continued to 12 months after surgery. Similarly, Nerhus *et al.* (2017) observed the same trend, except that the time at which the first significant improvements in pain and activity levels occurred was at 6 months rather than 3 months. It is possible that the longer time needed to achieve the first significant reduction in pain in the Nerhus *et al.* (2017) study was due to the inclusion of autografts in all patients, since they are known to be associated with more pain post-operatively as discussed earlier. It therefore stands to reason that it would take longer for pain to be significantly reduced compared to pre-operative levels.

Saier *et al.* (2017) reported that the first significant reduction in pain occurred as soon as 6 weeks after surgery. No direct comparison between studies was possible in this case since no other study reported pain 6 weeks after surgery. However, Chapter 9 found a decrease in pre-operative pain levels (6.1 ± 2.5) at 1 month post-operatively (5.1 ± 2.9). While this decrease was not statistically significant, it demonstrates a similar trend to the results of Saier *et al.* (2017) and – had a measurement been taken at 6 weeks – it is not unreasonable to predict that a significant decrease in pain levels may have been detected. Saier *et al.* (2017) did not assess physical activity levels. Krych *et al.* (2017) did assess activity levels and showed a significant decrease at 3 months, which then increased significantly by 12 months. They did not assess pain levels in their study.

Considering the aim of HTO is to reduce pain, and a key indication for surgery is an active patient, overall it seems that the 6 weeks to 3 months post-operative period is pivotal in the recovery from HTO, since it is where the first major pain and activity milestones were reached. Where autografts were used, recovery from surgery regarding pain and activity was delayed (Nerhus *et al.*, 2017), but patients can expect improvements in pain and physical activity to continue for the first 12 post-operative months.

Where Chapter 9 investigated the interaction of pain and activity in the short-term, Chapter 10 examined this relationship in the mid-term. It confirmed findings that residual pain is common among HTO patients after surgery (Bonnin *et al.*, 2013). However, it also showed that this level of pain was not significantly higher compared to healthy control subjects during low-impact activity, and that pain levels were very low during high-impact activity. This had not previously been investigated and the results call into question the underlying cause behind the generally observed pre- to post-operative shift in high- to low-impact activities (Hoorntje *et al.*, 2017). If residual pain is not necessarily an issue when performing high-impact activities, other factors must account for a larger proportion of the effect.

Chapter 7 identified that the fear of pain; a lack of confidence in the knee; and a lack of guidance after the recovery from surgery were cited as common reasons behind decisions about post-operative physical activity behaviours. Each factor related to information about, and the expectation of, the operated knee. Patients tend to over-estimate the likelihood of being pain-free after surgery (Mannion *et al.*, 2009). When patients then experience residual pain after surgery, they may feel less satisfied with the outcome since their expectation was not met (Baker *et al.*, 2007; Scott *et al.*, 2010; Longo *et al.*, 2015). It is logical to predict that this results in a level of uncertainty around the success of the operation, and therefore a fear of pain or re-injury when performing certain activities. Regarding pain, the results of Chapters 9 and 10 may be used to help moderate patient expectations and give better guidance regarding the likely progression of pain after surgery. These results can also be used to demonstrate that residual pain after surgery is common and it is not necessarily an indication of a need to avoid high-impact activities.

11.4 Patient expectations

The accuracy of patient expectations of post-operative outcome is highly correlated with satisfaction with the result of surgery (Baker *et al.*, 2007; Scott *et al.*, 2010). Grünwald *et al.* (2018) found that patients had high expectations for the outcome of HTO. Specifically, large proportions of patients placed some, or high, importance on key factors that have been examined throughout this thesis: pain relief (92.9%), improvement in daily activities (90.2%), improvement in the ability to exercise (82.7%), and improvement in the ability to run (78.9%).

The literature shows that HTO is largely successful in achieving pain relief (Brouwer *et al.*, 2014; Saier *et al.*, 2017). However, as discussed above, only a small proportion of patients improve upon their pre-operative physical activity levels (Hoorntje *et al.*, 2017; Kunze *et al.*, 2019), and the generally-observed shift from high- to low-impact activities after surgery, suggests that running after HTO is largely avoided by patients (Hoorntje *et al.*, 2017; Kim *et al.*, 2018). The disparity between the proportion of patients who place high importance on running after surgery versus those who actually achieve it, implies that patient expectations for HTO are often overestimated in terms of physical activity outcomes.

As mentioned above, there are a number of allusions to the importance of realistic patient expectations in the HTO literature (Bonnin *et al.*, 2013; Saragaglia *et al.*, 2014; Ekhtiari *et al.*, 2016; Hoorntje *et al.*, 2017; Grünwald *et al.*, 2018; Hoorntje *et al.*, 2019) but studies aiming specifically to achieve them are lacking. The qualitative study presented in Chapter 8 demonstrated that surgeons dedicate a significant proportion of time towards the management of patient expectations. However, a lack of consensus regarding the time it takes to reach numerous post-operative physical activity milestones was found. This may hinder the accuracy to which patient expectations – which are known to be high for HTO (Grünwald *et al.*, 2018) – can be moderated to within realistic parameters.

The Tegner activity scale is the most commonly reported measure specifically for physical activity used in the HTO literature (Hoorntje *et al.*, 2017; Kunze *et al.*, 2019). Monitoring changes in physical activity levels by using questionnaires such as the Tegner scale are a good indication of overall activity but are not sensitive to changes in the frequency or type of activity performed. Since physical activity preferences differ between individuals, more information relating to specific types of activity would allow for patient expectations to be better tailored on a patient-to-patient basis. A limited number of studies (including Chapter 7) have reported more detailed findings in this regard: generally reporting a shift from high- to low-impact activities after surgery (Salzmann *et al.*, 2009; Bonnin *et al.*, 2013; Saragaglia *et al.*, 2014; Faschingbauer *et al.*, 2015; Hoorntje *et al.*, 2017; Kim *et al.*, 2018; Hoorntje *et al.*, 2019). These studies all reported pre- to post-operative changes in the number and type of activity performed, with follow-up ranging from 22-69 months after surgery. Of those that reported the number of activities performed pre- and post-operatively (Salzmann *et al.*, 2009; Faschingbauer *et al.*, 2015; Hoorntje *et al.*, 2017; Hoorntje *et al.*, 2019), the general trend was that patients participated in the same number of activities post-operatively as they did pre-operatively. This differs from the results presented in Chapter 9, which showed a significant mean increase in the number of activities performed from 6.0 ± 2.6 pre-operatively to 9.9 ± 2.4 post-operatively at 12 months.

Comparisons between this thesis and other studies pertaining to the number of activities performed are difficult due to inconsistencies regarding what constituted an activity. For example, most studies focused solely on sporting activities (Salzmann *et al.*, 2009; Saragaglia *et al.*, 2014; Faschingbauer *et al.*, 2015; Hoorntje *et al.*, 2019), whereas others (including Chapter 9) also included activities of daily living (Bonnin *et al.*, 2013). By including more activities in the analysis, surgeons and patients have access to more detailed information which may be useful for tailoring and managing patient expectations on an individual basis. Furthermore, Chapter 9 was the first study to outline the precise time at which patients returned to different activities after surgery. For the purposes of managing patient expectations, Chapter 9 provides unique insight into the progression of recovery from surgery in terms of pain and physical activity.

Activities in Chapter 9 were grouped according to whether they were activities of daily living, low-impact activities, or high-impact activities and were assigned to those categories in line with other studies that have also made such distinctions (Bonnin *et al.*, 2013; Faschingbauer *et al.*, 2015; Hoorntje *et al.*, 2017; Hoorntje *et al.*, 2019). A total of 20 activities were identified during data collection (8 activities of daily living, 4 low-impact activities, and 8 high-impact activities). Only 3 of the 8 high-impact activities were performed pre-operatively. On average, the increase in activity participation pre-operatively to 12 months after surgery was 27% for activities of daily living, 19.8% for low-impact activities, and 10.5% for high-impact activities. This could be interpreted as agreement with the general trend in the literature: showing a shift from high- to low-impact activities after surgery. However, activities of daily living and low-impact activities were more popular pre-operatively than high-impact activities. This suggests a propensity for patients to prioritise participation in lower impact activities independently of the HTO. It is therefore unsurprising that the largest increase in participation post-operatively was in the lower-impact activities. The fact that participation rates and the number of high-impact activities were increased post-operatively suggests that HTO allowed those patients to return to high-impact activities after surgery who wanted to.

Chapter 9 showed that most patients were able to perform activities of daily living within the first 12 months after surgery regardless of whether they had been able to do so pre-operatively. The same was true to a lesser extent of low- and high-impact activities. Participation rates for all activities increased pre- to post-operatively, suggesting that patients tended to increase the number of activities they performed after surgery in addition to returning to the ones they used to perform pre-operatively.

Some studies (including Chapter 8) noted that some surgeons discourage patients from participating in high-impact activities after surgery, which has been suggested as a reason behind the observed shift from high- to low-impact activities after surgery (Faschingbauer *et al.*, 2015; Kim *et al.*, 2018). The results of Chapter 9 showed that participation in high-impact activities after surgery was achievable in the short-term, particularly if those activities were already performed pre-operatively. Furthermore, Chapter 10 and previously published studies (Salzmann *et al.*, 2009; Bonnin *et al.*, 2013; Faschingbauer *et al.*, 2015) supported the notion that this remains possible in the mid-term after surgery. A number of the activities mentioned in those studies were the same as those included in Chapter 9. Table 11.1 shows a side-by-side comparison of the participation rates for these activities in each published study against those pertaining to 12 months post-HTO from Chapter 9. With the exception of skiing activities – where participation rates were far greater in the previously published studies compared with the results from Chapter 9; probably because of the countries in which they were conducted (Germany, Switzerland, France versus the UK) – similar trends between the results of Chapter 9 and the published studies can be seen. This could suggest that activity participation within the first 12 months of HTO is maintained in the mid-term since the other three studies had mean follow-up times of 22 months (Faschingbauer *et al.*, 2015), 36 months (Salzmann *et al.*, 2009), and 50 months post-operatively (Bonnin *et al.*, 2013). However, this comparison is subject to confirmation by larger scale studies that should be conducted.

Table 11.1: *Comparison in activity participation rates between studies at final follow-up (%)*

Activity	Chapter 9	Bonnin *et al.* (2013)	Faschingbauer *et al.* (2015)	Salzmann *et al.* (2009)
Heavy domestic work	79.3	51.0	-	-
Cycling	58.6	42.0	58.4	71.2
Swimming	55.2	22.0	39.5	45.5
Jogging	37.9	4.0	9.3	-
Golf	17.2	5.0	-	-
Football (soccer)	6.9	-	4.7	-
Racquet sports	6.9	1.5	-	3.0
Downhill skiing	3.5	25.0	11.6	27.7
Cross-country skiing	3.5	10.0	-	7.6

Patients who performed activities prior to surgery were able to return to the same activities within 3 months after surgery. This was true regardless of whether the activity fell into low- or high-impact categories, with a few exceptions. These exceptions were activities likely to involve twisting of the knee, which took either 6 months (golf, downhill skiing, and cross-country skiing) or 12 months (football/rugby and tennis/badminton) before those patients who had performed the activity prior to surgery were able to do so again. All patients who were able to walk on even ground prior to surgery, could do so again within 1 month of surgery. Those who were not able to walk on even ground before surgery could do so within 3 months.

Overall, patients returned to the same physical activities, at the same level, performed prior to surgery. In most cases, this was achieved within 3 months but activities involving twisting of the knee took 6-12 months. Almost all patients increased the number of activities they performed pre- to post-operatively, and high-impact activities could be performed if desired. The data presented in Chapters 9 and 10 pertaining to activity participation in the short- and mid-term may throw into question the discouragement of participation in high-impact activities for patients by some surgeons. Furthermore, there is evidence to suggest that running (high-impact) possibly helps to reduce pain and does not affect the progression of knee osteoarthritis, which may be relevant to osteotomy survivorship (Lo *et al.*, 2018). Nevertheless, it is not known whether participation in high-impact activities after HTO affects the survival of an osteotomy in the long-term. A recent study showed 10 year survivorship of 87.1%, which included a cohort of active patients (Lau *et al.*, 2020). While this survival rate is in line with previously published meta-analysis (84.4%; Spahn *et al.*, 2013), the authors did not define or quantify the term “active”. Investigation into survivorship of HTO in active patients is therefore necessary to confirm the appropriateness of advice from surgeons regarding restricting high-impact activities after surgery.

The information presented here is the first to show the progression of recovery after HTO regarding returning to physical activity after surgery. Pain and physical activity are negatively correlated. Continuous improvements in both can be expected throughout the first post-operative year but it is the 3-month mark that appears to be the first major milestone. A significant reduction in pain is likely to be experienced between 6 weeks and 3 months after surgery, at which point patients should mostly have returned to their pre-operative level of activity. With the exception of those involving twisting of the knee, even high-impact activities can be performed within 3 months of surgery, provided they were already performed pre-operatively. Pain and activity levels continue to improve past 3 months to 12 months, allowing patients to increase the number of activities they perform compared to pre-operatively. Although confirmatory research would be useful, these findings provide a basis from which timelines for post-operative milestones can be created. Consequently, these results can help to achieve greater consensus among surgeons and the management of realistic patient expectations can be improved. In turn, this would then lead to improvements in patient satisfaction with the procedure (Mahomed *et al.*, 2002; Rossi *et al.*, 2015; Hoorntje *et al.*, 2017).

11.5 Clinical implications

The evidence presented in this thesis strongly supports the continued use of HTO for the treatment of painful unicompartmental medial osteoarthritis in physically active patients. Recent research suggests that the indications for alternative procedures, namely UKA, have been expanded to include some young and active patients (Krych *et al.*, 2017; Kim *et al.*, 2018). However, the systematic review presented in Chapter 4 demonstrated that the literature remains in favour of HTO for these patients in terms of post-operative physical activity levels. When considering the further positive effect that HTO with allograft bone grafting has on physical activity levels (Chapter 6), the case for the superiority of HTO over UKA in active patients is strengthened. Given the decreasing incidence of HTO, versus an increase in the number of UKA performed each year (Kley, 2020), efforts should be made to ensure that this trend is not a result of expanding UKA indications to include patients who would benefit more from HTO.

The evidence presented in Chapters 5 and 6 resulted in a recommendation being made for the routine use of allograft wedges during HTO. This thesis has argued that allograft wedges are the optimal graft type due to their low-risk disadvantages compared to other graft types and the positive clinical, radiological, and biomechanical outcomes associated with their use (Chapters 5 and 6; Han *et al.*, 2015; Lash *et al.*, 2015; Slevin *et al.*, 2016). Furthermore, HTO with allograft wedges is preferable to HTO without grafting due to the better post-operative physical activity levels patients achieve (Chapter 6). This is of particular relevance in cases of physically active patients, who are likely to comprise a significant proportion of those who undergo HTO due to the surgical indication of an active patient.

Similarly, the stability that graft materials provide to an osteotomy construct (Chapter 5) may have implications for patients with a high BMI (>30 kg/m^2). Traditionally, patients with a high BMI would be contraindicated for HTO due to the increased likelihood of poor outcomes and further progression of osteoarthritis (Felson *et al.*, 1988; Preston *et al.*, 2005; Spahn, Kirschbaum and Kahl, 2006; van Houten *et al.*, 2013). However, recent studies have reported satisfactory outcomes in patients with a high BMI so there remains some controversy over the appropriateness of BMI as a contraindicative factor for surgery (Dettoni *et al.*, 2010; Floerkemeier *et al.*, 2014; Siboni *et al.*, 2018). The apparent attitude change with regard to high BMI and osteotomy is likely due to the improvement in the design and strength of modern fixation plates compared to older methods of fixation (Agneskirchner *et al.*, 2006; Diffo Kaze *et al.*, 2019). The advent and success of strong fixation plates, plus the extra stability provided to an osteotomy by graft materials, suggests that a high BMI may not necessarily need to be considered as a contraindication for HTO. Although this would require further research to be confirmed, the European Society of Sports Traumatology, Knee Surgery, and Arthroscopy recently recommended the use of bone grafts during HTO in patients with a high BMI based, in part, upon the results of Chapter 5 (Belsey *et al.,* 2019a; Belsey *et al.*, 2019b). This suggests that the contraindication for HTO of a high BMI is not necessarily always applicable and further research may be able to demonstrate or clarify this.

Despite the recommendation made in this thesis for the routine use of allograft wedges during HTO, it has been recognised that it is not always a feasible option: often due to financial or logistical reasons (Jung *et al.*, 2010; Hung and Noi, 2012; van Heerwaarden *et al.*, 2018). Due to the commonly occurring disadvantages associated with other graft types, HTO without grafting is a better option for patients where the use of allograft wedges is not an option. The exception to this rule is in the case of patients at particular risk of complications (high BMI, smoker, large osteotomy gap size) where it is accepted that the benefits of using autografts outweigh the negatives (Aryee *et al.*, 2008; Amendola and Bonasia, 2010; Santic *et al.*, 2010). The previous point notwithstanding, there is clearly still a role for HTO without bone grafting in patients where allograft wedges are unavailable. Therefore, research should continue to strive to improve outcomes for this technique: which is why such patients continued to be included in the studies presented in Chapters 9 and 10.

Chapters 7 and 8 showed that surgeons place high importance on the management of patient expectations, which was reflected in the amount of time dedicated to informing patients as to the purpose and probable outcomes of HTO. However, a lack of consensus pertaining to timelines for post-operative milestones suggests that providing patients with expectations that are likely to match their outcome is difficult. This is compounded by the lack of research in the HTO literature regarding inherently individual differences between patients such as motivation, confidence, fear, personal interests, and personal circumstances; all of which were highlighted in Chapter 7 as contributing to post-operative physical activity behaviours. The management of realistic patient expectations, and therefore patient-reported outcomes of HTO and satisfaction with the procedure, will always be limited as long as psychosocial factors remain unresearched in the HTO literature.

Chapters 9 and 10 provided deeper insight into the role that pain plays pertaining to post-operative physical activity levels. The evidence presented suggests that patients were able to perform high-impact activities as soon as 3 months after surgery, particularly if they performed the same activities pre-operatively. Chapter 10 showed that this remained the case years after surgery and that participation in high-impact activity did not modify levels of residual pain in the knee. This further supports the use of HTO in active patients – particularly as a preferable option over UKA – as it allows not only an increase in post-operative activity levels but a return to the same activities regardless of the amount of forces exerted through the knee. This may have implications for those surgeons who currently advise HTO patients to consider limiting their post-operative participation in high-impact activities. A recent study into patients with knee osteoarthritis (who had not undergone osteotomy or arthroplasty) showed that running did not negatively affect the progression of symptoms (Lo *et al.*, 2018). Based on this, recommendations not to participate in high-impact activities after HTO should not be predicated on the risk of disease progression. This thesis has demonstrated that high-impact activities after HTO are possible in the short- to mid-term after surgery, but the long-term effects remain unknown. Until long-term studies of the effect of participation in high-impact activities after surgery are conducted, recommendations against advising patients to restrict their post-operative physical activity cannot yet be confidently made.

11.6 Strengths & limitations

This thesis had a number of strengths and limitations, which should be mentioned to better contextualise the findings presented. The systematic review presented in Chapter 4 provided a more detailed justification for the focus of this thesis on HTO, which is a strength of the project. Plus, the use of multiple databases and the inclusion of a second independent reviewer reduced the likelihood of reviewer bias and of relevant articles being missed. However, systematic reviews tend to be prone to common limitations (Moher *et al.*, 2009; Harris *et al.*, 2017). Firstly, the quality and heterogeneity of included studies made it difficult to draw definitive conclusions due to methodological differences of the studies, which may have confounded their findings. This was an issue for Chapter 4, hence the inability to perform a comprehensive meta-analysis of the data. It is also possible that some relevant articles were not identified during the literature search, including clinically relevant but unpublished negative results, meaning that they could not included in the final review and analysis.

Some studies were limited by small sample sizes (namely, Chapters 5 and 10), which again limited the degree to which definitive conclusions could be made. However, the study in Chapter 5 was only the second to test the biomechanical strength of graft materials in HTO (Takeuchi *et al.*, 2010), and was one of only a handful of similar biomechanical analyses that used the same test protocols (Maas *et al.*, 2013; Diffo Kaze *et al.*, 2015, 2017, 2019). Each of these previously published studies included sample sizes equal to, or smaller than, those in Chapter 5. Financial limitations were the primary reason behind the small sample size in this case, however the number of specimens tested built upon the precedent set in the literature.

The small sample sizes in Chapters 7 and 8 could also be perceived as limitations. However, sample sizes are less relevant for qualitative research as it is based on a different set of underlying assumptions and does not strive to produce data that is generalisable in the same way that quantitative research does. Qualitative data are collected and analysed to provide deeper meaning and understanding about a given subject. Rather than being reliable in terms of reproducibility, qualitative studies are instead judged by their trustworthiness and their credibility (Petty, Thomson and Stew, 2012b). The inclusion of a second coder (Chapter 7); continuous verification and probing during data collection; and reflection and questioning of the data during analysis all contribute to the trustworthiness and credibility of qualitative research (Petty, Thomson and Stew, 2012b). These points were adhered to in Chapters 7 and 8, which provided unprecedented insight into the experiences and views of patients and highly experienced osteotomy surgeons. New research questions were generated that otherwise might not have been realised through quantitative measures. Since qualitative research is non-existent in the HTO literature, the inclusion of qualitative studies in this thesis is one of the project’s major strengths.

The inclusion of control groups in Chapters 5, 6, and 10 were major strengths of their respective studies, particularly the age-matched control group in the latter. However, the lack of randomisation of participants into each group in Chapters 6 and 10 limit the studies somewhat. Randomisation was not possible in Chapter 6 due to its retrospective nature, and it would have been inappropriate for the study design in Chapter 10 for ethical reasons. Chapters 6 and 9 were limited by the risk of recall bias – inherent due to their retrospective designs – and the use of self-reported questionnaires meant that there was a risk of subjectivity bias. Similar questionnaires were used for the gait study in Chapter 10 (meaning subjectivity bias was a possible limitation) but the prospective lab-based design of that study was one of its strengths.

Each of the studies presented in this thesis had various strengths and limitations, meaning that definitive conclusions are therefore difficult to make solely based on them. Similar trends and examples of similar phenomena previously reported in the literature – for example, pertaining to high-impact activity participation after surgery – lend support to the presented data and their interpretations. Future research involving randomised controlled trials would provide high level evidence that would serve to confirm or reject the claims made throughout this thesis. However, such study designs are often difficult to conduct for various financial, temporal, practical, and ethical reasons. Therefore, studies such as the ones presented in this thesis offer potential insights into the effectiveness of surgical treatments and, when combined with the results of similar studies elsewhere in the literature, can help justify or question the continuation of practices in order to provide the best possible outcomes for patients.

11.7 Future research

Throughout this thesis, each study was conducted to answer a number of research questions and to satisfy various aims. However, a by-product of those studies arose in the form of the generation of questions for future research that could either act as a complimentary continuation of this PhD project, or as a starting point for other research within the field of HTO more generally.

Chapter 5 supported the use of allograft wedges during HTO, particularly considering that post-operative rehabilitation protocols involving early full weightbearing are increasingly being reported with positive results (Brinkman *et al.*, 2010; Brosset *et al.*, 2011; Hernigou *et al.*, 2015; Schröter *et al.*, 2017). The added stability that graft materials were shown to provide to the osteotomy construct may translate to more favourable results with an early weightbearing protocol compared to HTO with an unfilled gap. A comparative study to compare the effect of HTO with and without graft materials on the results of an early weightbearing protocol would therefore be of merit.

An additional implication for the results presented in Chapter 5 related to the suitability of a high BMI (>30 kg/m^2) as a relative contraindication for HTO. Traditionally, a high BMI would preclude patients from HTO surgery due to being associated with less favourable results in terms of functional outcome, complication rate, and time to conversion to arthroplasty (Spahn, Kirschbaum and Kahl, 2006; Miller *et al.*, 2007; Song *et al.*, 2010; Meidinger *et al.*, 2011; Zuiderbaan *et al.*, 2016). However, it has also been suggested that patients with high BMI should not necessarily be automatically contraindicated for HTO, since satisfactory outcomes are possible (Kolb *et al.*, 2012; Floerkemeier *et al.*, 2014; Siboni *et al.*, 2018; Parkar, Pastides and Khakha, 2020). Furthermore, the published results from Chapter 5 have recently been used as partial justification for the recommendation of bone graft use during HTO specifically for patients with a high BMI, due to the added strength they provide to the osteotomy construct (Parkar, Pastides and Khakha, 2020). Studies comparing the outcomes of patients with high and low BMI that undergo HTO with graft materials are lacking and should therefore be conducted to confirm this apparent move away from a high BMI as a surgical contraindication.

Chapter 6 found a difference in pre- to post-operative physical activity levels between patients who underwent HTO with and without allograft bone wedges at a mean 2.8 ± 1.2 years after surgery. The literature indicates that patients who underwent HTO with graft materials generally experienced a pre- to post-operative increase in activity within the first two years (Brinkman *et al.*, 2010; Nerhus *et al.*, 2017). A longer-term study suggested that increases in activity levels were still observable at a mean 6.4 ± 1.6 years after surgery (Schröter *et al.*, 2013). Conversely, research is equivocal regarding whether a pre- to post-operative increase in activity levels occurs within the first two years after surgery in patients who underwent HTO without graft materials (Faschingbauer *et al.*, 2015; Krych *et al.*, 2017).

Furthermore, Salzmann *et al.* (2009) and Saragaglia *et al.* (2014) conducted longer-terms studies and found that activity levels in HTO patients where no graft was used did not change, or decreased, compared to pre-operative levels at a mean 3.0 ± 0.7 years and 5.8 ± 1.3 years after surgery, respectively.

The results presented in Chapter 6 support the suggestion that HTO with grafting results in a sustained increase in pre- to operative activity levels, whereas HTO without grafting results in the maintenance of pre-operative levels in the mid-term. However, it is not known how these patterns progress in the long-term to the endpoint of the osteotomy. Understanding this would provide insight into the sustained, long-term impact of bone grafting on activity levels and the longevity of the osteotomy. This would have implications for long-term health-related quality of life since that is correlated with physical activity levels (Bize, Johnson and Plotnikoff, 2007). If differences in survivorship were significant, this may also have financial implications regarding the cost-effectiveness of using bone grafts during HTO (Bhandari *et al.*, 2012; Konopka *et al.*, 2015; Smith *et al.*, 2017). Therefore, a longitudinal multiple follow-up comparative study measuring activity levels and survivorship in patients who undergo HTO with and without graft materials is warranted.

The inclusion of participants who underwent HTO with different internal plate fixators in Chapter 6 was cited as a potential confounding variable. Different plate fixators affect the osteotomy in terms of time-to-union, complication rates, and biomechanical stability (Amendola and Bonasia, 2010; Cotic *et al.*, 2015; Diffo Kaze *et al.*, 2019). However, the degree to which different plate fixators interact with post-operative physical activity levels is unknown. This makes it difficult to determine whether plates were a confounding variable that significantly skewed the data in Chapter 6. A study to investigate a link between different plate fixators and post-operative activity levels would help determine the validity of the results in Chapter 6. It would also be of interest more generally when considering that HTO is indicated for active patients.

The need to eventually remove the fixation plate was a controversy unearthed in Chapter 8, which coincided with a lack of research in this area. There is limited evidence to support a possible link between the removal of the plate and an observed increase in functional outcome in the second post-operative year, however this remains to be confirmed and is largely anecdotal (Niemeyer *et al.*, 2010; Bode *et al.*, 2015; Goshima *et al.*, 2019). Irritation around the site of the fixation plate has been reported as a relatively common occurrence for HTO patients (Kolb *et al.*, 2012; Uquillas *et al.*, 2014). The implications this may have on outcomes in the mid- to long-term, if left in-situ, are unknown. Therefore, comparative studies investigating plate removal are warranted.

This thesis has provided evidence that supports the routine use of allograft bone wedges during HTO. However, acknowledgement has also been given to issues that prevent the possibility of using bone grafts: surgeon’s preference (Chapter 8), financial costs, and access to a bone bank with sufficient stock and capability to properly sterilise grafts in order to minimise the risk of disease transmission (Amendola and Bonasia, 2010; Santic *et al.*, 2010; Hung and Noi, 2012; Parkar, Pastides and Khakha, 2020). As such, there remains a place for HTO where the gap is left unfilled. Further research is required to improve the consistency and level of functional outcomes of HTO without grafting, which were shown to be inferior to HTO with grafting in Chapter 6. Investigations into steps that can be taken to achieve consensus between surgeons and to reduce the financial costs of, and increase access to, allograft bone wedges may similarly be helpful.

The qualitative studies presented in Chapters 7 and 8 highlighted a need for future research to be conducted on the need for, and impact of, plate removal on overall outcome. The literature suggests that irritation and plate-related pain are the major reasons that implants are removed after surgery (Aryee *et al.*, 2008; Bode *et al.*, 2015; Ghinelli *et al.*, 2016; Goshima *et al.*, 2019). Some of the participants in Chapter 8 reported routinely removing the plates irrespective of whether patients developed complications or not; citing an observed further incremental improvement in outcome once the plate was removed. This observation has been noted by some in the literature, although also anecdotally, as an aside to the main focus of the study (Niemeyer *et al.*, 2010; Bode *et al.*, 2015; Goshima *et al.*, 2019). Literature around plate removal specifically is lacking, and where it exists the focus is mainly on the optimal time to remove the plate (12-18 months after surgery), rather than any subsequent effect on the outcome (Aryee *et al.*, 2008; Brinkman *et al.*, 2008; Lind-Hansen *et al.*, 2016; Goshima *et al.*, 2019). This clear gap in the research, combined with the anecdotal observations of incremental improvements after removal, suggest that there is scope for this area to be investigated further.

The final recommendation for future research relates to building upon the results and conclusions presented in Chapter 10. The exercise protocol performed by each participant was relatively short (8 bouts of 3 minutes), meaning that caution should be taken when making recommendations relating to longer periods of exercise like prolonged jogging. Chapter 10 demonstrated that pain levels remained low and that a normal gait was exhibited by HTO patients compared with age-matched healthy controls, irrespective of exercise intensity.

Studies investigating the effects of time on these variables would allow for firmer conclusions to be made as to the ability of patients to perform high-impact exercise after HTO, which would have implications for patient expectation management and health-related quality of life.

The research in this thesis more generally can only be said to be applicable to the outcomes of HTO in the short- to mid-term after surgery. Future research is needed to investigate physical activity over time and the effects of higher activity levels – particularly the participation in high-impact activities – on survivorship of the osteotomy. HTO is intended to delay the need for a knee replacement, therefore survivorship is of utmost importance and should become a focus for future research as it pertains to post-operative physical activity.

11.8 Recent updates in the literature

The studies presented in this thesis were justified, in part, by the literature review conducted prior to any of the investigations taking place. Since the beginning of this project, many studies have subsequently been published. These studies have not been added to the initial literature review as it would be misleading to suggest that they were considered prior to this project taking place. However, some of these publications are extremely relevant to the findings presented in this thesis, therefore the following section briefly presents an overview of these studies and an explanation of their implications for the conclusions drawn from this project.

11.8.1 Return to physical activity

Several studies have been published recently relating to physical activity and HTO. Jacquet *et al.* (2020) conducted a retrospective cohort study comparing return to physical activity after HTO and UKA in patients who reported having high activity levels pre-symptomatically (UCLA score >8). HTO patients returned to physical activity sooner after surgery than UKA patients, and at 24 months post-operatively activity scores were significantly higher in HTO patients. Post-operative UCLA scores in both groups were higher than pre-operative UCLA scores, however neither group returned to pre-symptomatic levels. The difference between pre-symptomatic UCLA scores and post-operative scores was significantly smaller in HTO patients, suggesting that they experienced a larger benefit from the surgery in terms of physical activity levels. Furthermore, 62% of HTO patients participated in impact sports at final follow-up compared with 28% of UKA patients. These results verify and support the findings of the systematic review in Chapter 4, which concluded that HTO is preferable to UKA for physically active patients.

Kanto *et al.* (2020) also conducted a study involving HTO patients who were highly active pre-symptomatically (Tegner scores >5). Similar to the results of Jacquet *et al.* (2020), most patients (75.3%) returned to high-impact activities 24 months after surgery but mean pre-symptomatic Tegner activity levels were not achieved. Pre-operative activity levels were not assessed; however it was reported that patients decreased their activity levels prior to surgery (due to pain) compared to their pre-symptomatic levels. The operated knee was cited as a limiting factor for activity in 22% of patients, although only 14% did not return to their pre-symptomatic level of activity: 5% of whom cited a lack of interest in sports participation as the reason for their reduction in activity levels.

There was a clear difference in the graft material used during HTO and the mean time to return to physical activities between the two aforementioned studies. Jacquet *et al.* (2020) included allograft wedges in all HTO patients, who returned to activity at a mean 4.9 ± 2.2 months after surgery versus 8.7 ± 2.7 months in the Kanto *et al.* (2020) study where synthetic grafts were used. Chapter 9 – which included patients who underwent HTO with an allograft wedge or without grafting – identified the 3-6 month period as when most patients returned to high-impact activities. These recent studies lend further support to the argument that HTO with allograft wedges and HTO without grafting are preferable options to HTO with synthetic grafting in physically active patients.

A final study – which included a case report of patients who underwent HTO with and without synthetic grafts – observed similar patterns to the two previously mentioned publications (Nakamura *et al.*, 2020). Mean pre-symptomatic Tegner scores (5.9 ± 1.1) were significantly higher than pre-operative Tegner scores (2.8 ± 1.1), and patients returned to a level similar to their pre-symptomatic status 24 months after HTO (5.8 ± 1.1). The study did not mention time to return to pre-operative activity levels but did report a mean time of 14.2 ± 3.9 months for a return to pre-symptomatic physical activity. Each of these studies support the conclusions drawn in this thesis that HTO suitably allows patients to return to high-impact activities after surgery, and there is some evidence to support the claim that allograft wedges or no grafting are superior options to synthetic grafts with regard to post-operative outcomes.

The results of these three recently published studies demonstrate an important difference between the terms “pre-operative” and “pre-symptomatic”, which are often not clearly defined in other publications. It is difficult to acquire pre-symptomatic data prospectively for obvious reasons, and recall bias is therefore an issue when being retrospectively estimated. However, HTO outcomes should strive to allow patients to return to activity levels as close to pre-symptomatic levels as possible. Returning merely to pre-operative levels should not be the aim of HTO since it is likely that these levels were already reduced due to arthritic pain (Kanto *et al.*, 2020). This further supports the notion that techniques to improve upon, rather than equal, pre-operative activity levels should be recommended for active patients.

11.8.2 Graft materials

The main source of autografts for use in HTO is from the iliac crest, which is considered the gold-standard (Slevin *et al.*, 2016; Parkar, Pastides and Khakha, 2020). However, their associated disadvantages of prolonged operative time, donor site morbidity, and increased post-operative pain make alternative graft options attractive. This thesis recommends the use of allograft wedges over autografts (and synthetic wedges) due to their comparative low-risk disadvantages and comparable, or superior, clinical outcomes (Chapters 5 and 6; Han *et al.*, 2015; Lash *et al.*, 2015; Slevin *et al.*, 2016).

A biomechanical study was published comparing gap pressures in HTO against the compressive strength of allograft wedges (Yoon *et al.*, 2020). It found that gap pressure increased with gap size and that the compressive strength of allograft wedges was up to 13.7 times greater than an HTO with a (large) 14 mm gap size. This supports previously reported recommendations for the use of grafts in HTO with a gap size >10 mm (Lobenhoffer and Agneskirchner, 2003; Yacobucci and Cocking, 2008; Jung *et al.*, 2010; Santic *et al.*, 2010). The results also support the findings presented in Chapter 5 pertaining to the additional strength and stability that allograft wedges provide to an osteotomy construct.

Clinically, a recent study compared the use of synthetic chips versus allograft bone chips as a filler for HTO (Lee *et al.*, 2020). 24 months after surgery, functional results between groups were similar, however the synthetic grafts displayed inferior absorbability compared to the allografts. A similar finding was reported 4 years post-operatively when synthetic grafts were used during HTO (Putnis *et al.*, 2020). Although functional outcomes remained good at follow-up, the continued radiological evidence of the presence of synthetic grafts demonstrated that resorption did not fully occur. If this trend were also to be observed in the long-term, it was suggested that there may be implications for the performance of a future TKA (Putnis *et al.*, 2020). Therefore, allograft wedges remain preferable to synthetic grafts.

A final study investigated the outcome of HTO filled with a combination of synthetic grafts and autografts sourced from the distal femur (Group A) compared against HTO with no grafting (Group B) and HTO with solely synthetic grafting (Group C) (Jung *et al.*, 2020). Group A resulted in significantly reduced time-to-union (3.4 ± 1.5 months versus 7.2 ± 3.2 months in

Group B and 8.3 ± 3.1 months in Group C). It also found that Group A outcome scores were significantly higher (better) at 6 months compared to the other two groups but that these differences disappeared at final follow-up (22 months post-HTO). The study supports claims made in this thesis that HTO with synthetic grafts is less desirable than other options in terms of time-to-union. However, the combination of synthetic grafting with an autograft eliminated this disadvantage and resulted in a significantly quicker improvement in functional outcomes compared to HTO without grafting.

Furthermore, the sourcing of the autografts from the distal femur seemingly negated the known disadvantages associated with iliac crest autografts. It was reported that the total operative time between groups was "minimally longer" in Group A and that there was no associated donor site morbidity due to the minimally invasive approach taken. Mild pain was experienced as a result of the autograft harvesting procedure, but it required no extra intervention. Since the study did not include a group with allograft wedges, comparisons to studies in this thesis are difficult to make. However, these results show promise for alternative methods of incorporating synthetic and autografts in HTO, since it appears that some of the disadvantages associated with both types can be mitigated to a significant degree. Until such time that future research confirms the findings of Jung *et al.* (2020), allograft wedges remain the recommended graft type by this thesis.

11.8.3 Lateral hinge fractures

Studies investigating the effects of lateral hinge fractures confirmed previous findings with regard to increased delayed union (Kumagai *et al.*, 2020; Song *et al.*, 2020). Once union had been achieved, functional outcomes did not appear to be affected within 12 months of surgery (Song *et al.*, 2020). One study included patients who underwent HTO with synthetic grafts (Kumagai *et al.*, 2020), and another comprised a single group of patients who underwent HTO with allograft bone chips (n=123), no filler (n=8), and one patient who received an autograft due to being a smoker (Song *et al.*, 2020). Delayed union occurred in patients who experienced a lateral hinge fracture irrespective of whether they underwent HTO with allograft, synthetic wedges, or no filler. These findings support current recommendations for the use autografts in cases where hinge fractures occur due to their superior osteoconductive properties (Slevin *et al.*, 2016).

CHAPTER 12 – CONCLUSION

This thesis aimed to investigate return to physical activity after high tibial osteotomy with and without graft materials, with the intention of providing evidence-based recommendations for future practice to improve physical activity outcomes for patients. High tibial osteotomy was shown to be preferable to unicompartmental knee arthroplasty for young, active patients and the long-term implications pertaining to subsequent total knee arthroplasty revisions and cost-effectiveness remain favourable over UKA.

Outcomes after HTO are generally positive when performed in appropriately selected patients. Much of the literature indicates improved knee function, reduced pain, and a return to physical activity to a level equal to, or greater than, a patient's pre-operative status after surgery. However, the proportion of patients who equal their pre-operative activity levels is significantly larger than those who improve pre- to post-operatively. Since being physically active is an indicative criterion for HTO over other treatment options, it is important that patients can return to physical activity after surgery with as little restriction caused by the operated knee as possible. Nevertheless, the operated knee is often cited by patients as a limiting factor regarding post-operative participation in physical activities; particularly those involving high-impact movements.

This thesis found that allograft wedges are superior overall in comparison to other graft materials due to their comparable positive outcomes and lower-risk disadvantages. Including allograft wedges in HTO is preferable to leaving the gap unfilled because of the superior strength and stability they provide to the osteotomy construct. The biomechanical advantage that allograft wedges provide compared to an unfilled osteotomy gap translated clinically to differences in pre- to post-operative physical activity levels. Those patients who underwent HTO with allograft wedges significantly improved their pre- to post-operative physical activity levels, and were more likely to have clinically significant improvements in their knee function, compared with those who underwent HTO without grafting. Therefore, the routine use of allograft wedges during HTO is recommended.

A lack of confidence in the knee, fear of pain or reinjury, residual pain, and a reported lack of guidance from 6 months after surgery were also highlighted as factors that influence HTO patients regarding post-operative physical activity levels. Surgeons reported that informing patients and managing realistic expectations of the post-operative outcome were of prominent importance. However, a lack of consensus around predicted post-operative ability and timelines for achieving post-operative milestones suggested that there was scope for improving the accuracy of patient expectations. Understanding pain and providing information pertaining to post-operative milestones became a major focus of this thesis.

Physical activity levels were negatively correlated with pain. Pre-operative pain levels were shown to have decreased within 1 month of surgery (significantly so by 3 months), which continued to decline until 12 months post-operatively. Patients can expect to return post-operatively to the same activities they performed pre-operatively, and can often increase the number of activities participated in. Walking on even ground within 1 month of surgery and returning to most pre-operative activities by 3 months, including "high-impact" ones that do not involve twisting of the knee, is expected. Twisting activities can be performed after 6 post-operative months. Residual pain was more noticeable during high-impact physical activity although levels remained very low on average. Spatiotemporal gait parameters during low- and high-impact activity were comparable to those of age-matched healthy controls. Low post-operative pain levels are commonly seen as the prime indicator of a successful outcome after HTO. While this is appropriate, maximising pre- to post-operative changes in physical activity levels should also be viewed as a major aim, since being active is a key indication for the procedure.

Osteotomy is a form of surgery based on a principle that dates back hundreds of years. Adjusting a weightbearing line that passes through a painfully overloaded joint compartment, and preserving the native knee, is still very much relevant today. This is despite the advent of reconstructive techniques that have gained prominence over the last few decades. In a world where many developed countries comprise of aging populations, methods of maintaining a good quality life in old age are becoming increasingly important. By undergoing a joint preserving opening-wedge HTO with allografts – where expectations have been accurately managed – patients can return to physical activity after surgery with few restrictions, while simultaneously delaying the need for reconstructive surgery. This has obvious implications for patients who require a high level of function to work, or for those who are recreationally active for social, physical health, and mental health reasons. Osteotomy is a procedure with a long past. But what about its future? Participant S14 from Chapter 8 said it best:

> "I'm excited about [osteotomy]. I always have been, I always will be. I think it is going to make a change to the way that we conduct knee surgery. I would really like to see us move away from the somewhat binary approach to how we approach this problem. If you look at diversity on this planet […] everybody's an individual and what they need

is a bespoke approach to their problem. And osteotomy, because it is a bespoke operation, is actually capable of offering that.

It's a subject I feel passionately about and I really genuinely think that we have an opportunity in the next decade or two to change the way in which we conduct knee surgery. It's probably going to come from educating younger surgeons and patients to the possibilities; so they're aware of this as an option. But the more we do the surgery, the more it will become available, the more other patients will talk about it to their friends. That's where we should be heading so that we avoid this inevitable revision burden that is massively going to escalate. And instead of addressing the problem by training more revision surgeons to spend forever chopping knees out and replacing them with bigger pieces of metal, we should just think a little bit more carefully about what we're doing at the outset before we embark upon arthroplasty as the first operation. So who knows where it's going to go? It seems to be expanding and I hope it continues to do so."

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Clinical Sports Medicine Update

Return to Physical Activity After High Tibial Osteotomy and Unicompartmental Knee Arthroplasty

A Systematic Review and Pooling Data Analysis

James Belsey,*† MA, Sam K. Yasen,‡ MBBS, Simon Jobson,† PhD, James Faulkner,† PhD, and Adrian J. Wilson,§ MBBS, BSc
Investigation performed at Department of Sport, Exercise and Health, University of Winchester, Winchester, UK

Background: The 2 most common definitive surgical interventions currently performed for the treatment of medial osteoarthritis of the knee are medial opening wedge high tibial osteotomy (HTO) and medial unicompartmental knee arthroplasty (UKA). Research exists to suggest that physically active patients may be suitably indicated for either procedure despite HTO being historically indicated in active patients and UKA being more appropriate for sedentary individuals.

Purpose: To help consolidate the current indications for both procedures regarding physical activity and to ensure that they are based on the best information presently available.

Study Design: Systematic review.

Methods: A search of the literature via the MEDLINE, Embase, and PubMed databases was conducted independently by 2 reviewers in accordance with the PRISMA (Preferred Reporting Items for Systematic Meta-Analyses) guidelines. Studies that reported patient physical activity levels with the Tegner activity score were eligible for inclusion. Patient demographics, operative variables, and patient-reported outcome scores were abstracted from the included studies.

Results: Thirteen eligible studies were included, consisting of 401 knees that received HTO (399 patients) and 1622 that received UKA (1400 patients). The patients' mean age at surgery was 48.4 years for the HTO group and 60.6 years for the UKA group. Mean follow-up was 46.6 months (HTO) and 53.4 months (UKA). All outcome scores demonstrated an equal or improved score for activity and knee function regardless of the operation performed. Operative variables during HTO had a larger effect on outcome than during UKA.

Conclusion: Patients who underwent HTO were more physically active pre- and postoperatively, but patients undergoing UKA experienced an overall greater increase in their physical activity levels and knee function according to Tegner and Lysholm scores. Activity after HTO may be influenced by operative factors such as the implant used and the decision to include graft material in the osteotomy gap, although this requires further research. Some studies found that patients were able to return to physical activity postoperatively despite having an age or body mass index that would traditionally be a relative contraindication for HTO or UKA.

Keywords: high tibial osteotomy; unicompartmental knee arthroplasty; unicondylar knee arthroplasty; physical activity; return to sport; outcome; quality of life; indications; knee replacement

The 2 most common definitive surgical interventions currently performed for the treatment of medial osteoarthritis (OA) of the knee are medial opening wedge (OW) high tibial osteotomy (HTO) and medial unicompartmental knee arthroplasty (UKA). The traditional indications for HTO include unicompartmental OA, tibial deformity, no extreme knee instability, >120° range of motion, age <60 years, physically active, and body mass index (BMI) <30 kg/m^2.[1,7,60] The traditional indications for UKA include unicompartmental OA, age >60 years, angular deformity <15°, low functional demands, and BMI <82 kg.[14,15,60] However, a wide body of research exists to suggest that good outcomes can be achieved with either procedure well outside these traditional indications. Specifically, physically active patients may be suitably indicated for either procedure.[10,14]

Surgeons have historically favored HTO when presented with physically active patients and opted for UKA in cases of more sedentary individuals.[50] A recent study, however, showed that patients who underwent UKA for

The American Journal of Sports Medicine
1–9
DOI: 10.1177/0363546520948861

APPENDIX B – PUBLICATIONS FROM CHAPTER 5

Belsey *et al. Journal of Experimental Orthopaedics* (2019) 6:13
https://doi.org/10.1186/s40634-019-0184-6

Journal of Experimental Orthopaedics

RESEARCH Open Access

Graft materials provide greater static strength to medial opening wedge high tibial osteotomy than when no graft is included

James Belsey[1,5*], Arnaud Diffo Kaze[2,3], Simon Jobson[1], James Faulkner[1], Stefan Maas[2], Raghbir Khakha[5], Adrian J. Wilson[4] and Dietrich Pape[3]

Abstract

Background: The purpose of this study was to compare the stability of medial opening-wedge high tibial osteotomy (MOWHTO) with and without different graft materials. Good clinical and radiological outcomes have been demonstrated when either using or not using graft materials during MOWHTO. Variations in the biomechanical properties of different graft types, regarding the stability they provide a MOWHTO, have not been previously investigated.

Methods: A 10 mm biplanar MOWHTO was performed on 15 artificial sawbone tibiae, which were fixed using the Activmotion 2 plate. Five bones had OSferion60 wedges (synthetic group), five had allograft bone wedges (allograft group), and five had no wedges (control group) inserted into the osteotomy gap. Static compression was applied axially to each specimen until failure of the osteotomy. Ultimate load, horizontal and vertical displacements were measured and used to calculate construct stiffness and valgus malrotation of the tibial head.

Results: The synthetic group failed at 6.3 kN, followed by the allograft group (6 kN), and the control group (4.5 kN). The most valgus malrotation of the tibial head was observed in the allograft group (2.6°). The synthetic group showed the highest stiffness at the medial side of the tibial head (9.54 kN·mm^{-1}), but the lowest stiffness at the lateral side (1.59 kN·mm^{-1}). The allograft group showed high stiffness on the medial side of the tibial head (7.54 kN·mm^{-1}) as well as the highest stiffness on the lateral side (2.18 kN·mm^{-1}).

Conclusions: The use of graft materials in MOWHTO results in superior material properties compared to the use of no graft. The static strength of MOWHTO is highest when synthetic grafts are inserted into the osteotomy gap. Allograft wedges provide higher mechanical strength to a MOWHTO than when no graft used. In comparison to the synthetic grafts, allograft wedges result in the stiffness of the osteotomy being more similar at the medial and lateral cortices.

Keywords: Tibial osteotomy, Allograft, Synthetic graft, Biomechanical analysis, Static strength, Activmotion plate

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Full list of author information is available at the end of the article

PLOS ONE

RESEARCH ARTICLE

The biomechanical effects of allograft wedges used for large corrections during medial opening wedge high tibial osteotomy

James Belsey[1,2☯*], Arnaud Diffo Kaze[3,4☯], Simon Jobson[1‡], James Faulkner[1‡], Stefan Maas[3‡], Raghbir Khakha[2], Dietrich Pape[4☯], Adrian J. Wilson[5‡]

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☯ These authors contributed equally to this work.
‡ These authors also contributed equally to this work.
* jbelsey89@gmail.com

OPEN ACCESS

Citation: Belsey J, Diffo Kaze A, Jobson S, Faulkner J, Maas S, Khakha R, et al. (2019) The biomechanical effects of allograft wedges used for large corrections during medial opening wedge high tibial osteotomy. PLoS ONE 14(5): e0216660. https://doi.org/10.1371/journal.pone.0216660

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Data Availability Statement: All raw data files are available from the FigShare database at the following link: https://figshare.com/articles/Data_for_Plos_One_xlsx/7498835.

Funding: The allograft wedges used in this study were provided by RTI Surgical Inc (http://www.rtix.com), who also sponsor the PhD course being undertaken by the lead author [JB] at the University of Winchester, UK. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Abstract

The inclusion of an allograft wedge during medial opening wedge high tibial osteotomy has been shown to lead to satisfactory time-to-union in larger corrections (>10˚). Such large corrections are associated with greater incidences of intraoperative hinge fracture and reduced construct stability. The purpose of this study was to investigate the biomechanical stability that an allograft wedge brings to an osteotomy. Ten medium-size fourth generation artificial sawbone tibiae underwent 12 mm biplanar medial opening wedge high tibial osteotomy with a standard Tomofix plate. Five tibiae had an allograft wedge inserted into the osteotomy gap prior to plate fixation (allograft group). The gap in the remaining tibiae was left unfilled (control group). Each group underwent static compression testing and cyclical fatigue testing until failure of the osteotomy. Peak force, valgus malrotation, number of cycles, displacement and stiffness around the tibial head were analysed. Intraoperative hinge fractures occurred in all specimens. Under static compression, the allograft group withstood higher peak forces (6.01 kN) compared with the control group (5.12 kN). Valgus malrotation was lower, and stiffness was higher, in the allograft group. During cyclical fatigue testing, results within the allograft group were more consistent than within the control group. This may indicate more predictable results in large osteotomies with an allograft. Tibial osteotomies with allograft wedges appear beneficial for larger corrections, and in cases of intraoperative hinge fracture, due to the added construct stability they provide, and the consistency of results compared with tibial osteotomies without a graft.

APPENDIX C – LETTER OF ETHICAL APPROVAL FOR STUDY IN CHAPTER 5

THE UNIVERSITY OF WINCHESTER

Friday 13th January

James Belsey

Department of Sport & Exercise

University of Winchester

Sparkford Road

Winchester SO22 4NR

Dear Mr James Belsey,

Re: Faculty of Business, Law and Sport RKE Ethics Application [BLS/17/01]

Title: *The use of bone grafts on the strength & stability of high tibial osteotomy*

Thank you for your submission to the University of Winchester, Faculty of Business Law and Sport (BLS) ethics panel.

On behalf of the Faculty of BLS RKE Ethics Committee I am pleased to advise you that the ethics of your application have been approved. Approval is for five years and is for the documentation submitted for review on 12/12/16. If the project has not been completed within five years from the date of this letter, re-approval must be requested.

If the nature, content, location, procedures or personnel of your approved application change, please advise the Head of the Faculty BLS ethics committee.

Yours sincerely

Prof. M. Burke.

Prof. Maria Burke

Head of Research & Knowledge Exchange

University of Winchester

Dr James Faulkner, Head of Ethics in the Faculty of BLS
Email: James.Faulkner@winchester.ac.uk; Tel: +44 (0)1962 624932

APPENDIX D – METHODS AND PRELIMINARY TRENDS IN ONGOING RESEARCH

It was mentioned in Chapter 6 that the study presented was not the one originally planned that aimed to investigate differences in physical activity levels between patients who underwent HTO with and without allograft wedges. For reasons that were outlined in Section 6.2, the original study was not able to be completed within the timeframe of this PhD project, and data collection is ongoing. In the interest of transparency and completeness, the methods and early results will now be presented.

i) Methods

Study design

This is a non-randomised prospective comparative study containing an experimental group and a control group. A repeated measures design is being employed with data collection occurring at four time points, which coincide with normally-scheduled patient appointments at the hospital: pre-operatively, 1 day post-operatively, 6 weeks post-operatively, and 12 weeks post-operatively.

Participants

Patients scheduled to undergo medial opening wedge HTO either with or without an allograft wedge are being prospectively recruited to participate in this study. Patients undergoing simultaneous procedures (other than arthroscopy) are excluded from participation.

A power analysis was performed a priori using the results of a previous study (Ryan *et al.*, 2009) which used accelerometery data to track the physical activity of patients with lower back pain compared to healthy controls. To achieve an effect size of d=0.58, with an alpha error probability of 0.05 and power of 0.8, and to account for dropouts and data corruption due to hardware failure, a total of 60 patients (30 per group) were required to participate. At the time of writing, 6 patients have completed participation in the allograft group and only 1 in the control group has returned a complete data set. Consequently, comparisons between groups are not yet possible. However, early trends within the allograft group can be seen, and it is these that are presented here.

Outcome measures

Knee function and physical activity levels are measured at each time point using a combination of subjective and objective methods. KOOS, Tegner, and UCLA scores provide subjective patient-reported measures, and an accelerometer worn for 7 days at each time point collects objective activity information pertaining to number of steps, energy expenditure, and time spent lying/sitting, standing, and stepping.

Data analysis

A repeated measures ANOVA will be conducted once a full dataset has been collected to analyse any differences that may emerge between groups in the subjective and objective measures. Correlations (Pearson's *r*) will be calculated to assess the relationship between the subjective and objective measures of physical activity. The subjective measures are commonly used in clinical practice to assess surgical outcome. Correlating these scores with the objective measures of activity will help determine the extent to which the commonly used subjective measures offer an accurate reflection of the patient's outcome.

As mentioned above, there are only complete datasets for 6 patients in the allograft group and 1 in the control group. For the purposes of reporting early trends in the data, no comparisons between groups could be made. However, graphs showing the mean subjective and objective results of the allograft group have been plotted and presented below. Due to the small number of patients, statistical analysis has not been conducted and conclusions based on the preliminary emerging trends are tentative and subject to change.

ii) Results

Baseline demographic characteristics of the included patients can be found in Table D1 below.

Table D1: *Baseline patient demographics*

Characteristic	(Mean ± SD)
Patients (n)	6
Age at surgery (y)	50.0 ± 8.6
Sex (male:female)	4:2
BMI (kg/m^2)	31.4 ± 6.7
Smoking status (smoker:non-smoker)	1:5
Gap size (mm)	8.5 ± 1.9
Knee (right:left)	2:4

Figure D1 shows the mean changes in knee function over time according to the subscales of the KOOS questionnaires. Each subscale shows a similar trend: an initial reduction in knee function followed by a sharp improvement in function at 6 and 12 weeks post-operatively, with the exception of "Sports and recreation" and "Quality of life" where the observed improvement between 1 week and 6 weeks post-operatively was not as dramatic.

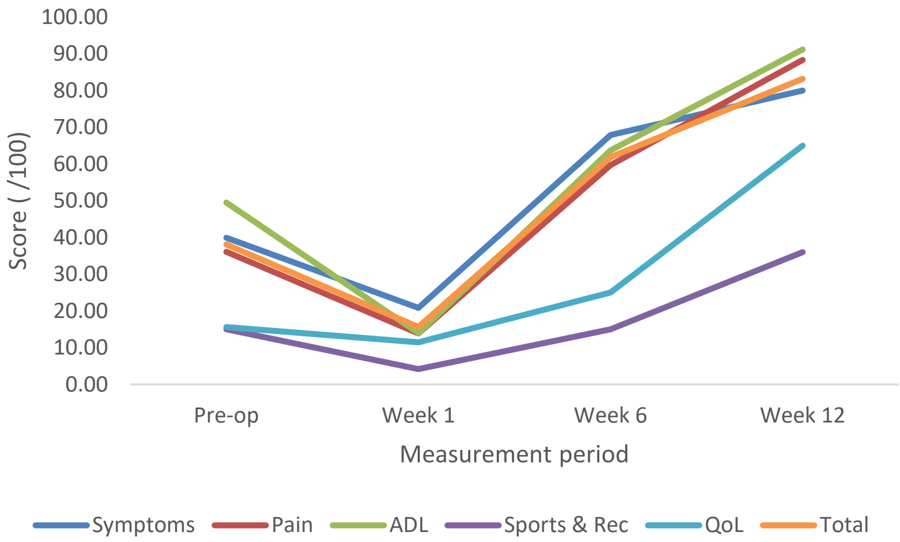

Figure D1: Mean KOOS subscale scores at each measurement period

ADL = Activities of daily living; QoL = Quality of life.

Figure D2 shows the changes in mean Tegner and UCLA activity scores over time. Pre-operative activity levels were significantly reduced 1 week after surgery, slightly reduced 6 weeks after surgery, and slightly increased 12 weeks post-HTO.

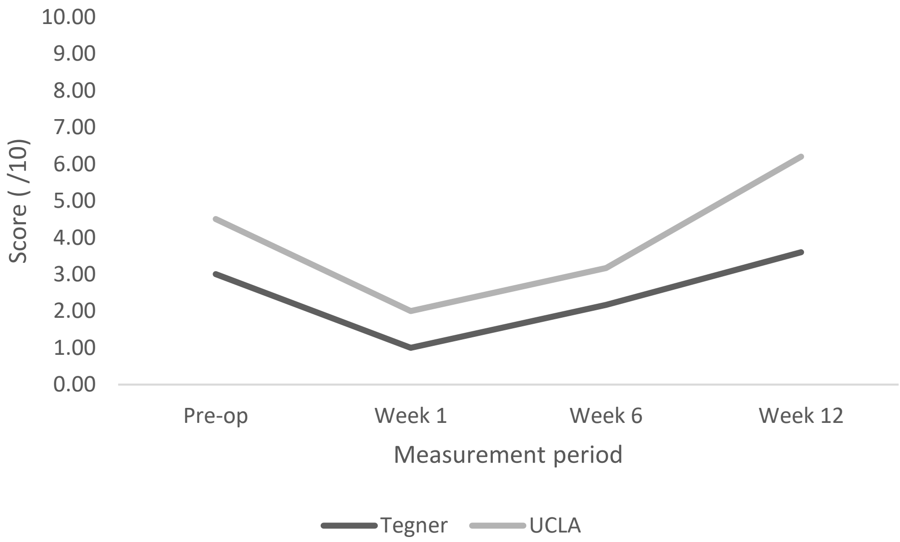

Figure D2: Mean Tegner and UCLA activity scores at each measurement period

Figure D3 shows the change in the mean number of steps taken daily at each time point. Pre-operative step numbers were not equalled or exceeded within the first 12 weeks after HTO.

Steps were drastically reduced in the first post-operative week but then sharply increased at 6 and 12 weeks after surgery.

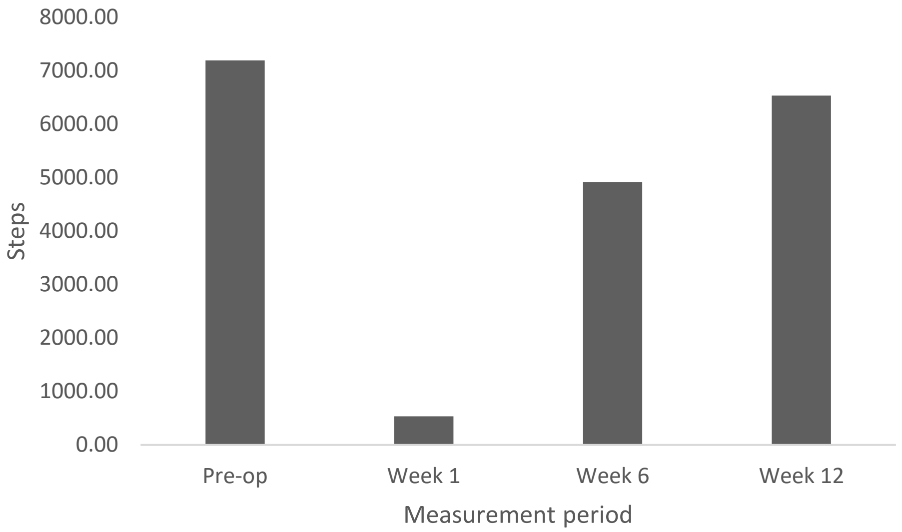

Figure D3: Mean daily step count at each measurement period

A similar trend can be seen in the changes in the mean number of daily sit-to-stands over time (Figure D4).

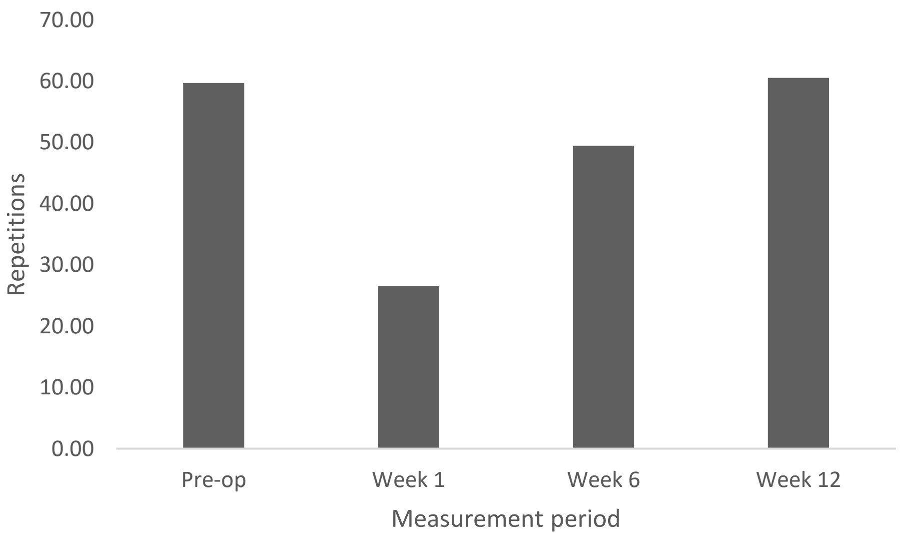

Figure D4: Mean daily sit-to-stands performed at each measurement period

Figure D5 shows the change in mean number of hours per day spent standing, stepping, or in a seated/lying position. A majority of a given day was spent either seated or lying down, <5 hours was spent standing, and <2 hours was spent stepping. This trend was reflected in Figure D6, which shows the number of hours per day spent performing activities at different exercise intensities. >20 hours per day was sedentary activity, <5 hours per day was light activity, and <1 hour per day was moderate-to-vigorous physical activity.

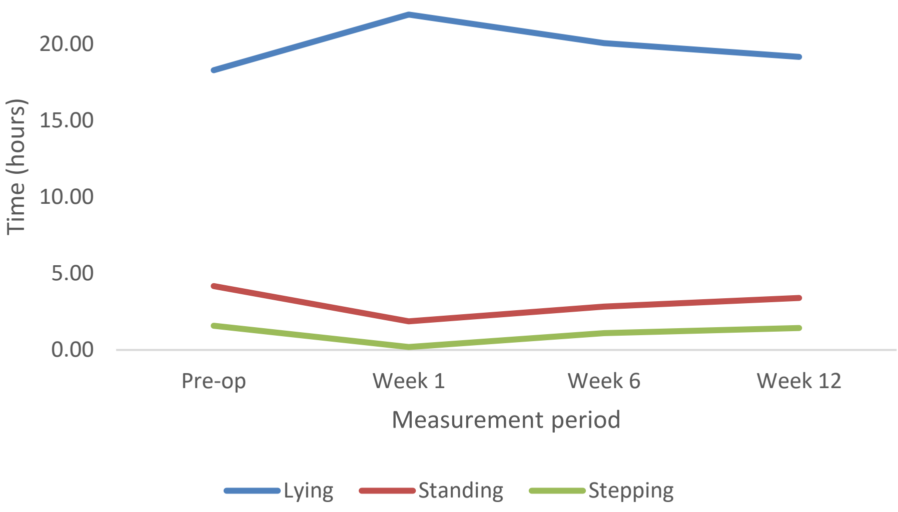

Figure D5: Mean daily hours spent seated/lying, standing, or stepping

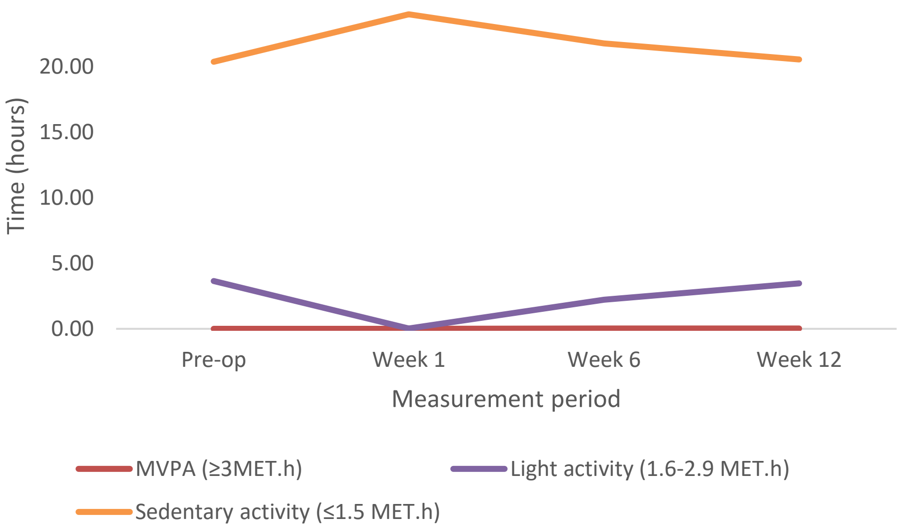

Figure D6: Mean daily hours spent at different activity intensities

MVPA = moderate-to-vigorous physical activity; MET.h = Metabolic equivalent of task, hours.

iii) Discussion

All of the results show a drop in function and activity levels in the first week after surgery combined with a noticeable increase in time spent lying/seated. Symptoms, pain, daily living activities and general knee function increased the most between week 1 and week 6 – rising to a level above that which was observed pre-operatively – and continued to improve up to 12 weeks post-operatively. Quality of life and subjective physical activity levels returned to pre-operative levels by week 6 and showed the greatest improvement between weeks 6 and 12. Objective activity levels showed the greatest improvement between week 1 and week 6 with a smaller continued improvement occurring until 12 weeks after surgery. Pre-operative activity levels were equalled, but not exceeded, within 12 weeks post-operatively, according to the objective measures. This may suggest that subjective measures of physical activity slightly overestimate the pre- to post-operative change in activity levels after HTO.

The pattern of the KOOS "pain" subscale was very similar to the pattern reported in Chapter 9 where pain significantly worsened in the first week after surgery but improved within 4-6 weeks and continued to improve to 12 weeks. The same can be said for the Tegner score, which was used in both studies, where pre-operative activity levels were decreased at 1 week and 6 weeks after surgery, but had returned close to pre-operative levels within 12 weeks. The results of the KOOS "activities of daily living" subscale support the findings in Chapter 9 whereby such activities were largely possible within 4-6 weeks of surgery with further increases at 12 weeks. The difference in pattern between the KOOS "ADL" and "Sports & Rec" subscales suggest that it is important to differentiate between types of physical activity since they require different lengths of time before they can be performed post-operatively. This is supported by the results of Chapter 9, which showed that a return to pre-operative rates of participation in different activities occurred at either 1 month, 3 months, or 6 months after surgery. The trend in the mean number of steps performed daily add context to the findings of Chapter 9 by showing that walking was clearly possible within 6 weeks of surgery, but the amount of walking performed was reduced compared to pre-operative levels. It was not until 12 weeks that number of daily steps approached pre-operative levels, which may explain why other physical activities were not performed at the same rate as pre-operatively until 12 weeks after surgery in Chapter 9.

iv) Conclusion

Knee function and pain improve at a different rate to physical activity and quality of life after HTO, but all measures equalled or exceeded pre-operative levels within 12 weeks of surgery.

Subjective measures of physical activity may overestimate actual post-operative activity levels. Although the results of this study are ongoing, the emerging preliminary trends largely support the retrospectively collected data presented in Chapter 9. Once finished, this study will be the first to provide objective physical activity data of HTO patients. It will also be the first prospectively conducted study to investigate differences in physical activity outcomes over time between patients that undergo HTO with and without graft materials. The results will build upon the findings of the first retrospectively conducted study with the same aim, which can be found in Chapter 6.

APPENDIX E – FORMS RELATING TO STUDY IN CHAPTER 6

i) Letter of ethical approval (University of Winchester)

UNIVERSITY OF WINCHESTER

Wednesday 9th January 2019

James Belsey

Department of Sport, Exercise & Health

Faculty of Business, Law and Sport

University of Winchester

Hants, SO22 4NR

Dear Mr James Belsey

Re: Faculty of Business, Law and Sport RKE Ethics Application [BLS/19/02]

Title: *Assessing physical activity of patients following high tibial osteotomy with and without bone grafting.*

Thank you for your submission to the University of Winchester, Faculty of Business Law and Sport (BLS) ethics panel.

On behalf of the Faculty of BLS RKE Ethics Committee I am pleased to advise you that you have received a favourable opinion for the ethical content of your application. Favourable opinion is for five years and is only for the documentation submitted for review on 06/01/19. If the project has not been completed within five years from the date of this letter, re-approval must be requested.

If the nature, content, location, procedures or personnel of your approved application change, please advise the Head of the Faculty BLS ethics committee.

Yours sincerely

Prof M. Burke

Professor Maria Burke

Head of Research, Faculty of BLS

University of Winchester

ii) **Letter of ethical approval (NHS)**

NHS
Health Research Authority

East Midlands - Leicester Central Research Ethics Committee
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

<u>Please note</u>: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

20 June 2018

Mr James Belsey
PhD student at University of Winchester and Honorary Researcher at Basingstoke & North Hampshire Hospital
University of Winchester
Dept of Sport, Exercise & Health
Sparkford Road
Winchester
SO22 4NR

Dear Mr Belsey

Study title:	**Assessing physical activity levels of patients following high tibial osteotomy (HTO) with and without bone grafting.**
REC reference:	**18/EM/0174**
Protocol number:	**UMT057/13**
IRAS project ID:	**242284**

Thank you for your letter of 15th June 2018, responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the sub-committee.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point,

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Mr James Belsey
PhD student at University of Winchester and Honorary Researcher at Basingstoke & North Hampshire Hospital
University of Winchester
Dept of Sport, Exercise & Health
Sparkford Road
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Email: hra.approval@nhs.net
Research-permissions@wales.nhs.uk

17 July 2018

Dear Mr Belsey

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Assessing physical activity levels of patients following high tibial osteotomy (HTO) with and without bone grafting.**
IRAS project ID:	**242284**
Protocol number:	**UMT057/13**
REC reference:	**18/EM/0174**
Sponsor	**University of Winchester**

I am pleased to confirm that HRA and Health and Care Research Wales (HCRW) Approval has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

How should I continue to work with participating NHS organisations in England and Wales?
You should now provide a copy of this letter to all participating NHS organisations in England and Wales, as well as any documentation that has been updated as a result of the assessment.

Following the arranging of capacity and capability, participating NHS organisations should **formally confirm** their capacity and capability to undertake the study. How this will be confirmed is detailed in the "*summary of assessment*" section towards the end of this letter.

You should provide, if you have not already done so, detailed instructions to each organisation as to how you will notify them that research activities may commence at site following their confirmation of capacity and capability (e.g. provision by you of a 'green light' email, formal notification following a site initiation visit, activities may commence immediately following confirmation by participating organisation, etc.).

iii) Letter of invitation to participate for study in Chapter 6

Department of Sport Exercise & Health
University of Winchester
Sparkford Road
Winchester
Hampshire
SO22 4NR

Address

Re: High Tibial Osteotomy Research

Dear <insert name here>

I am writing to inform you of a piece of research that is currently being conducted with patients of <insert surgeon name> who have previously undergone high tibial osteotomy.

Since you had your surgery in <insert year here> I would like to invite you to participate in a study that is being conducted in collaboration with the Knee Research Team at Basingstoke & North Hampshire Hospital and the University of Winchester for a PhD project, which will investigate patients returning to physical activity after their surgery.

If you choose to take part, your participation in the study should take no longer than 15 minutes of your time. You will be requested to complete two sets of questionnaires pertaining to your physical activity levels prior to your surgery as well as your physical activity levels today. These questionnaires can either be sent to you via email or in the post and, once completed, can also be returned using either of these methods (if you would prefer to post the questionnaires back to me then you will be provided with a stamped, addressed envelope so that you do not incur any expenses).

Your participation in this study would be greatly appreciated and the results will go towards the furthering of scientific knowledge in this area, the informing of future surgical practice, and importantly, the improvement of treatment and care for future osteotomy patients.

If you think you may be interested in participating in the study, please feel free to contact me (the chief investigator) at the following email address for more information: james.belsey@winchester.ac.uk or by phone on +44 (0) 7748 365022

Yours Sincerely,

James Belsey
Chief Investigator & PhD Candidate

iv) Participant information sheet for study in Chapter 6

ASSESSING PHYSICAL ACTIVITY LEVELS OF PATIENTS FOLLOWING HIGH TIBIAL OSTEOTOMY WITH, AND WITHOUT, BONE GRAFTING

PARTICIPANT INFORMATION SHEET

The Knee Research Team at Basingstoke & North Hampshire Hospital is constantly working to produce research that is at the cutting edge of science in the field of knee surgery. As a patient who has undergone high tibial osteotomy, we would like to invite you to participate in this study. In conjunction with the Department of Sport, Exercise and Health at the University of Winchester, we aim to assess the post-operative physical activity levels of patients who have undergone high tibial osteotomy.

Taking part in this study is completely voluntary. If you decide not to participate, you are not obliged to give a reason, and the care you receive at the hospital will not be affected at all. If you decide now that you would like to participate, but later change your mind, you reserve the right to remove yourself from the study at any time without giving a reason.

What is the purpose of this research?
The inclusion of a bone graft during high tibial osteotomy divides opinion among orthopaedic surgeons across the world, with some preferring to use them with their patients, and some electing not to. Previous research has shown that both methods can result in positive outcomes for the patient. However, a recent study has shown that the inclusion of a bone graft during the procedure increases the strength and stability of the osteotomy. With this study, we aim to compare the differences in post-operative levels of physical activity between patients who undergo high tibial osteotomy with a bone graft, and those who have the surgery without a bone graft. The results of this research will help to inform opinions regarding the arguments for, and against, the use of bone grafts during high tibial osteotomy. This will help to benefit surgeons as well as patients in the future.

What is involved?
If you are interested in participating in this study, then we kindly ask that you read this Participation Information Sheet carefully. Once you have done so, we welcome any questions you may have regarding any aspects of the study and/or your participation in the study. Once you believe that any initial questions have been answered to your satisfaction, you will also be required to sign a consent form. Again, this should be read thoroughly and carefully before confirming your willingness to participate.

Please note: this will not be the only opportunity you have to ask questions. You are free, and encouraged, to ask questions at any stage of your participation in the study.

Procedures:
If you decide to participate, you will be asked to complete two sets of three questionnaires. These questionnaires consist of multiple choice questions and aim to find out your own perspective about your physical activity levels prior to, and since your osteotomy.

The first three questionnaires will require you to complete them while considering the condition of your knee and your physical activity levels pre-surgery – the time period between knowing you were going to have the operation but before undergoing the procedure. The second three questionnaires will require you to complete them while considering the condition of your knee and your physical activity levels currently. It should take around 15 minutes to complete all questionnaires

What do you get out of it?
You will have the opportunity to voice any concerns/worries you may have regarding how your return to physical activity post-surgery matches with your expectations. You will also be helping future patients who undergo this surgery, because the results from the study will contribute to scientific literature, which is used to help inform surgical practice globally.

Are there any risks?
There are no major risks or concerns regarding participation in this study.

The University of Winchester is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The University of Winchester will keep paperwork with identifiable information about you from this study for 7 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information at https://winchester.ac.uk/about-us/leadership-and-governance/privacy-and-cookie-policy/

Basingstoke & North Hampshire Hospital (BNHH) will collect information from you and your medical records for this research study in accordance with our instructions. BNHH will keep your name, NHS number, and contact details confidential and will not pass this information to the University of Winchester. BNHH will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from the University of Winchester and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The University of Winchester will only receive information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

What are the rights of participants in the study?

Participation in this study is voluntary, and as such, you are free to decline to participate or to withdraw yourself from the study at any time, without experiencing any disadvantage in the care you would normally receive from the hospital. Some parts of your medical notes may be accessed by the researchers, who are either full-time NHS employees or are in possession of NHS honorary contracts. You will be informed of any results that come out of this study, which may have an impact on the management of your health. All personal data that is collected throughout the entire duration of this study will be kept confidential, and will be kept locked in a cabinet in a secure office at the University of Winchester. Your identity will only be known to the researchers involved, and any results that are presented or published in scientific journals will be anonymised and untraceable back to you. You will not be paid to participate in this study, nor will you be charged for taking part.

What happens after the study or if you pull out?
You no longer will be contacted to further participate in the study. The healthcare you receive related to your osteotomy will not be affected. You will be provided with written information regarding your data within two weeks of the conclusion of the study. All data will be stored in a locked cabinet in a secure office for a period of 7 years.

Who is in the study team?
Mr. James Belsey, PhD Student, Department of Sport, Exercise & Health, University of Winchester, Tel. 07748 365022

Professor Simon Jobson, Director of Research & Knowledge Exchange, University of Winchester.

Dr. James Faulkner, Senior Lecturer, Department of Sport, Exercise & Health, University of Winchester.

Mr. Sam Yasen, Consultant in Trauma & Orthopaedics, Basingstoke & North Hants Hospital.

Mr. Michael Risebury, Consultant Knee Surgeon, Basingstoke & North Hants Hospital.

Professor Adrian Wilson, Consultant Orthopaedic Surgeon, BMI The Hampshire Clinic.

This study has been approved to be undertaken by the Hampshire Hospitals NHS Foundation Trust Research Department and the NHS Research Ethics Committee (ref. 18/EM/0174)

Can I speak to anyone outside of the study team if I have concerns about this research?
You can speak with the Hampshire Hospitals Foundation Trust Patient Advisory and Liaison Service (PALS) Manager on 01256 486766 or by email customercare@hhft.nhs.uk

THIS PROJECT IS FUNDED BY:

The Knee Preservation Fund at the University of Winchester.

v) **Consent form for study in Chapter 6**

Patient Study Number: ☐☐☐

ASSESSING PHYSICAL ACTIVITY LEVELS OF PATIENTS FOLLOWING HIGH TIBIAL OSTEOTOMY WITH, AND WITHOUT, BONE GRAFTING

CONSENT FORM

Name of Researchers: Mr. James Belsey, Professor Simon Jobson, Dr. James Faulkner, Mr. Sam Yasen, Mr. Michael Risebury, Professor Adrian Wilson

Please initial boxes below

1. I confirm that I have read and understood the Patient Information Sheet for the above study and have had the opportunity to ask questions. I understand that the data in this study will be included in future related clinical research projects. ☐
2. I confirm that I have had sufficient time to consider whether or not to take part in the study. ☐
3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
4. I understand that sections of my medical notes may be looked at by responsible individuals from regulatory authorities where it is relevant to my taking part in research. Medical records may also be viewed by the named researchers in possession of honorary NHS contracts. I give permission for these individuals to have access to my patient records. ☐
5. I agree to take part in the above study. ☐

Name of participant (please PRINT)	Date (DD/MM/YY)	Signature of participant
James Belsey		
Name of person taking consent (please PRINT)	Date (DD/MM/YY)	Signature of person taking consent

APPENDIX F – FORMS RELATING TO STUDY IN CHAPTER 7

i) Ethical approval for study in Chapter 7

UNIVERSITY OF WINCHESTER

Tuesday 1st May 2018

James Belsey

Department of Sport, Exercise & Health

Faculty of BLS

University of Winchester

Hants, SO22 4NR

Dear James Belsey,

Re: Faculty of Business, Law and Sport RKE Ethics Application [BLS/18/08]

Title: *Investigating the decision to return to physical activity after high tibial osteotomy*

Thank you for your submission to the University of Winchester, Faculty of Business Law and Sport (BLS) ethics panel.

On behalf of the Faculty of BLS RKE Ethics Committee I am pleased to advise you that you have received a favourable opinion for the ethical content of your application. Favourable opinion is for five years and is only for the documentation submitted for review on 27/04/18. If the project has not been completed within five years from the date of this letter, re-approval must be requested.

If the nature, content, location, procedures or personnel of your approved application change, please advise the Head of the Faculty BLS ethics committee.

Yours sincerely

Prof M. Burke.

Prof Maria Burke

Head of Research and Knowledge Exchange in Faculty BLS

University of Winchester

Dr James Faulkner, Head of Ethics in the Faculty of BLS
Email: James.Faulkner@winchester.ac.uk; Tel: +44 (0)1962 624932

ii) Letter of invitation for study in Chapter 7

James Belsey
Department of Sport, Exercise & Health
University of Winchester
Sparkford Road
Winchester
SO22 4NR

<address>

Dear <insert name here>

I am writing to you today to invite you to attend an interview that will be used as part of a piece of scientific research into patient physical activity levels after high tibial osteotomy. I am a PhD candidate at the University of Winchester and work for Prof. Wilson, who is one of the top osteotomy surgeons in the world and is responsible for producing world-leading research in the area of knee osteotomy.

Since you underwent high tibial osteotomy in 2017 under the care of Prof. Wilson, I am interested in talking to you about a number of things, positive and negative, regarding your physical activity levels before and after your surgery.

This study will allow us to get a deeper understanding of things like your physical activity expectations prior to surgery, and how they compare with the outcome you have had. Rather than simply filling out a questionnaire, which can often prevent patients from giving their full opinion, I want to know exactly what you think and would be very interested in meeting with you to have a one-to-one conversation. This will be a one-time commitment and should take no longer than 60 minutes. The location can be agreed to suit your preferences (e.g. Basingstoke, Winchester or your home).

If you think you might be interested in participating in this research, which will help to inform practice for future patients, then please contact me either by email, text or phone and I can provide you with more information. Please note: replying to this letter and asking me for more information does not commit you to participating in this study and if you decide that you no longer wish to continue with it, you are free to withdraw yourself at any time without giving a reason.

I very much look forward to hearing from you soon.

Best Regards

James Belsey

iii) Participant information sheet for study in Chapter 7

Investigating the decision to return to physical activity after high tibial osteotomy

The Basingstoke Knee Research Team is constantly working to produce research that is at the cutting edge of science in the field of knee surgery. As a patient who has undergone high tibial osteotomy, we would like to invite you to participate in this study. In conjunction with the Department of Sport, Exercise and Health at the University of Winchester, we aim to investigate your opinions regarding the factors behind your post-operative physical activity levels.

Taking part in this study is completely voluntary. If you decide not to participate, you are not obliged to give a reason. If you decide now that you would like to participate, but later change your mind, you reserve the right to remove yourself from the study at any time without giving a reason.

What is the purpose of this research?

The inclusion of a bone graft during high tibial osteotomy divides opinion among orthopaedic surgeons across the world, with some preferring to use them with their patients, and some electing not to. Previous research has shown that both methods can result in positive outcomes for the patient. However, a recent study has shown that the inclusion of a bone graft during the procedure increases the strength and stability of the osteotomy. As a result, we think that this may help patients return to their own desired physical activity level after the operation. With this study, we aim to determine whether your pre-surgery expectations of your post-surgery physical activity levels have been achieved, and if not, why not? The results of this study will help to inform future research into how osteotomy patients are able to achieve desired physical activity levels post-surgery. This will be of benefit to surgeons as well as patients in the future.

What is involved?

If you are interested in joining in, then we kindly ask that you read this Participation Information Sheet carefully. Once you have done so, we welcome any questions you may have regarding any aspects of the study and/or your participation in the study. Once you believe that any initial questions have been answered to your satisfaction, you will also be required to sign a consent form. Again, this should be read thoroughly and carefully before confirming your willingness to participate.

Please note: this will <u>not</u> be the only opportunity you have to ask questions. You are free, and encouraged, to ask questions at any stage of your participation in the study.

Procedures:

If you decide to take part, you will be asked to complete two questionnaires. One questionnaire consists of multiple choice questions and aims to assess your knee function and your ability to perform various movements (kneeling, squatting, jumping etc). The second questionnaire requires you to indicate your level of participation in physical activity on a scale of 1-10. After this, you will be invited to attend a face-to-face interview with one of the researchers in which you will be asked questions, based on your answers to the questionnaires, about how your levels of physical activity have been as a result of your osteotomy. This will also be an opportunity for you to elaborate on any points from the questionnaires that you feel should be clarified and expanded on. This interview will be a one-time thing and will likely last between 30 and 60 minutes. The results from the interview will help us to develop an understanding as to why your post-surgery physical activity levels are as high or low as they are. The interview can be scheduled to suit you, and can take place either at the University of Winchester, a location of your choice, or at your home, depending on your preferences.

What do you get out of it?
You will have the opportunity to voice any concerns/worries you may have regarding how your return to physical activity post-surgery matches with your expectations. You will also be helping future patients who undergo this surgery, because the results from the study will contribute to scientific literature, which is used to help inform surgical practice globally.

Are there any risks?
The risks for taking part in this study are extremely low. You are only completing questionnaires and participating in one interview. The questions asked during the interview are not going to be psychologically demanding or exhausting, and if you are not obliged to share anything you do not wish to.

What are the rights of participants in the study?
Participation in this study is voluntary, and as such, you are free to decline to participate or to withdraw yourself from the study at any time, without experiencing any disadvantage in the post-operative care you would normally receive from the hospital. All personal data that is collected throughout the entire duration of this study will be kept confidential, and will be kept locked in a cabinet in a secure office at the University of Winchester. Your identity will only be known to the researchers involved, and any results that are presented or published in scientific journals will be anonymised and untraceable back to you. You will not be paid to participate in this study, nor will you be charged for taking part.

What happens after the study or if you pull out?
You will be provided with written information regarding your data within two weeks of the conclusion of the study. All data will be stored in a locked cabinet in a secure office for a period of 7 years.

Who is in the study team?
Mr. James Belsey, PhD Student, Department of Sport, Exercise & Health, University of Winchester, Tel. (+44) 07748 365022

Professor Simon Jobson, Director of Health & Wellbeing, University of Winchester.

Dr. James Faulkner, Senior Lecturer, Department of Sport, Exercise & Health, University of Winchester.

Professor Adrian Wilson, Consultant Orthopaedic Surgeon, BMI The Hampshire Clinic.

This study has been approved to be undertaken by the University of Winchester Research Ethics Committee.

iv) Consent form for study in Chapter 7

Patient Study Number: ☐☐☐

Investigating the decision to return to physical activity after high tibial osteotomy

Names of Researchers: Mr. James Belsey, Professor Simon Jobson, Dr. James Faulkner, Professor Adrian Wilson

Please initial boxes below

1. I confirm that I have read and understood the Patient Information Sheet for the above study and have had the opportunity to ask questions. I understand that the data in this study will be used to inform future related clinical research projects. ☐
2. I confirm that I have had sufficient time to consider whether or not to take part in the study. ☐
3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
4. I agree to take part in the above study. ☐

Name of participant (please PRINT)	Date (DD/MM/YY)	Signature of participant

v) Question guide for study in Chapter 7

Before we get started talking about your current physical activity levels, I'd just like to establish where you're coming from with regard to your physical activity levels before you were having the issues with your knee that eventually led to you having the osteotomy. So, on this Tegner scale you've marked your pre-surgery physical activity levels as **?** which means **?** Can you remember how this compared with your physical activity levels before you really started having these knee issues?
Could you talk a little bit about the sorts of things you were doing?

When you knew that you were going to have surgery on your knee, what were your thoughts regarding your ability to be physically active again after the procedure?
Were you worried that you wouldn't be able to go back to normal? Did you hope that it would allow you to do more than previously?

When we look at were you marked yourself on the Tegner scale for your physical activity levels at the moment, you said you're around **?**, which means **?** and is higher/lower/the same as what you said were your levels before you were having knee issues. Can you describe the sorts of thing that you do with regard to physical activity? How do you feel about that current level of physical activity that you're at?

How long did it roughly take after your surgery for you to reach the physical activity levels you're currently at? Were you satisfied with the progress you made after your surgery? Was it longer, shorter or about what you expected?

What were the reasons behind your decision to start/not increasing your physical activity levels after your surgery?

Did you have any thoughts or feelings of uncertainty when you were beginning to increase the physical activity after your surgery?

Was there anything stopping you from increasing your physical activity levels sooner after surgery?

Let’s take a look at some of the external factors that might have influenced your physical activity levels. Can you think of anyone or anything external to you that has impacted or guided your choices with regards to the physical activity you do? Would there be any external factor that you didn’t experience but that you think could have affected your return to physical activity if you had experienced it (e.g. comparing your progress with other patients, having a surgeon or physio tell you that you can do more)?

If we look to the future now, do you wish/expect to be able to increase your physical activity levels at some point or are you thinking that things are likely to stay about where they are?

Have you had your plate removed?
How did this affect your physical activity levels? In the run up to and recover from the surgery, as well as after you were healed?

APPENDIX G – FORMS RELATING TO STUDY IN CHAPTER 8

i) Ethical approval for study in Chapter 8

UNIVERSITY OF WINCHESTER

Wednesday 24th April 2019

James Belsey

Department of Sport, Exercise & Health

Faculty of Business, Law and Sport

University of Winchester

Hants, SO22 4NR

Dear Mr Belsey,

Re: Faculty of Business, Law and Sport RKE Ethics Application [BLS/19/12]

Title: Investigating pain and return to physical activity after high tibial osteotomy.

Thank you for your submission to the University of Winchester, Faculty of Business Law and Sport (BLS) ethics panel.

On behalf of the Faculty of BLS RKE Ethics Committee I am pleased to advise you that you have received a favourable opinion for the ethical content of your application. Ethical approval is for five years and is only for the documentation submitted for review on 06/04/19. If the project has not been completed within five years from the date of this letter, re-approval must be requested.

If the nature, content, location, procedures or personnel of your approved application change, please advise the Head of the Faculty BLS ethics committee.

Yours sincerely

Prof. M. Burke.

Prof. Maria Burke

Head of Ethics in Faculty BLS

University of Winchester

Dr James Faulkner, Head of Ethics in the Faculty of BLS
Email: James.Faulkner@winchester.ac.uk; Tel: +44 (0)1962 624932

ii) Participant information sheet for study in Chapter 8

INVESTIGATING PAIN AND RETURN TO PHYSICAL ACTIVITY AFTER HIGH TIBIAL OSTEOTOMY

PARTICIPANT INFORMATION SHEET

In conjunction with the Department of Sport, Exercise and Health at the University of Winchester, we are currently inviting previous high tibial osteotomy (HTO) patients and orthopaedic surgeons to participate in this research. We aim to assess the actual experiences that previous patients have had with regard to the amount of pain experienced and the type of physical activity performed in the first year after surgery. This will then be compared with the information given to patients prior to surgery relating to these aspects. This will help to ensure the accuracy of this information and improve the expectations patients have of the first 12 months after their osteotomy.

Taking part in this study is completely voluntary. If you decide not to participate, you are not obliged to give a reason. If you decide now that you would like to participate, but later change your mind, you reserve the right to remove yourself from the study at any time without giving a reason.

What is the purpose of this research?
This study will form part of a PhD thesis being written by a student at the University of Winchester. A previous study from this project showed that patients sometimes experience more pain in the immediate aftermath of their surgery than they initially expected. It also showed that patients would have liked to have been given information suggesting what types of physical activity the "average" patient is able to perform throughout the first year after surgery. This study aims to create a "12 month timeline" that will show this information based on the experiences of patients who have previously undergone high tibial osteotomy. It is believed that this will help to improve overall patient satisfaction with the surgery due to this information assisting the formulation of realistic expectations of the surgical outcome.

What is involved?
If you are interested in participating in this study, then we kindly ask that you read this Participation Information Sheet carefully. Once you have done so, we welcome any questions you may have regarding any aspect of the study and/or your participation in the study. Once you believe that any initial questions have been answered to your satisfaction, you will also be required to sign a consent form. Again, this should be read thoroughly and carefully before confirming your willingness to participate.

Please note: this will not be the only opportunity you have to ask questions. You are free, and encouraged, to ask questions at any stage of your participation in the study.

Procedures*:*
Through a recorded short interview, you will be asked to outline the information you would normally give to prospective HTO patients regarding their expected return to physical activity and level of pain within the first 12 months post-operatively. Answers you give during the interview will be analysed and compared against those from other interviews in order to uncover common themes in the information that consultants tend to provide their prospective patients.

What do you get out of it?
Results from this study will be submitted to scientific journals for peer-review and publication and will provide consultants and future patients with a resource that demonstrates a 12 month timeline of pain and return to physical activity in the "average" HTO patient. This would be something you could use in your own practice, if you think it could be useful to help manage patient expectations prior to their surgery.

Are there any risks?
No risk to participants is expected in this study.

We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information at https://winchester.ac.uk/about-us/leadership-and-governance/privacy-and-cookie-policy/

What are the rights of participants in the study?
Participation in this study is voluntary, and as such, you are free to decline to participate or to withdraw yourself from the study at any time. All personal data that is collected throughout the entire duration of this study will be kept confidential, and will be kept locked in a cabinet in a secure room at the University of Winchester. Your identity will only be known to the researchers involved, and any results that are presented or published in scientific journals will be anonymised and untraceable back to you. You will not be paid to participate in this study, nor will you be charged for taking part.

What happens after the study or if you pull out?
You no longer will be contacted to further participate in the study. The healthcare that HTO patients receive related to their osteotomy will not be affected. All participants will be provided with written information regarding their data within two weeks of the conclusion of the study.

Who is in the study team?

Mr. James Belsey, PhD Student, Department of Sport, Exercise & Health, University of Winchester, Tel. 07748 365022, Email. james.belsey@winchester.ac.uk

Professor Simon Jobson, Director of Research & Knowledge Exchange, University of Winchester.

Dr. James Faulkner, Senior Lecturer, Department of Sport, Exercise & Health, University of Winchester.

Mr. Sam Yasen, Consultant in Trauma & Orthopaedics, Basingstoke & North Hants Hospital.

Mr. Michael Risebury, Consultant Knee Surgeon, Basingstoke & North Hants Hospital.

Professor Adrian Wilson, Consultant Orthopaedic Surgeon, BMI The Hampshire Clinic.

THIS PROJECT IS FUNDED BY:

The Knee Preservation Fund at the University of Winchester.

iii) Consent form for study in Chapter 8

Patient Study Number: ☐☐☐

INVESTIGATING PAIN AND RETURN TO PHYSICAL ACTIVITY AFTER HIGH TIBIAL OSTEOTOMY

CONSENT FORM

Name of Researchers: Mr. James Belsey, Professor Simon Jobson, Dr. James Faulkner, Mr. Sam Yasen, Mr. Michael Risebury, Professor Adrian Wilson

Please initial boxes below

1. I confirm that I have read and understood the Participant Information Sheet for the above study and have had the opportunity to ask questions. I understand that the data in this study will be included in future related clinical research projects. ☐
2. I confirm that I have had sufficient time to consider whether or not to take part in the study. ☐
3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
4. I agree to take part in the above study. ☐

Name of participant (please PRINT)	Date (DD/MM/YY)	Signature of participant
Name of person taking consent (please PRINT)	Date (DD/MM/YY)	Signature of person taking consent

iv) Interview questions for study in Chapter 8

Can you tell me what information you would typically give a prospective HTO patient, who would be undergoing solely an osteotomy with no concurrent procedures such as an ACL reconstruction?

- Procedure
- Recovery period
- Time to walk
- Time off work
- Post-operative pain levels
- Return to normal activity levels

What kind of physical activities would you expect patients to be able to return to after their HTO?
How long would you tell a patient it might take to get to the level where they can perform/participate in such activities?

Do you expect patients, on average, to eventually be pain free in their knee after surgery?
How long until they reach that point?
Also the same during physical activity?

How many HTO's roughly do you perform in a year/month?
At which intervals do you see your patients post-operatively?

Any other comments regarding recovery, pain and physical activity in the first 12 months post-operatively?

APPENDIX H – FORMS RELATING TO STUDY IN CHAPTER 9

i) Ethical approval for study in Chapter 9

UNIVERSITY OF WINCHESTER

Wednesday 24th April 2019

James Belsey

Department of Sport, Exercise & Health

Faculty of Business, Law and Sport

University of Winchester

Hants, SO22 4NR

Dear Mr Belsey,

Re: Faculty of Business, Law and Sport RKE Ethics Application [BLS/19/12]

Title: Investigating pain and return to physical activity after high tibial osteotomy.

Thank you for your submission to the University of Winchester, Faculty of Business Law and Sport (BLS) ethics panel.

On behalf of the Faculty of BLS RKE Ethics Committee I am pleased to advise you that you have received a favourable opinion for the ethical content of your application. Ethical approval is for five years and is only for the documentation submitted for review on 06/04/19. If the project has not been completed within five years from the date of this letter, re-approval must be requested.

If the nature, content, location, procedures or personnel of your approved application change, please advise the Head of the Faculty BLS ethics committee.

Yours sincerely

Prof. M. Burke.

Prof. Maria Burke

Head of Ethics in Faculty BLS

University of Winchester

Dr James Faulkner, Head of Ethics in the Faculty of BLS
Email: James.Faulkner@winchester.ac.uk; Tel: +44 (0)1962 624932

ii) Participant information sheet for study in Chapter 9

INVESTIGATING PAIN AND RETURN TO PHYSICAL ACTIVITY AFTER HIGH TIBIAL OSTEOTOMY

PARTICIPANT INFORMATION SHEET

In conjunction with the Department of Sport, Exercise and Health at the University of Winchester, we are currently inviting previous high tibial osteotomy (HTO) patients to participate in this research. High tibial osteotomy is a form of knee surgery, often intended to treat osteoarthritis, and is commonly performed on patients wishing to remain physically active post-operatively. We aim to assess the actual experiences that previous patients have had with regard to the amount of pain experienced and the type of physical activity performed in the first year after surgery. This will help to improve the accuracy of information given to future patients to improve their expectations of the first 12 months after osteotomy.

Taking part in this study is completely voluntary. If you decide not to participate, you are not obliged to give a reason. If you decide now that you would like to participate, but later change your mind, you reserve the right to remove yourself from the study at any time without giving a reason.

What is the purpose of this research?
This study will form part of a PhD thesis being written by a student at the University of Winchester. A previous study from this project showed that patients sometimes experience more pain in the immediate aftermath of their surgery than they initially expected. It also showed that patients would have liked to have been given information suggesting what types of physical activity the "average" patient is able to perform throughout the first year after surgery. This study aims to create a "12 month timeline" that will show this information based on the experiences of patients who have previously undergone high tibial osteotomy. It is believed that this will help to improve overall patient satisfaction with the surgery due to this information assisting the formulation of realistic expectations of the surgical outcome.

What is involved?
If you are interested in participating in this study, then we kindly ask that you read this Participation Information Sheet carefully. Once you have done so, we welcome any questions you may have regarding any aspect of the study and/or your participation in the study. Once you believe that any initial questions have been answered to your satisfaction, you will also be required to sign a consent form. Again, this should be read thoroughly and carefully before confirming your willingness to participate.

Please note: this will not be the only opportunity you have to ask questions. You are free, and encouraged, to ask questions at any stage of your participation in the study.

Procedures*:*
You will initially be required to sign a form stating that you consent to participate in this study. Following this, using a series of questionnaires, you will be asked to recall the level of pain you experienced and the types of physical activities you were capable of doing 1 day before your surgery, and 1 week, 1 month, 3, months, 6 months, and 1 year after your surgery. This will provide us with an idea of your progress in the first 12 months post-operatively, which will be aggregated with the answers from other patients in order to compile a timeline of the average progression of HTO patients in the short-term.

What do you get out of it?
At the end of the study, you will receive a summary of the results from the study, which you can use to see how your individual experience compared against that of the "average" patient.

You will also be helping future patients who undergo this surgery because the results from the study will contribute to the scientific literature, which is used to help inform surgical practice globally.

Are there any risks?
No risk to participants is expected in this study.

We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information at https://winchester.ac.uk/about-us/leadership-and-governance/privacy-and-cookie-policy/

What are the rights of participants in the study?
Participation in this study is voluntary, and as such, you are free to decline to participate or to withdraw yourself from the study at any time. All personal data that is collected throughout the entire duration of this study will be kept confidential, and will be kept locked in a cabinet in a secure room at the University of Winchester. Your identity will only be known to the researchers involved, and any results that are presented or published in scientific journals will be anonymised and untraceable back to you. You will not be paid to participate in this study, nor will you be charged for taking part.

What happens after the study or if you pull out?
You no longer will be contacted to further participate in the study. The healthcare that HTO patients receive related to their osteotomy will not be affected. All participants will be provided with written information regarding their data within two weeks of the conclusion of the study.

Who is in the study team?

Mr. James Belsey, PhD Student, Department of Sport, Exercise & Health, University of Winchester, Tel. 07748 365022, Email. james.belsey@winchester.ac.uk

Professor Simon Jobson, Director of Research & Knowledge Exchange, University of Winchester.

Dr. James Faulkner, Senior Lecturer, Department of Sport, Exercise & Health, University of Winchester.

Mr. Sam Yasen, Consultant in Trauma & Orthopaedics, Basingstoke & North Hants Hospital.

Mr. Michael Risebury, Consultant Knee Surgeon, Basingstoke & North Hants Hospital.

Professor Adrian Wilson, Consultant Orthopaedic Surgeon, BMI The Hampshire Clinic.

THIS PROJECT IS FUNDED BY:

The Knee Preservation Fund at the University of Winchester.

iii) **Consent form for study in Chapter 9**

Patient Study Number: ☐☐☐

INVESTIGATING PAIN AND RETURN TO PHYSICAL ACTIVITY AFTER HIGH TIBIAL OSTEOTOMY

CONSENT FORM

Name of Researchers: Mr. James Belsey, Professor Simon Jobson, Dr. James Faulkner, Mr. Sam Yasen, Mr. Michael Risebury, Professor Adrian Wilson

Please initial boxes below

1. I confirm that I have read and understood the Patient Information Sheet for the above study and have had the opportunity to ask questions. I understand that the data in this study will be included in future related clinical research projects. ☐
2. I confirm that I have had sufficient time to consider whether or not to take part in the study. ☐
3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
4. I understand that sections of my medical notes may be looked at by responsible individuals from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my patient records. ☐
5. I agree to take part in the above study. ☐

Name of participant (please PRINT)	Date (DD/MM/YY)	Signature of participant
Name of person taking consent (please PRINT)	Date (DD/MM/YY)	Signature of person taking consent

iv) Non-validated Activity Participation Questionnaire from study in Chapter 9

Please indicate which of the following activities (if any) that you participate in currently.

Walking on even ground….	☐	Walking on uneven ground…..	☐
Work…………………………….	☐	Light domestic work…………….	☐
Heavy domestic work……..	☐	Stair climbing……………………….	☐
Golf……………………………….	☐	Driving a car………………………..	☐
Driving a motorcycle………	☐	Swimming…………………………….	☐
Cycling…………………………..	☐	Yoga/Pilates………………………….	☐
Jogging on even ground…	☐	Jogging on uneven ground……..	☐
Jumping………………………..	☐	Kneeling……………………………….	☐
Cross country running…..	☐	Cross country skiing……………….	☐
Downhill skiing………………	☐	Motocross/Speedway…………….	☐
Basketball/Handball………	☐	Tennis/Badminton…………………	☐
Squash…………………………..	☐	Ice hockey/Bandy…………………	☐
Football/Rugby………………	☐	Gymnastics……………………………	☐

Other (please list):

APPENDIX I – FORMS RELATING TO STUDY IN CHAPTER 10

i) Ethical approval for study in Chapter 10

UNIVERSITY OF WINCHESTER

Thursday 14th March 2019

James Belsey

Department of Sport, Exercise & Health

Faculty of Business, Law and Sport

University of Winchester

Hants, SO22 4NR

Dear Mr Belsey,

Re: Faculty of Business, Law and Sport RKE Ethics Application [BLS/19/07]

Title: *Gait and residual pain at different physical activity intensities in high tibial osteotomy patients and healthy controls.*

Thank you for your submission to the University of Winchester, Faculty of Business Law and Sport (BLS) ethics panel.

On behalf of the Faculty of BLS RKE Ethics Committee I am pleased to advise you that you have received a favourable opinion for the ethical content of your application. Ethical approval is for five years and is only for the documentation submitted for review on 05/03/19. If the project has not been completed within five years from the date of this letter, re-approval must be requested.

If the nature, content, location, procedures or personnel of your approved application change, please advise the Head of the Faculty BLS ethics committee.

Yours sincerely

Prof. M. Burke.

Prof. Maria Burke

Head of Ethics in Faculty BLS

University of Winchester

Dr James Faulkner, Head of Ethics in the Faculty of BLS
Email: James.Faulkner@winchester.ac.uk; Tel: +44 (0)1962 624932

ii) **Participant information sheet for study in Chapter 10**

GAIT AND RESIDUAL PAIN AT DIFFERENT PHYSICAL ACTIVITY INTENSITIES IN HIGH TIBIAL OSTEOTOMY PATIENTS AND "HEALTHY" CONTROLS

PARTICIPANT INFORMATION SHEET

In conjunction with the Department of Sport, Exercise and Health at the University of Winchester, we are currently inviting previous high tibial osteotomy (HTO) patients and "healthy" controls to participate in this research. High tibial osteotomy is a form of knee surgery, often intended to treat osteoarthritis. It achieves this by altering the weight-bearing line through the knee to relieve symptoms, while preserving the joint and delaying the need for a knee replacement. We aim to assess gait and perceived knee pain during walking and running at a number of self-regulated exercise intensities.

Taking part in this study is completely voluntary. If you decide not to participate, you are not obliged to give a reason. If you decide now that you would like to participate, but later change your mind, you reserve the right to remove yourself from the study at any time without giving a reason.

What is the purpose of this research?
It has been reported that HTO patients may experience some residual pain after their surgery, however studies have shown that patients can also return to physical activity at a level similar to that prior to their knee issues. It stands to reason that more intense physical activities, which exert higher forces through the knee, may result in higher levels of residual pain. This research will be the first to investigate the effect that exercise intensity has on the residual pain, if any, that HTO patients tolerate during physical activity. This will be compared with "healthy" control subjects who have no prior history of knee pain or lower limb surgery and will help to benefit surgeons as well as patients in the future.

What is involved?
If you are interested in participating in this study, then we kindly ask that you read this Participation Information Sheet carefully. Once you have done so, we welcome any questions you may have regarding any aspect of the study and/or your participation in the study. Once you believe that any initial questions have been answered to your satisfaction, you will also be required to sign a consent form. Again, this should be read thoroughly and carefully before confirming your willingness to participate.

Please note: this will not be the only opportunity you have to ask questions. You are free, and encouraged, to ask questions at any stage of your participation in the study.

Procedures*:*
If you decide to participate, you will be invited to attend a single testing session in the sports biomechanics laboratory at the University of Winchester, in which your current knee function and pain levels will first be assessed through the implementation of a questionnaire. Once this has been done, a "Physical Activity Readiness" questionnaire will need to be completed in

order to determine your suitability to undergo the exercise testing described below. Your blood pressure, resting heart rate, mass, and height will be measured as part of this process. Your mass and height will be used to calculate your body mass index (BMI), which will be included in the final data analysis. You will then be asked to wear a clip-on belt containing a sensor that will analyse your gait while you are performing the following walking and jogging protocols on a flat treadmill.

The treadmill testing will consist of 8 bouts (4 walking, 4 jogging) with each bout lasting 3 minutes. The intensity at which you walk/jog during each bout will be self-regulated and guided by your "rate of perceived exertion" (RPE), determined using a scale between 6 and 20 where 6 equals "no exertion at all" and 20 equals "maximal exertion". However, you will not be required to maximally exert yourself for this study. The intensity of each bout will fall between 9 (very light) and 15 (hard) on the RPE scale. Please see the table below, which clearly illustrates the test protocol.

Bout number	Exercise	Intensity (RPE)	Length (minutes)
1	Walking	9	3
2	Walking	11	3
3	Walking	13	3
4	Walking	15	3
5	Jogging	9	3
6	Jogging	11	3
7	Jogging	13	3
8	Jogging	15	3

Please note that you will not necessarily conduct the bouts in the exact order presented in the above table. The order of bouts will be randomised in advance of your arrival to the university.

Half way through, and at the end of, each bout you will report any levels of pain experienced in the knee by completing 2 pain scales. You will be required to rest in a seated position in between bouts until your heart rate returns to normal resting levels. If at any point, you experience any knee pain at an intolerable level, you are free to stop the treadmill and end a bout of exercise.

Gait, pain, and distance covered on the treadmill will be analysed and comparisons will be made between the HTO patients and the "healthy" controls. All data will be anonymised and will not be traceable back to you.

Your visit to the University of Winchester should take no longer than 2 hours.

What do you get out of it?
The "Physical Activity Readiness" questionnaire that will be completed at the beginning of the testing session will include a BMI measurement, blood pressure test, and resting heart rate measurement. You may find this useful as these measurements pertain to your current health status and you will be able to take a copy of these measurements home with you, for your reference. You will also have access to all of your data, including from the gait sensor, once the final analysis has been performed.

You will also be helping future patients who undergo this surgery because the results from the study will contribute to the scientific literature, which is used to help inform surgical practice globally.

Are there any risks?
Due to the nature of the study, participants (mainly HTO patients) may experience some discomfort in their knee during the treadmill testing, however you will not be required to continue through any intolerable levels of discomfort or pain. You will decide for yourself what constitutes an intolerable level. All participants are allowed to terminate a bout of exercise and/or remove themselves from the study at any point without having to give a reason.

Other than this and the usual hazards associated with exercising on a treadmill, no further risk to participants are expected in this study.

We will be using information from you (all participants) and your medical records (HTO patients only) in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information at https://winchester.ac.uk/about-us/leadership-and-governance/privacy-and-cookie-policy/

What are the rights of participants in the study?
Participation in this study is voluntary, and as such, you are free to decline to participate or to withdraw yourself from the study at any time. All personal data that is collected throughout the entire duration of this study will be kept confidential, and will be kept locked in a cabinet in a secure room at the University of Winchester. Your identity will only be known to the researchers involved, and any results that are presented or published in scientific journals will be anonymised and untraceable back to you. You will not be paid to participate in this study, nor will you be charged for taking part.

What happens after the study or if you pull out?
You no longer will be contacted to further participate in the study. The healthcare that HTO patients receive related to their osteotomy will not be affected. All participants will be provided with written information regarding their data within two weeks of the conclusion of the study.

Who is in the study team?
Mr. James Belsey, PhD Student, Department of Sport, Exercise & Health, University of Winchester, Tel. 07748 365022, Email. james.belsey@winchester.ac.uk

Professor Simon Jobson, Director of Research & Knowledge Exchange, University of Winchester.

Dr. James Faulkner, Senior Lecturer, Department of Sport, Exercise & Health, University of Winchester.

Mr. Sam Yasen, Consultant in Trauma & Orthopaedics, Basingstoke & North Hants Hospital.

Mr. Michael Risebury, Consultant Knee Surgeon, Basingstoke & North Hants Hospital.

Professor Adrian Wilson, Consultant Orthopaedic Surgeon, BMI The Hampshire Clinic.

THIS PROJECT IS FUNDED BY:

The Knee Preservation Fund at the University of Winchester.

iii) **Consent form for study in Chapter 10**

Patient Study Number: ☐☐☐

GAIT AND RESIDUAL PAIN AT DIFFERENT PHYSICAL ACTIVITY INTENSITIES IN HIGH TIBIAL OSTEOTOMY PATIENTS AND "HEALTHY" CONTROLS

CONSENT FORM

Name of Researchers: Mr. James Belsey, Professor Simon Jobson, Dr. James Faulkner, Mr. Sam Yasen, Mr. Michael Risebury, Professor Adrian Wilson

Please initial boxes below

1. I confirm that I have read and understood the Patient Information Sheet for the above study and have had the opportunity to ask questions. I understand that the data in this study will be included in future related clinical research projects. ☐
2. I confirm that I have had sufficient time to consider whether or not to take part in the study. ☐
3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
4. I understand that sections of my medical notes may be looked at by responsible individuals from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my patient records. ☐
5. I agree to take part in the above study. ☐

Name of participant (please PRINT)	Date (DD/MM/YY)	Signature of participant
Name of person taking consent (please PRINT)	Date (DD/MM/YY)	Signature of person taking consent

iv) **Physical Activity Readiness Questionnaire (PAR-Q) from Chapter 10**

Participant Consent Form

I ____________________________________ consent to take in part in this research study titled:

Gait and residual pain at different physical activity intensities in high tibial osteotomy patients and healthy controls.

The investigator has explained the full details and parameters of all tests and procedures to me, and/or I have read the Information Sheet. I confirm that I have understood what participation will involve, and confirm that I have been made aware of all the potential benefits and risks of participation.

I declare that I have completed and signed the accompanying Physical Activity Readiness Questionnaire truthfully to the best of my knowledge, and that I have never been advised to abstain from any form of exercise by a medical practitioner. I know of no reason why participation in these testing procedures might present a risk to my safety.

I understand that any medical information that I have submitted will be treated as highly confidential.

I would like to be provided with a copy of the following for my personal records *(please tick)*:

Information Sheet ☐

Consent Form ☐

PAR-Q ☐

Signed: _____________________ ***(Participant)*** **Date:** ________________________

Signed: _____________________ ***(Witness)*** **Date:** ________________________

Physical Activity Readiness Questionnaire (PAR-Q)

Date of Birth		Blood pressure (mmHg)	
Height (m)		Body Mass (kg)	

Please tick <u>either</u> 'Yes' <u>or</u> 'No' for all of the following questions. If you are unsure about any question, please ask the investigator.				***Yes***	***No***
Are you used to vigorous exercise?					
Has your medical doctor said that you must not undertake vigorous activity?					
Do you have:	***Yes***	***No***		***Yes***	***No***
heart disease			any blood disorder		
frequent chest pains			diabetes mellitus		
raised blood pressure			thyroid disease		
episodes of excessive breathlessness			arthritis that is made worse by exercise		
a persistent cough			back pain that is made worse by exercise		
asthma			hiatus (chest) hernia or heartburn		
a recent chest infection			inguinal (groin) hernia		
				Yes	***No***
Do you lose your balance because of dizziness?					
Do you have episodes where you regularly lose consciousness?					
To the best of your knowledge, are you pregnant?					
Do you have an allergy to silver?					
Do you have any implanted electronic devices such as cardiac pace-makers or similar assistive devices?					
Do you have any other condition that may prevent you either exercising or taking part in this project? Please give details below:					

If you have any other concerns or questions with regard to completing this form or are unsure as to your general state of health please contact the investigator in person or at the following email address: Edward.Tasker@winchester.ac.uk

For Official Use only

Details of any further discussions with research subject regarding health indications stated above:

Signed: ____________________ ***(Participant)*** **Date:** ____________________

Signed: ____________________ ***(Lab Supervisor)*** **Date:** ____________________