Body composition analysis using abdominal scans from routine clinical care in patients with Crohn’s Disease

Darcy Quinn Holt, Boyd Josef Gimnicher Strauss, Kenneth K Lau, and Gregory Thomas Moore

INTRODUCTION

Crohn’s Disease is a gastrointestinal inflammatory condition associated with malnutrition,[1–4] lower bone mineral density,[5] lower body mass index (BMI), and lower fat-free mass (FFM).[6] Body weight, weight loss, and BMI are insufficiently sensitive to assess FFM.[7,8] In clinical practice, the most accessible[9] and accurate[10] means of determining these body composition compartments is whole body dual-energy X-ray absorptiometry (DXA).

Despite recommendations that patients with inflammatory bowel disease (IBD) undergo regular DXA for monitoring bone mineral density (BMD),[11] screening prevalence is low: approximately one in five patients.[12] However, abdominal computed tomography (CT) scans are often obtained as part of routine care of Crohn’s Disease for assessment of disease complications or activity.[13]

In other disease states, such as cancer[14] and obesity,[15] analysis of single slice abdominal CT or magnetic resonance imaging (MRI) images at the level of the third lumbar vertebra (L3) has been shown to highly correlate with FFM as determined by DXA. This correlation has not previously been described in patients with inflammatory bowel disease.

Similarly, evaluation of intra-abdominal fat area in a single CT or MRI slice at the level of the L4–5 intervertebral disc has been shown to correlate highly with total visceral adipose tissue volume.[14,16–18] The use of single-slice abdominal scans to estimate total body skeletal muscle, visceral adipose tissue and subcutaneous adipose tissue as measured by total body MRI scan has shown that the L3 level provides the most robust single scan for estimating all parameters.[19]

We sought to determine whether single slice analysis of CT scans at the L3 and L4–5 levels, obtained as part of routine clinical care in patients with Crohn’s Disease, was able to predict body composition compartments with accuracy.

MATERIALS AND METHODS

Patients who had CT scans (Discovery CT 750HD, GE Healthcare, Little Chalfont, UK) and total body DXA (GE Lunar Prodigy, GE Healthcare, Little Chalfont, UK) performed within a 12-month period as part of routine clinical care at a single tertiary health care service (Monash Health, Victoria, Australia) were retrospectively identified by a search of radiology and clinical databases, with a diagnosis of Crohn’s disease confirmed by chart review. CT DICOM (Digital Imaging and Communications in Medicine) images at the L3 and L4–5 levels were analysed for body composition by a single experienced operator using SliceOmatic 4.3 (TomoVision, Montreal, Quebec, Canada). CT scans were acquired on a 64-section CT scanner (Discovery CT 750HD, GE Healthcare, Little Chalfont, UK). The acquisition protocol consisted of an automatic exposure control (AEC) technique with a slice thickness of 1.25 mm and a pitch of 1.5.

Abdominal CT images of patients with Crohn’s disease were analyzed and comparison was made with total body fat-free mass, total body fat mass, femoral neck t-score, and other parameters reported from DXA, the reference method.

RESULTS

Thirty-seven subjects were identified, 15 male and 22 female, with a mean age of 43.8 years. There was significant correlation (Pearson $r = 0.923, p < 0.001$) between skeletal muscle area from CT and total fat-free mass measured by DXA. Similarly, total body fat mass correlated strongly ($r = 0.928, p < 0.0001$) with subcutaneous fat area. In this cohort of ambulatory Crohn’s Disease patients, low muscle mass/sarcopenia was prevalent and predictive of lower bone mineral density.

CONCLUSIONS

Fat mass, fat-free mass, and appendicular skeletal muscle index can be predicted by analysis of a single CT slice in patients with Crohn’s Disease. Similar to published data from healthy subjects, the L3 vertebral body level provided the most robust correlation with most parameters. This study represents the first published use of routinely obtained abdominal imaging to demonstrate this relationship – and to predict body composition components – in patients with inflammatory bowel disease.
Statistical analysis
Pearson correlation coefficients were calculated and multivariate linear regression analysis was performed. Variables included for linear modelling included basic demographic and anthropometric information (age, gender, height, and weight) and the CT measurement with highest correlation to the DXA-measured body composition compartment being estimated. When individual values were missing from the dataset, subjects were excluded from the relevant analysis. Akaike’s information criteria [20] were used to discard variables from linear modelling. A Bland–Altman plot was used to evaluate bias and trend of predicting FFM and FM from cross-sectional images compared to DXA measurements. A p value of less than 0.05 was considered significant. GraphPad Prism 6 (GraphPad Software, La Jolla, CA) and R version 3.1.2 (The R Foundation for Statistical Computing, Vienna, Austria) were used.

Ethical considerations
This research was approved by the Monash Health Human Research Ethics Committee (project number 11264A).

Results
Thirty-seven subjects were identified, 15 male and 22 female, with a mean age of 43.8 years (Table 1).

CT scans were obtained for a variety of clinical indications (Table 1).

There was significant correlation (Pearson r = 0.924, p < 0.001) between the L4–5 skeletal muscle area from CT and total FFM as measured by DXA (Figure 1A); the correlation was equally strong at the L3 level (Table 2). The median time between CT and DXA scans was 21 days; there was no correlation between the interval between scans and the difference between predicted (CT) and measured (DXA) lean tissue mass (r = −0.124, p = 0.520).

Similarly, total body fat mass showed a high degree of correlation (r = 0.928, p < 0.0001, n = 37) with subcutaneous fat area at an L3 level; correlation was equally strong at the L4–5 level (Figure 1B).

A formula previously described by Mourtzakis, and referenced by Baker,[14,15] for CT-derived FFM was able to predict DXA FFM in this patient group (R² 0.852, p < 0.0001). Likewise, DXA-measured ASMI was predicted by Mourtzakis’ formula using measurement of skeletal muscle area at the L3 level (R² 0.730, p < 0.0001).

In these two previously published studies, a statistically significantly older and heavier patient cohort was studied. To ascertain whether closer prediction of DXA measures of body composition may be possible in this Crohn’s Disease patient cohort, multivariate linear modelling was used.

Table 1. Characteristics of the study cohort.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number (n)</th>
<th>Mean ± SD</th>
<th>p (t-test male vs. female)</th>
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<tbody>
<tr>
<td>Number (n)</td>
<td>37</td>
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<td></td>
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<tr>
<td>Age (years)</td>
<td>43.8 ± 2.6</td>
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<tr>
<td>Male</td>
<td>21 ± 3.5</td>
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<tr>
<td>Female</td>
<td>16 ± 3.7</td>
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<tr>
<td>Mean weight (kg)</td>
<td>67.2 ± 3.6</td>
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<tr>
<td>Male</td>
<td>78.4 ± 6</td>
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<tr>
<td>Female</td>
<td>74.8 ± 13</td>
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<tr>
<td>Mean DXA FFM</td>
<td>23.9 ± 1</td>
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<tr>
<td>Male</td>
<td>26.1 ± 1.8</td>
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<tr>
<td>Female</td>
<td>22.4 ± 1.2</td>
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<td>0.103</td>
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<tr>
<td>Mean DXA FM</td>
<td>46 ± 2.3</td>
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<tr>
<td>Male</td>
<td>58.5 ± 3.1</td>
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<tr>
<td>Female</td>
<td>38.4 ± 1.5</td>
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<td>&lt;0.001</td>
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<td>Mean ASMI (kg/m²)</td>
<td>6.6 ± 0.4</td>
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<tr>
<td>Male</td>
<td>7.81 ± 0.49</td>
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<tr>
<td>Female</td>
<td>5.49 ± 0.19</td>
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<td>&lt;0.001</td>
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<tr>
<td>Mean L3 skeletal muscle area (cm²)</td>
<td>128 ± 7.5</td>
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<tr>
<td>Male</td>
<td>161.9 ± 11.8</td>
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<tr>
<td>Female</td>
<td>104.8 ± 6.1</td>
<td></td>
<td>&lt;0.001</td>
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<tr>
<td>Mean L4–5 skeletal muscle area (cm²)</td>
<td>123.9 ± 7.3</td>
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<td></td>
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<tr>
<td>Male</td>
<td>158 ± 11.2</td>
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<tr>
<td>Female</td>
<td>99.5 ± 5</td>
<td></td>
<td>&lt;0.001</td>
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<tr>
<td>Mean L3 visceral adipose tissue area</td>
<td>97 ± 14.4</td>
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<td></td>
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<tr>
<td>Male</td>
<td>129.6 ± 28.3</td>
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<tr>
<td>Female</td>
<td>74.8 ± 13.1</td>
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<td>0.09</td>
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<tr>
<td>Mean L3 subcutaneous adipose tissue area (cm²)</td>
<td>171.9 ± 18.8</td>
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<tr>
<td>Male</td>
<td>182 ± 30.2</td>
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<tr>
<td>Female</td>
<td>165 ± 24.5</td>
<td></td>
<td>0.66</td>
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<tr>
<td>Mean L4–5 visceral adipose tissue area (cm²)</td>
<td>92.8 ± 10.7</td>
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<tr>
<td>Male</td>
<td>111.6 ± 21.2</td>
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<tr>
<td>Female</td>
<td>79.3 ± 9.7</td>
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<td>0.18</td>
</tr>
<tr>
<td>Mean L4–5 subcutaneous adipose tissue area (cm²)</td>
<td>218.7 ± 23.5</td>
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<td></td>
</tr>
<tr>
<td>Male</td>
<td>234.4 ± 39.3</td>
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</tr>
<tr>
<td>Female</td>
<td>207.6 ± 29.5</td>
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<td>0.59</td>
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To ascertain and test a specific formula in this setting, subjects were randomly assigned into either a formula-finding cohort (n = 19) or a validation cohort (n = 18). From the formula-finding cohort, a model incorporating age, gender, weight, height, and skeletal muscle area at L3 level was tested. Using Akaike’s information criteria, weight was discarded. The resulting formula predicted measured FFM from DXA with R² of 0.9301, p < 0.0001.

Fat – free mass = (0.11687 × L3 skeletal muscle area in cm²) + (0.12883 × age in years) + (34.64221 × height in m) + (4.6485 if male gender) − 35.18862

In the validation cohort, this formula had an R² of 0.918, p < 0.0001 (Figure 1C).

A Bland–Altman plot of the resulting predicted measures for the entire dataset (Figure 2A) suggests that at larger values of FFM, this formula may tend to underestimate the actual value (Pearson r of average vs. difference 0.589, p < 0.001), although the bias (+0.005, SD 4.446) is small.
From the formula-finding cohort, a model incorporating age, gender, weight, height, and subcutaneous adipose tissue area at L3 level was tested. No variables were excluded after use of Aikaike’s information criteria. The resulting formula predicted measured fat mass from DXA with $R^2$ of 0.942, $p < 0.0001$.

\[
\text{Fat mass} = 0.03377 \times \text{L3 subcutaneous adipose tissue area in cm}^2 \\
- (0.16216 \times \text{age in years}) \\
- (6.16599 \text{ if male gender}) \\
- (24.29556 \times \text{height in m}) \\
+ (0.57833 \times \text{weight in kg}) + 26.49794
\]

In the validation cohort, this model had an $R^2$ of 0.930, $p < 0.0001$ (Figure 1D).

A Bland–Altman plot (2B) of the difference between predicted fat mass and measured fat mass vs. the average between the two values demonstrated small bias ($0.76$, SD $4.32$) and did not reveal a trend ($p = 0.237$) towards systematic difference.

### Bone mineral density

8.3% of subjects had a lumbar spine t-score $<-2.5$; 14.3% had a femoral neck t-score $<-2.5$. There was a strong correlation between L3 skeletal muscle area and femoral neck BMD ($r = 0.746, p < 0.001$), total body BMD ($r = 0.651, p < 0.001$) and a weaker – although statistically significant – correlation with lumbar spine BMD ($r = 0.355, p = 0.031$). All subjects with femoral neck osteoporosis had lower than median skeletal muscle area.

### Sarcopenia

Low muscle mass was prevalent in this cohort. 45.4% of male subjects and 50% of female subjects had a DXA-measured ASMI more than two standard deviations below a young adult population mean, as previously defined.[21] Although the LTMI formula of Mourtzakis had poor sensitivity and specificity for detection of DXA-measured sarcopenia in this cohort (AUROC 0.76, $p = 0.08$), we sought to determine whether multivariate linear regression would find a more accurate model: \[
\text{LTMI} = (0.0247 \times \text{L4–5 skeletal muscle area in cm}^2) + (0.01879 \times \text{weight in kg}) - (3.47054 \times \text{height in m}) + (0.89309 \times \text{gender})
\]
if male gender) + 7.6514] have improved sensitivity and specificity (AUROC 0.86, p 0.02).

**Obesity**

Thirty-nine percent subjects had a BMI greater than 25 kg/m² and 19% greater than 30 kg/m². The prevalence of sarcopenic obesity, defined as a BMI ≥30 kg/m² in conjunction with an ASMI <2 SD below young adult mean, was low: only one subject fulfilled these criteria.

**Longitudinal studies**

A small number of identified subjects had repeated paired scans available for comparison, and in some subjects, changes in body composition had occurred. While only one pair of scans from each subject was included in the main dataset, repeated measurements were analysed with one-way ANOVA to determine that there was no variation in the mean difference between observed measures of skeletal muscle area by DXA and CT-predicted measures (p = 0.677).

**Male vs. female**

While significant differences in body composition existed between male and female subjects (Table 1), the formula for predicting fat mass showed equal applicability in male and female subjects (Figure 2C and D), with linear regression analysis demonstrating no significant difference between the lines (p = 0.275). However, the formula for predicting FFM demonstrated a difference between the observed and predicted values in male and female subjects that was of statistical significance (p = 0.009). Despite a high degree of accuracy in both genders, model prediction of FFM was slightly better in male subjects (R² = 0.902) than female subjects (R² = 0.885).

**Discussion**

Analysis of body composition and identification of low FFM may have important implications for prognosis and treatment of patients with IBD and yet, such screening does not form a part of treatment algorithms or recommendations from professional bodies.

A recent systematic review of body composition studies in inflammatory bowel disease found that body composition parameters often varied from population norms, but that detailed analyses and outcome data were scarce[8] the authors recommend further investigation and publication of better quality data to ascertain the role of body composition analysis in clinical practice.

Sarcopenia – defined as the condition of low muscle mass, strength, and/or function [22] – is prevalent in Crohn’s Disease,[8,23–25] with inflammatory cytokines such as tumour necrosis factor alpha (TNF) implicated.[26,27] The TNF antagonist infliximab reverses sarcopenia in Crohn’s Disease [25]; early cachexia may also be amenable to treatment of underlying inflammation, nutritional support, orexigenic agents, and exercise.[28–30] In a case-control
study.[24,31] Crohn’s Disease patients in clinical remission were three times more likely than healthy controls to have sarcopenia, as defined by an ASMI more than one standard deviation below the young adult mean measured by whole body DXA. Screening for sarcopenia in inflammatory bowel disease may enable more aggressive, and perhaps more effective, early therapy.

Steroid exposure and body composition parameters such as weight, skinfold thickness, BMI, muscle strength, skeletal muscle mass, and ASMI have been associated with altered BMD in patients with IBD.[23,32] Osteopenia has been reported as having a 50% prevalence in patients with Crohn’s Disease.[33] with osteoporosis in 30%; a systematic review has shown that 87% of Crohn’s Disease patients have a significant reduction in BMD measured by DXA compared to controls.[8] In the patient group reported in our study, a lower incidence of osteoporosis and osteopenia was found, but there was significant correlation between CT measures of body composition and BMD.

Many studies show a reduction in BMI and reduced fat mass in Crohn’s disease compared with the general population,[6,34] and in this cohort, rates of overweight and obesity were less than the Australian population (63.4% self-report a BMI > 25 kg/m²).[35]

Axial CT slices at the L3 level and L4–5 level can be used to estimate fat mass, FFM, and ASMI measured by DXA in patients with Crohn’s Disease, allowing analysis of body composition using images otherwise obtained as part of routine clinical care. Although not all paired CT and DXA studies were obtained contemporaneously, the median interval was less than one month; there was no correlation between interval and difference between measured and expected values, suggesting that body composition remained relatively constant during the interval between scans. A limitation of this study is the small number of subjects with both CT and DXA studies performed within the constrained time period. Although robust linear relationships were demonstrated, a larger cohort may have permitted further analysis of gender differences or the role of other variables.

Similar to published data from healthy subjects,[19] the L3 vertebral body level provided the most robust correlation with most parameters, with no significant difference between genders in terms of degree of correlation.

In this cohort of ambulatory Crohn’s Disease patients, low muscle mass was prevalent, and was predictive of lower BMD. We have described the first use of routinely obtained abdominal imaging to demonstrate this relationship – and to predict body composition components – in patients with inflammatory bowel disease. This study validates a method of body composition analysis using abdominal scans otherwise obtained as part of routine clinical care in patients with Crohn’s Disease.

The technique described may allow not only further research into the role of body composition in inflammatory bowel disease: prospectively, but also by permitting retrospective analysis of existing patient cohorts with accessible CT scans. Possible important applications include optimising drug dosing, predicting treatment response or complications, and improving the accuracy of prognosis.

Disclosure statement
The authors report no conflict of interest.

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