Routine abdominal magnetic resonance imaging can determine psoas muscle area in paediatric Crohn's disease and correlates with bioelectrical impedance measures of lean mass

James J Ashton^{1,2}, Dilane Peiris³, Zachary Green¹, Luise Marino⁴, Mark Griffiths³, Mark Beattie¹

- Department of Paediatric Gastroenterology, Southampton Children's Hospital, Southampton, UK
- Human Genetics and Genomic Medicine, University of Southampton, Southampton, UK
- Department of Paediatric Radiology, Southampton Children's Hospital, Southampton, UK
- Department of Dietetics/SLT, University Hospital Southampton Foundation NHS Trust, Southampton, UK

Correspondence to-

Professor R Mark Beattie

Department of Paediatric Gastroenterology,

Southampton Children's Hospital,

University Hospitals Southampton

Tremona Road

Southampton

SO16 6YD

UK

Mark.beattie@uhs.nhs.uk

<u>Abstract</u>

<u>Background-</u> Paediatric-onset Crohn's disease (CD) has been associated with undernutrition, and nutritional supplementation is common. Accurate and accessible measures of body composition would provide data to personalise nutritional therapy, whilst avoiding adiposity in this disease group. We assessed the feasibility of MRI-derived measures of psoas crosssectional area in paediatric CD and correlated with anthropometric and bioelectrical impedance (BIA) measures.

<u>Methods-</u> MRI small bowel/pelvis images of patients with CD, aged less than 18 years, were retrieved. Patients with concurrent anthropometric and BIA measurements were eligible for inclusion. The psoas cross-sectional area at L3 was calculated by two assessors and combined to give the combined psoas cross-sectional area. To assess reproducibility of measures we calculated the coefficient of variation (CoV). BIA, age, height-Z-scores and weight-Z-scores were correlated with psoas area.

<u>Results-</u> 10 patients were included. Psoas cross-sectional area was able to be calculated for all MRI scans. There was high reproducibility between measurers, mean CoV 0.099. There was a significant positive correlation between psoas area and BIA-derived lean mass, Pearson correlation coefficient (PCC) 0.831, p=0.003.

Height-Z-score, weight-Z-score and age all positively correlated with psoas area but none were significant, PCC 0.343 p=0.33, PCC=0.222 p=0.54, and PCC 0.6034, p=0.065, respectively.

<u>Conclusions-</u> These demonstrate the feasibility of deriving measures of body composition from routine MRI imagine. There was significant positive correlation between psoas area

and BIA-derived estimates of lean mass. Further studies are required to derive normal measures prior to routine clinical implementation to aid personalisation of nutritional therapy.

Introduction

Paediatric inflammatory bowel disease (IBD) is a chronic relapsing and remitting condition with long term nutritional sequalae. Historically, paediatric onset Crohn's disease has presented with weight loss, growth delay and malnutrition¹. Whilst recent data has pointed to improved linear growth, patients continue to present underweight and may continue to have nutritional compromise². There is emerging adult data indicating many patients with Crohn's disease have persistent body composition abnormalities, with sarcopenia associated with poor disease outcomes³. Whilst there is less data in paediatric Crohn's disease there are established reports of lower muscle mass when compared to the general population^{4,5}. Body composition assessment remains challenging with limited technology and difficulty of interpretation of values in the context of different ages. A wide range of methods have been used to establish estimates of muscle mass in paediatric IBD, although these generally employ additional measurements of children performed through dual energy X-ray absorptiometry (DEXA) or computerised tomography (CT) scans^{6–8}. Whilst these data produce meaningful results, the additional radiation exposure makes justification of routine measurements in children difficult. Contemporary data from Israel utilised small bowel magnetic resonance imaging (MRI) in paediatric IBD patients⁹. The authors found significant correlation with disease severity, and sarcopenia was a predictor of severe clinical disease course and need for escalation to biologic therapy.

Nutritional therapy is established as key element of Crohn's disease treatment, including exclusive enteral nutrition and newer exclusion diets such as CD-ED and CD-TREAT^{10–12}. However, the utility of maintenance enteral nutrition to prevent relapse remains controversial, with no high quality evidence present^{13,14}. Despite this, the use of nutritional supplements in Crohn's disease is widely practiced, and can be useful as a targeted strategy for malnourished patients¹⁵. It is increasingly evident that obesity is a problem in IBD patients, resulting in poorer outcomes and increased incidence of additional noncommunicable disease¹⁶. Whilst simple anthropometry remains a key tool in nutritional assessment we should be looking towards routine measures of body composition to better characterise patients, identify sarcopenia and target nutritional interventions⁵.

Within this study we aimed to use MRI scans routinely performed on paediatric patients with Crohn's disease to establish feasibility of psoas muscle cross-sectional area calculation. We aimed to relate psoas cross-sectional area to anthropometric and bioelectrical impedance (BIA) measures.

Methods

Patients were recruited from the paediatric gastroenterology service at Southampton Children's Hospital. To be included patients had to have a diagnosis of Crohn's disease in line with the modified Porto criteria¹⁷, be aged under 18 years of age and be attending routine appointments at Southampton Children's Hospital. All patients, or parents, gave informed consent.

MRI scans

Patients who had undergone a routine MRI scan within 4 months of recruitment were eligible for inclusion in the analysis. The MRI must have included the L3 segment of the psoas muscle and therefore was restricted to small bowel and pelvic MRIs.

Bioelectrical impedance measurements

At the time of recruitment all patients had bioelectrical impedance (BIA) measurements performed. We utilised the derived estimate of total lean mass (in kg), alongside the percentage lean mass, as a proxy for sarcopenia. These measures have previously been utilised in paediatric IBD to determine body composition¹⁸.

Psoas muscle mass calculation

Muscle mass was measured independently by two radiologists (DP and MG). The crosssectional area of the left and right psoas muscles was calculated using SyngoVia software¹⁹, with the measurement taken outlining the psoas muscle using the freehand ROI tool and nudge tool for adjustment of the margin at the level of the mid L3 vertebral body. These measures were then combined to give an overall 'combined' psoas area. These data are reported as psoas cross-sectional area in cm².

Anthropometric measurements

At recruitment patients had routine height, weight and BMI data collected. These were converted into height Z-score, weight Z-score and BMI Z-scores using the WHO reference data.

Data and statistical analysis

For each left psoas measurement and each right psoas measurement we calculated the coefficient of variation from the two radiological measurements to determine the reproducibility. We used Pearson correlation to determine the relationship between individual anthropometric and BIA derived variables and the psoas muscle cross sectional area.

Ethical approval

Ethical approval was granted by the London (Westminster) research ethics committee (18/LO/1457).

<u>Results</u>

Ninety-seven patients were recruited and eligible for inclusion in the MRI scan arm of the study. Following application of inclusion criteria, 10 patients had MRI imaging available within 4 months of recruitment and were included for further analysis.

Feasibility of measures

Free-hand annotation at the level of mid L3 vertebral body was performed as an addition to routine reporting of MRI scans. All scans retrieved for analysis were annotated. Measures of psoas cross-sectional area were able to be calculated in 100% of scans.

Coefficient of variation

We assessed the reproducibility of measurements between measurers using the coefficient of variation. Multiple measures were available for 8 patients, table 1. The mean coefficient of variation was equivalent to 9.9% (range 1.4-29.4%). Assuming a linear relationship, these data would expect a 2.72cm² increase of psoas area for each increase in year of age from the age of 11-16 years, the mean individual psoas area for all ages, was 7.83cm² (range 4.98-13.9cm²).

Psoas cross sectional area correlates with BIA-derived lean mass

BIA analysis utilises a derived measure of lean mass and fat mass to estimate the total lean mass in a patient of known weight. Pearson correlation identified a significant positive correlation between combined psoas crossed sectional area and BIA-derived lean mass, Pearson correlation coefficient (PCC) 0.831, p=0.003, figure 1A. There was also a positive correlation between age and BIA-derived lean mass, PCC 0.759, p=0.011, figure 1B.

Relationship of psoas area with age, height and weight

We correlated the height and weight Z-score with the mean combined L3 psoas crosssectional area. Height Z-score positively correlated with psoas area, PCC=0.343 but this was not significant p=0.33, figure 2A. Similarly, weight Z-score positively correlated with psoas area, PCC=0.222 but this was also not significant p=0.54, figure 2B.

Age at the time of MRI scan was correlated with mean combined L3 psoas cross-sectional area. The PCC 0.6034, p=0.065 demonstrating a positive, but non-significant, relationship between age and psoas muscle area, figure 2C.

Discussion

These data demonstrate that routine MRI scans, performed on patients with Crohn's disease, can be used to derive measures of psoas cross-sectional area. These measures significantly correlate with BIA-derived estimates of lean mass. Reproducibility of psoas area measures was relatively high with around 10% variability in measures across all patients. Overall, these measures are highly feasible as part of routine MRI reporting. These data may enable future definitions of normal muscle mass to be formulated and assessment of sarcopenia in children with IBD to be performed as part of routine scanning.

There is increasing interest in personalised nutritional therapy for Crohn's disease⁵. The increase in childhood obesity has presented novel challenges in a disease previously typified by undernutrition¹⁶. The role of dietary management for induction of remission in paediatric Crohn's disease is well established, however the place of routine supplemental nutrition is less certain^{10,14,20}. In adult IBD, sarcopenia is associated with increased morbidity and mortality, and worse outcomes including the need for surgery^{3,21}. However, obesity is also associated with worse long-term outcomes in IBD and increased risk of additional non-communicable disease¹⁶. The balance of ensuring patients are nutritionally replete, without promoting adiposity, requires a personalised approach to nutrition. More recent body composition data has indicated that up to 25% of children with IBD have excess adiposity, which may be missed by routine anthropometric screening²². Beyond this, exclusive enteral nutrition has been shown to increase lean mass, but not fat mass, at induction in newly diagnosed Crohn's disease patients¹⁸. Clearly, a practical and easy measure of body composition is required to tailor nutritional therapy to patients.

MRI scans for small bowel assessment should be routinely performed at diagnosis in all children with Crohn's disease¹³. This provides an opportunity to utilise measures of body composition derived from these data to personalise ongoing nutritional intervention. In this study we demonstrate the feasibility of gathering MRI derived psoas cross-sectional area, alongside the strong correlation with age and BIA-estimated lean mass. Whilst this is currently a manual process a neural network has been trained on CT to identify the L3 level and calculate psoas volumes and this would be a technique to automate the calculation on MRI imaging²³.

An additional element for MRI scans would be the role of fat infiltration of psoas. The fat fraction could be calculated within the area of the psoas muscle. A Dixon sequence provides measurement to visualise water content and fat content separately²⁴. This can be utilised to calculate the fat fraction within the muscle, a calculation performed following segmentation within SyngioVia software tools. The addition Dixon sequence requires no contrast administration and takes less than a minute to acquire in the scanner. This would allow further estimation of adiposity as part of routine MRI imaging.

We acknowledge that there are several limitations of these data. We were able to perform the analysis on only 10 patients due to time differences between BIA measures and MRI imaging. The role of sex and puberty was not able to be examined due to the low patient number. In order to provide clinically useful measures, it would be vital to construct sexspecific centile charts for psoas cross-sectional area, which would require higher numbers of patients. Formulation of these charts would enable children with Crohn's disease to have accurate assessment of the degree of sarcopenia at diagnosis, and at any subsequent MRI imaging, without the need for additional scans or hospital visits. The clinical team could then target nutritional intervention more concisely and avoid overnutrition in those patients without a lean mass deficit.

Conclusion

These data provide a strong indication of the utility of routine MRI imaging in the assessment of sarcopenia for children with Crohn's disease, with strong correlation between psoas area and BIA-derived estimates of lean mass. Further studies are required to derive normal measures and consider the implementation of additional MRI sequences to assess adiposity, prior to routine clinical implementation to aid personalisation of nutritional therapy.

Tables and Figures

Table 1- Coefficient of variation for eight patients with multiple measures of psoas cross-sectional area.

Figure 1A- Positive relationship between combined mean psoas cross-sectional area and bioelectrical impedance (BIA) derived whole body lean mass (Kg), Pearson correlation coefficient, 0.831, p=0.003, **1B**- Positive relationship between combined mean psoas cross-sectional area and age at MRI scan (years), Pearson correlation coefficient 0.759, p=0.011.

Figure 2A- Positive relationship between combined mean psoas cross-sectional area and height Z-score Pearson correlation coefficient, 0.343, p=0.33, **2B-** Positive relationship between combined mean psoas cross-sectional area and weight Z-score, Pearson correlation coefficient, 0.222, p=0.54, **2C-** Positive relationship between combined mean psoas cross-sectional area and age at MRI scan (years), Pearson correlation coefficient, 0.6034, p=0.065,

References

- Motil KJ., Grand RJ., Davis-Kraft L., Ferlic LL., Smith EO. Growth failure in children with inflammatory bowel disease: A prospective study. *Gastroenterology* 1993;**105**(3):681–91. Doi: 10.5555/URI:PII:001650859390883E.
- Ashton JJ., Green Z., Young A., Borca F., Coelho T., Batra A., et al. Growth failure is rare in a contemporary cohort of paediatric inflammatory bowel disease patients. *Acta Paediatr* 2020:apa.15383. Doi: 10.1111/apa.15383.
- Ryan E., McNicholas D., Creavin B., Kelly ME., Walsh T., Beddy D. Sarcopenia and inflammatory bowel disease: A systematic review. *Inflamm Bowel Dis* 2019:67–73. Doi: 10.1093/ibd/izy212.
- Davies A., Nixon A., Muhammed R., Tsintzas K., Kirkham S., Stephens FB., et al. Reduced skeletal muscle protein balance in paediatric Crohn's disease. *Clin Nutr* 2019. Doi: 10.1016/j.clnu.2019.05.017.
- Ashton JJ., Green Z., Beattie RM. Beyond bedside measures of malnutrition in paediatric Crohn's disease – Should we be thinking of sarcopenia. *Clin Nutr* 2020. Doi: 10.1016/j.clnu.2020.03.034.
- 6. Burnham JM., Shults J., Semeao E., Foster BJ., Zemel BS., Stallings VA., et al. Bodycomposition alterations consistent with cachexia in children and young adults with Crohn disease. *Am J Clin Nutr* 2005;**82**(2):413–20. Doi: 10.1093/AJCN.
- 7. Thayu M., Shults J., Burnham JM., Zemel BS., Baldassano RN., Leonard MB. Gender differences in body composition deficits at diagnosis in children and adolescents with Crohn's disease. *Inflamm Bowel Dis* 2007;**13**(9):1121–8. Doi: 10.1002/ibd.20149.

- Schneider SM., Al-Jaouni R., Filippi J., Wiroth J-B., Zeanandin G., Arab K., et al.
 Sarcopenia is prevalent in patients with Crohn's disease in clinical remission. *Inflamm Bowel Dis* 2008;**14**(11):1562–8. Doi: 10.1002/ibd.20504.
- Atlan L., Pratt LT., Cohen S., Shiran S., Yerushalmy-feler A. Sarcopenia is a predictor for severe disease course in paediatric inflammatory bowel disease. *J Crohn's Colitis* 2020;14(Supplement_1):S197–8. Doi: 10.1093/ECCO-JCC.
- 10. Ashton JJ., Gavin J., Beattie RM. Exclusive enteral nutrition in Crohn's disease: Evidence and practicalities. *Clin Nutr* 2018. Doi: 10.1016/j.clnu.2018.01.020.
- Levine A., Wine E., Assa A., Sigall Boneh R., Shaoul R., Kori M., et al. Crohn's Disease Exclusion Diet Plus Partial Enteral Nutrition Induces Sustained Remission in a Randomized Controlled Trial. *Gastroenterology* 2019;**157**(2):440-450.e8. Doi: 10.1053/j.gastro.2019.04.021.
- Svolos V., Hansen R., Nichols B., Quince C., Ijaz UZ., Papadopoulou RT., et al. Treatment of Active Crohn's Disease With an Ordinary Food-based Diet That Replicates Exclusive Enteral Nutrition. *Gastroenterology* 2018;**0**(0). Doi: 10.1053/j.gastro.2018.12.002.
- Van Rheenen PF., Aloi M., Assa A., Bronsky J., Escher JC., Fagerberg UL., et al. The Medical Management of Paediatric Crohn's Disease: an ECCO-ESPGHAN Guideline Update. *J Crohn's Colitis* 2020;**2020**:1–24. Doi: 10.1093/ecco-jcc/jjaa161.
- Gavin J., Ashton JJ., Heather N., Marino L V., Beattie RM. Nutritional support in paediatric Crohn's disease; Outcome at 12 months. *Acta Paediatr* 2017. Doi: 10.1111/apa.14075.

- Forbes A., Escher J., Hébuterne X., Kłęk S., Krznaric Z., Schneider S., et al. ESPEN guideline: Clinical nutrition in inflammatory bowel disease. *Clin Nutr* 2017;**36**(2):321– 47. Doi: 10.1016/j.clnu.2016.12.027.
- Singh S., Dulai PS., Zarrinpar A., Ramamoorthy S., Sandborn WJ. Obesity in IBD: epidemiology, pathogenesis, disease course and treatment outcomes. *Nat Rev Gastroenterol Hepatol* 2017;**14**(2):110–21. Doi: 10.1038/nrgastro.2016.181.
- Levine A., Koletzko S., Turner D., Escher JC., Cucchiara S., de Ridder L., et al. ESPGHAN revised porto criteria for the diagnosis of inflammatory bowel disease in children and adolescents. *J Pediatr Gastroenterol Nutr* 2014;**58**(6). Doi: 10.1097/MPG.0000000000239.
- Gerasimidis K., Talwar D., Duncan A., Moyes P., Buchanan E., Hassan K., et al. Impact of exclusive enteral nutrition on body composition and circulating micronutrients in plasma and erythrocytes of children with active Crohn's disease. *Inflamm Bowel Dis* 2012;**18**(9):1672–81. Doi: 10.1002/ibd.21916.
- syngo.via Siemens Healthineers United Kingdom. Available at: https://www.siemens-healthineers.com/en-uk/medical-imaging-it/advancedvisualization-solutions/syngovia. Accessed November 17, 2020.
- Sigall-Boneh R., Pfeffer-Gik T., Segal I., Zangen T., Boaz M., Levine A. Partial Enteral Nutrition with a Crohn's Disease Exclusion Diet Is Effective for Induction of Remission in Children and Young Adults with Crohn's Disease. *Inflamm Bowel Dis* 2014;**20**(8). Doi: 10.1097/MIB.00000000000110.
- 21. Bamba S., Sasaki M., Takaoka A., Takahashi K., Imaeda H., Nishida A., et al. Sarcopenia

is a predictive factor for intestinal resection in admitted patients with Crohn's disease. *PLoS One* 2017;**12**(6):e0180036. Doi: 10.1371/journal.pone.0180036.

- Dhaliwal J., Martincevic I., Williams B., Frost K., Uusoue K., Arpino V., et al. Body Composition Using Air Displacement Plethysmography in Children With Inflammatory Bowel Disease. *J Pediatr Gastroenterol Nutr* 2020;**71**(1):52–8. Doi: 10.1097/MPG.0000000002683.
- Hashimoto F., Kakimoto A., Ota N., Ito S., Nishizawa S. Automated segmentation of 2D low-dose CT images of the psoas-major muscle using deep convolutional neural networks. *Radiol Phys Technol* 2019;**12**(2). Doi: 10.1007/s12194-019-00512-y.
- 24. Ma J. Dixon techniques for water and fat imaging. *J Magn Reson Imaging* 2008;28(3):543–58. Doi: 10.1002/jmri.21492.

	Patient 1		Patient 2		Patient 3		Patient 4		Patient 5		Patient 6		Patient 7		Patient 8	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
Measure 1	10.42	12.09	4.98	5.75	8.5	8.85	7.5	8.3	7.62	7.82	7.59	8.19	6.28	5.54	10.24	10.37
Measure 2	12.26	13.9	4.97	5.91	8.33	8.17	6.1	6.19	8.02	7.19	6.84	7.05	5.8	5.89	7.06	6.8
Mean	11.34	12.995	4.975	5.83	8.415	8.51	6.8	7.245	7.82	7.505	7.215	7.62	6.04	5.715	8.65	8.585
Coefficient of variation	11.5%	9.9%	0.1%	1.9%	1.4%	5.7%	14.6%	20.6%	3.6%	5.9%	7.4%	10.6%	5.6%	4.3%	27.0%	29.4%





