



Sarcopenia and visceral obesity assessed by computed tomography are associated with adverse outcomes in patients with Crohn's disease

Julienne Grillot, Christelle d'Engremont, Anne-Laure Parmentier, Zaher Lakkis, Gaël Piton, Diane Cazaux, Claire Gay, Marjolaine de Billy, Stéphane Koch, Sophie Borot, et al.

► To cite this version:

Julienne Grillot, Christelle d'Engremont, Anne-Laure Parmentier, Zaher Lakkis, Gaël Piton, et al.. Sarcopenia and visceral obesity assessed by computed tomography are associated with adverse outcomes in patients with Crohn's disease. *Clinical Nutrition*, 2020, 39, pp.3024 - 3030. <10.1016/j.clnu.2020.01.001>. <hal-03492434>

HAL Id: hal-03492434

<https://hal.science/hal-03492434v1>

Submitted on 17 Oct 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons CC BY-NC 4.0 - Attribution - Non-commercial use - International License

Sarcopenia and visceral obesity assessed by computed tomography are
associated with adverse outcomes in patients with Crohn's disease

Julienne Grillo¹, Christelle D'Engremont¹, Anne Laure Parmentier², Zaher Lakkis³, Gaël
Piton⁴, Diane Cazaux¹, Claire Gay¹, Marjolaine De Billy⁵, Stéphane Koch¹, Sophie Borot⁶,
Lucine Vuitton¹

Short title: Body composition is associated with adverse outcomes in Crohn's disease

Affiliations

¹Department of Gastroenterology and Nutrition, University Hospital of Besançon, University
Bourgogne Franche-Comté, 25030 Besançon, France.

²Centre de Méthodologie Clinique, University Hospital of Besançon, Besançon, France.

³Department of Digestive and Oncologic Surgery – Liver Transplantation Unit, University
Hospital of Besançon, University Bourgogne Franche-Comté, 25030 Besançon, France.

⁴Intensive Care unit, University Hospital of Besançon, University Bourgogne Franche-Comté,
25030 Besançon, France.

⁵Department of Radiology, University Hospital of Besançon, University Bourgogne Franche-
Comté, 25030 Besançon, France.

⁶Department of Endocrinology and Nutrition, University Hospital of Besançon, University
Bourgogne Franche-Comté, 25030 Besançon, France.

23 Corresponding author:
24 Lucine Vuitton, MD, PhD,
25 Department of Gastroenterology and EA3181, University Hospital of Besançon, University
26 Bourgogne-Franche-Comté, 25030 Besançon, France.
27 Phone: + 33 3 81 66 8393; Fax: + 33 3 81 66 8417
28 Email: lvuitton@chu-besancon.fr; lucinevuitton@gmail.com
29
30 Abbreviations:
31 AT, Adipose Tissue; BMI, Body Mass Index; CD, Crohn's Disease; CRP, C Reactive Protein;
32 CT, Computed Tomography; DICOM, Digital Imaging and Communication in Medicine;
33 DXA, Dual-energy X-ray Absorptiometry; IBD, Inflammatory Bowel Disease; MRI,
34 Magnetic Resonance Imaging; NIH, National Institutes of Health; SFA, Subcutaneous Fat
35 Area; SM, Skeletal Muscle; SMI, Skeletal Muscle Index; TFA, Total Fat Area; TNF, Tumor
36 necrosis factor; VFA, Visceral Fat Area; WC, Waist Circumference.
37

ABSTRACT

Background: Altered body composition may impact on the clinical course of Crohn's disease (CD) but is not detected by the simple body mass index (BMI) assessment.

Aim: To assess the prevalence of sarcopenia and visceral obesity by a single computed tomography (CT) slice, and its association with adverse events in an adult hospitalized CD cohort.

Methods: 88 CD patients who had abdominal CT scans during hospitalization were retrospectively enrolled. The skeletal muscle index (SMI) at the third lumbar vertebra level was used to assess sarcopenia. Sarcopenia was defined as a SMI $<38.5\text{cm}^2/\text{m}^2$ in women, $<52.4\text{cm}^2/\text{m}^2$ in men and visceral obesity as a visceral fat area $\geq 130\text{ cm}^2$. Clinical malnutrition was defined by a BMI $<18.5\text{ kg}/\text{m}^2$. Univariate analysis was performed, and predictors for surgery in the follow-up were entered in a stepwise logistic regression model for multivariate analysis.

Results: The prevalence of sarcopenia was 58%, malnutrition 21.6%, and visceral obesity 19.3%. Among sarcopenic patients, 49% had a normal BMI, 13.7% were overweight, and 1(2%) was obese. Sarcopenic CD patients had significantly more abscesses (51% vs 16.7%, $p=0.001$), hospitalizations (61.2% vs 36.1%, $p=0.022$) and digestive surgery (63.3% vs 27.8%, $p=0.001$) than non-sarcopenic patients during the follow-up, whereas usual malnutrition assessment was not correlated with disease outcomes. In multivariate analysis, both sarcopenia and visceral obesity were associated with further occurrence of digestive surgery.

Conclusion: Both sarcopenia and visceral obesity were associated with adverse outcomes in severe CD patients whereas usual nutritional assessment was not.

Key words: Crohn's disease, body composition, sarcopenia, visceral obesity, CT scan, surgery

Introduction

Crohn's disease (CD) is a chronic progressive and disabling inflammatory bowel disease (IBD) which may lead to hospitalizations, surgery and impact quality of life. CD is well known to be associated with malnutrition,¹⁻⁴ lower body mass index (BMI)⁵ and lower lean body mass.^{6,7} Indeed, 75% of hospitalized CD patients are malnourished and 1/3 have a low BMI.⁸ There are multiple causes: limited food intake, malabsorption, increased nutrients losses and potentially treatment adverse events. Current data indicate that IBD patients, particularly CD patients, have alterations in their body composition (lean and fatty mass) that the simple BMI assessment may fail to detect.⁹⁻¹¹ Also, growing evidence suggests that altered body composition in IBD is associated with more severe phenotypes¹² and may negatively impact on the clinical course of the disease, response to treatments, and quality of life,¹³⁻¹⁶ although some discordant results have been reported regarding surgery indications and outcomes.¹⁷

While the deuterium oxide dilution method, or to a lesser extent a proxy by the whole-body dual-energy X-ray absorptiometry (DXA), would be the best measures of body composition, these techniques are neither routinely accessible nor feasible in clinical practice. Recently, the development of an accessible method to assess body composition, using a third lumbar (L3) computed tomography (CT) slice, has demonstrated its reliability and prognostic ability in other diseases such as cancer and obesity.¹⁸⁻²³ This tool has extended nutritional assessment possibilities in routine clinical care, and can be applied to CD patients.²⁴ CT can differentiate body tissues (adipose, muscular, skeletal), water and air, based on tissue specific attenuation values, and easily provides a body composition analysis, including quantification of abdominal circumference, abdominal adipose tissues (AT) (subcutaneous, visceral, and intermuscular), and skeletal muscle (SM).²⁵

The aims of this study were to assess the body composition of hospitalized CD patients by a L3 single CT slice and to investigate the association between body composition and adverse outcomes during the follow-up of this cohort of patients.

Methods

Study population

From our cohort of patients with a confirmed diagnosis of CD and follow-up at Besançon University Hospital, those aged 18 to 65 years who had an abdominal CT scan and were hospitalized in the Gastroenterology unit between the 1st of January 2010 and the 15th of June 2016, were retrospectively enrolled for this study. Only hospitalized CD patients were included, as they fulfilled the criteria to have both CT scan examination and full conventional nutritional assessment in the same time period and represent a population of special interest regarding the risk of malnutrition and altered body composition. Patients were excluded in the absence of height, weight and serum albumin parameters within two weeks of the CT scan. Patients with the following comorbidities were also excluded to alleviate potential nutritional confounding parameters: severe organ insufficiency (cardiac, renal, liver, and pulmonary), cancer, and infection with human immunodeficiency virus.

Demographic and clinical variables

Age, gender, CD duration, CD location and phenotype according to the Montreal classification,²⁶ treatment and smoking history were recorded at the date of abdominal CT. During hospitalisation, the Harvey-Bradshaw index (HBI), as a marker of CD clinical activity, nutritional supplementation, and medical and surgical treatments were recorded. BMI, healthy body weight and percentage of weight loss in the past month and 6 months were calculated. Normal BMI was defined as ≥ 18.5 kg/m² and < 25 kg/m², overweight as ≥ 25 kg/m² and < 30 kg/m², obesity as ≥ 30 kg/m². Malnutrition was defined by a BMI < 18.5

kg/m². Serum albumin was recorded but was not considered in the definition of malnutrition, as a low level in patients with acute inflammation does not necessarily reflect poor nutritional status. Follow-up data were obtained from patient's medical records. Outcomes: further hospitalizations, abscess(es) (intestinal and perianal), surgery (intestinal resection and perianal surgery, use of anti-Tumor necrosis factor (TNF) therapy, and change or dose optimization of anti-TNF therapy were recorded; bowel restorative surgery was not considered. The study was conducted through the current French reference methodology, MR-003, and registered at the University Hospital Research Unit of Besançon, France.

Radiological body composition measurement

CT images at L3 levels were analyzed to determine SM mass and corrected by the exclusion of the third lumbar SM, visceral AT and subcutaneous AT by a single operator, blinded to clinical and biological data, using the free public-domain software developed by the National Institutes of Health (NIH Image J1.47) (Figure 1). In case of repeated abdominal CTs during hospitalization, only the first one performed after admission was considered for analysis. The skeletal muscle index (SMI) (cm²/m²), which is the ratio of the cross-sectional area of skeletal muscles at the level of the L3 vertebra to the height squared (m²), was used to identify sarcopenia. As reported before in the literature, sarcopenia was defined as a SMI < 38.5 cm²/m² in women and < 52.4 cm²/m² in men²⁷ and visceral obesity was defined as a visceral fat area (VFA) ≥ 130 cm².²⁸

Statistical analyses

Quantitative variables were presented as mean ± standard deviation when normally distributed, or as median [interquartile range] if non-normally distributed. Normality was analysed using the Kolmogorov-Smirnov test. Qualitative variables were presented as

numbers (percentages). The Chi-square (X^2) test was used to compare categorical variables, and the Student t or Mann Whitney and Wilcoxon tests were used for quantitative variables. The univariate predictors for surgery in the follow-up with $p < 0.2$, and malnutrition defined by a BMI < 18.5 kg/m² were entered in a stepwise multivariate logistic regression model. The Odds ratio (OR) and 95% confidence intervals (CI) were presented in the final multivariate model. A p-value of less than 0.05 was considered significant. All analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC, USA), and R version 3.5.0 (R Development Core Team, 2005).

Results

Demographic and disease characteristics

Among our CD cohort patients, a total of 175 patients had an abdominal CT during the inclusion period, among them 105 were hospitalized and 88 were meeting all inclusion criteria (Supplementary figure 1). Follow-up data were subsequently available for 85 patients. The baseline characteristics of the 88 patients are shown in Table 1. Overall, median age was 35.4 ± 12.4 years, half were men (44 patients), half were current smokers (44 patients), and the mean HBI was 7.4 ± 4.4 . Regarding disease location, 53.4% of the patients had an ileocolonic disease, 34.1% an ileal disease, and 12.5% a colonic disease. The disease phenotype was stricturing in 43.2%, penetrating in 34.1% and non-stricturing, non-penetrating in 22.7% of patients; 27.3% had perianal disease. The mean duration of CD at the time of the CT scan was 170.2 ± 290.5 months; the mean duration of follow-up after the CT scan was 22.2 ± 20.1 months. The cause of hospital admission was abdominal pain in 52 (59.1%) patients, abdominal pain and diarrhoea in 27 (30.7%), diarrhoea in 5 (5.7%), and fever 4 (4.6%). During hospitalisation, 56 patients received oral nutritional supplementation

(Modulen® or oral supplements), 9 received enteral nutrition. None received parenteral nutrition. Medical and surgical treatments during hospitalisation are reported in Table 1. During the follow-up, 31/85 (36.5%) patients had abscesses (23 intestinal locations and 8 perianal locations), 43/85 (50.6%) were re-hospitalized; 41/85 (48.2%) had surgery (32 intestinal resections (13 right hemicolectomies, 13 ileocaecal resections, 5 small bowel resections and 1 stricturoplasty) and 9 had perianal surgery (surgical drainage of abscess and/or fistula), and a treatment with an anti-TNF agent was initiated in 42 (48.8%) patients (Table 1).

Nutritional status and Body composition

At the time of recruitment, mean BMI was 22.7 ± 4.6 kg/m², mean serum albumin level was 28.7 ± 6.4 g/L. BMI was less than 18.5kg/m² in 21.6% of patients; 46.6% had a normal BMI, 23.7% were overweight and 9.1% were obese (Table 1). Overall, malnutrition (as defined by BMI<18.5kg/m²) occurred in 19/88 (21.6%) patients. Sarcopenia, as assessed by the SMI on CT scan, was present in 51/88 (58%) patients, and visceral obesity, as assessed by the VFA, was present in 17/88 (19.3%) patients.

As shown in Table 2, there were no significant differences regarding age, gender, smoking status, disease location, and CD clinical activity according to the HBI, when comparing patients with or without sarcopenia and with or without malnutrition. More frequent perianal diseases were observed in patients with a BMI <18.5kg/m². Regarding treatments during hospitalisation, in sarcopenic patients, Modulen® supplementations and surgery were significantly more frequent, and treatment by thiopurines was less frequent (Table 2).

Sarcopenic patients had significantly lower BMI (20.6 ± 4 kg/m² vs 25.6 ± 3.7 kg/m², $p<0.0001$), lower serum albumin levels (27 ± 6.3 g/L vs 30.9 ± 6 g/L, $p=0.004$) and more frequent malnutrition (35.3% vs 2.7%, $p=0.0002$) than non-sarcopenic patients. However, among sarcopenic patients, 25 (49.0%) had a normal BMI, 7 (13.7%) were overweight, 1

(2%) was obese, and 8 (15.7%) had a visceral obesity assessed by CT scan. SFA was significantly lower than in non-sarcopenic patients, while VFA and visceral obesity were similar (Table 2). Conversely, all patients but one with malnutrition ($\text{BMI} < 18.5\text{kg/m}^2$) were sarcopenic, and all radiological measurements of body composition were significantly lower in the malnourished group (Table 2).

There were no significant differences regarding the main outcomes at follow-up (further hospitalizations, abscesses, surgeries) between malnourished and non-malnourished CD patients. However, sarcopenic CD patients had significantly more abscesses (51.0% vs 16.7%, $p=0.001$), further hospitalizations (61.2% vs 36.1%, $p=0.022$) and surgeries (63.3% vs 27.8%, $p=0.001$), than non-sarcopenic CD patients (Table 2).

In the group of patients with visceral obesity (Supplementary Table 1), only 2 (11,8%) patients were obese, 11 (64.7%) were overweight, 4 (23,5%) had a normal BMI, none had a $\text{BMI} < 18.5\text{kg/m}^2$. These patients with visceral obesity were significantly more female (76.5% vs 43.7%, $p=0.01$), older (mean age 45.3 vs 33.1 years, $p=0.0003$), and with longer CD duration (150 vs 46 months, $p=0.03$). During follow-up, they had significantly more surgeries (75% vs 42%, $p=0.02$) and switch of anti-TNF agent (43.3% vs 18.8%, $p=0.05$) (Supplementary Table 1).

Study of CD patients according to their surgical status during the follow-up

In CD patients who underwent surgery during the follow-up, sarcopenia and visceral obesity at baseline were significantly more frequent ($p=0.036$ and $p=0.002$, respectively), compared to patients who did not. Patients also had lower serum albumin levels ($p=0.014$). However, malnutrition according to BMI at baseline was not associated with further occurrence of surgery ($p=0.66$). Stricturing or penetrating behaviours (B2/B3) were significantly associated with more frequent digestive surgery ($p=0.013$) (Table 3). In univariate analysis (Table 4),

surgery in the follow-up was significantly associated with disease behaviour (B2 and B3, respectively, OR=3.75, 95% CI [1.05;13.39] and OR=6.75, 95% IC [1.76;25.96], p= 0.011), male gender (OR=3.03, 95% CI [1.25;7.34], p=0.012), serum albumin (OR=0.92, 95% CI [0.85;0.99], p=0.01), sarcopenia (OR=4.48, 95% IC [1.76;11.38], p=0.00) and also visceral obesity (OR=4.14, 95% CI [1.21;14.13], p=0.016), but not malnutrition (95% CI [0.45;3.49], p=0.663). In multivariate analysis, only sarcopenia and visceral obesity were independent factors of surgery (Table 4).

Discussion

In this observational cohort of hospitalized CD patients, we demonstrated that the evaluation of the body composition using a single CT slice was a suitable tool to assess their nutritional status, and was predictive of adverse events in the course of the disease: abscesses, digestive surgery and hospitalization, whereas BMI and/or serum albumin levels were not. We also found that both sarcopenia and visceral obesity were independently associated with surgery during the follow-up. This study showed a high prevalence of sarcopenia (58%) in hospitalised CD patients, confirming the previously reported results by Schneider et al. (60%)²⁹ and Holt et al. (68.5%).²⁴ In IBD care, especially in a hospitalization setting, systematic nutritional assessment using this simple and easily accessible method should be promoted, in addition to the more common assessment using BMI and albumin levels, to bring adequate nutritional support and prevent adverse outcomes.

We pointed out that 64.7% of sarcopenic CD patients had a falsely reassuring BMI ($\geq 18.5\text{kg/m}^2$), with similar visceral fat levels as compared to non-sarcopenic patients, and paradoxically 15% were overweight or obese. Sarcopenic CD patients had a significantly

lower BMI than non-sarcopenic patients, but still in the normal range. Furthermore, sarcopenia was associated with bad outcomes, whereas malnutrition assessed by conventional clinical data was not. Indeed, analysis of the body composition using a single CT slice is a better reflection of lean and fat mass than BMI. Recently, the Global Leadership Initiative on Malnutrition (GLIM)³⁰ published the global consensus on diagnostic criteria for malnutrition in adults, introducing reduced muscle mass as one of the phenotypic criteria to assess malnutrition. Sarcopenia was first suggested in 1989 to define an involuntary loss of muscle mass in elderly subjects that usually occurs in all individuals because of ageing. It has also been associated with disability, low quality of life, and death.^{31,32} Premature sarcopenia was previously described in IBD population by using dual-energy x-ray absorptiometry and was shown to correlate with low bone mineral density.²⁹ This premature sarcopenia may be a consequence of malnutrition (due to dietary restriction and/or malabsorption), inactivity (due to long-term disabling disease) and chronic inflammation. Supporting the role of inflammation, recently Subramaniam *et al.*³³ demonstrated that infliximab, potentially by decreasing inflammatory protein levels (IL6 and CRP), could reverse sarcopenia after 25 weeks of treatment.

To our knowledge, few studies focused on the prognosis of CD patients according to their body composition status evaluated by a single CT slice. Association of sarcopenia with early anti-TNF therapy failure¹⁶ and postoperative outcomes³⁴ was suggested. Conflicting results were reported concerning the association of sarcopenia with surgical events. As expected, stricturing and penetrating disease phenotypes were risk factors for surgery in our study. Sarcopenia was also an independent risk factor, confirming the results of Bamba S *et al.* in a similar population¹⁵. In the recently published study by Thiberge C *et al.*,¹⁷ SMI also tended

261 to be reduced in patients with adverse outcome, compared with patients without surgery nor
262 death ; however, the difference was not significant ($p=0.07$).

263 CT imaging has become the gold standard for the quantification of visceral adipose tissue;
264 using $VFA \geq 130 \text{cm}^2$ to define visceral obesity has proven to be an easy and reproducible
265 parameter for the assessment of visceral obesity.²⁸ Previous studies highlighted that visceral
266 obesity was a strong predictor of perioperative outcomes after digestive surgery.^{35,36} Ding *et*
267 *al.*³⁷ demonstrated that visceral obesity was significantly associated with an increase in bowel
268 resection length, postoperative ileus and postoperative complications overall ($p < 0.001$) in
269 patients with CD undergoing primary surgery. Erhayiem *et al.*³⁸ found that a higher
270 mesenteric fat index (visceral to subcutaneous fat area ratio), could predict a more
271 complicated course of the disease. In the post-operative setting, a post-hoc analysis of the
272 POCER study in 44 CD patients, demonstrated that regardless of the treatment, higher
273 visceral adiposity was significantly associated with CD recurrence.³⁹ To our knowledge, only
274 the above-mentioned study by Thiberge *et al.*¹⁷ found opposite results regarding fat body
275 composition in a severe CD population: in their retrospective cohort of patients, lower
276 subcutaneous and visceral adiposity indexes were significantly associated with surgery or
277 death, perhaps because of a longer and more severe course of disease in the patients with an
278 available CT scan¹⁷ or because they used surgery *and* death as an endpoint, without exclusion
279 of potential confounding comorbidities (cancer, organ failure...). Our results showed that
280 visceral obesity was an independent surgical outcome factor in multivariate analysis, whereas
281 BMI was not. Almost 20% of our patients had visceral obesity but only 9% were obese
282 according to BMI. Patients with penetrating or stricturing phenotypes had a higher VFA than
283 patients with non-structuring and non-penetrating disease. On the other hand, our findings,
284 corroborated by most of the studies mentioned above,³⁶⁻³⁸ support the hypothesis that human

fat tissue is not solely a reservoir for excess nutrients but also a dynamic tissue involved in the regulation of immunity and inflammation.⁴⁰

This study suffers from a few limitations that deserve to be underlined. Firstly, it is limited by its retrospective and single-centre design, although all patients were extracted from a prospective cohort of patients. We could not properly assess the history of corticosteroids intake in our patients' cohort as self-medication and prescription of corticosteroids by general practitioners are frequent, contrary to other immunomodulators which are precisely recorded in hospital files; thus we cannot exclude that, in addition to disease severity, sarcopenia was also due to higher corticosteroid intake that may lead to loss of muscle and central adiposity. Secondly, there is a selection bias linked to the study of hospitalised patients. We intentionally chose to include only hospitalised CD patients, as they fulfilled the criteria to have both CT scan examination and full conventional nutritional assessment. Also, **their** severe outcomes deserve appropriate management to decrease morbidity. We believed that the perspective of specific recommendations on nutritional assessment and supplementation in patients with such severe conditions warranted a dedicated study. A further step to our work will be to assess the feasibility and prognosis relevance of body composition evaluation by a non-invasive non-irradiating tool (abdominal MRI), to extend our results to the outpatient population with less severe CD.

Nutritional assessment by more appropriate tools than weight and BMI should be promoted in inflammatory bowel diseases to properly assess malnutrition, as sarcopenia is associated with pejorative outcome, but prevalent in patients with normal BMI. Body composition measurement also allows the detection of visceral obesity, another pejorative nutritional parameter underestimated by simple BMI monitoring. The third lumbar (L3) computed tomography (CT) slice analysis represents an alternative tool to measure the body

composition of CD patients that may be more easily accessible in all hospitals than the alternative measurement of bioelectrical impedance.⁴¹ Based on such analysis, a proper management of altered body composition is clearly a future goal for gastroenterologists; it may be achieved by improving nutritional status and promoting physical activity while controlling inflammation.

References

1. Dieleman LA, Heizer WD. Nutritional issues in inflammatory bowel disease. *Gastroenterol Clin North Am* 1998;27:435–451.
2. Krok KL, Lichtenstein GR. Nutrition in Crohn disease. *Curr Opin Gastroenterol* 2003;19:148–153.
3. Hebuterne X, Filippi J, Schneider SM. Nutrition in adult patients with inflammatory bowel disease. *Curr Drug Targets* 2014;15:1030–1038.
4. Forbes A, Escher J, Hébuterne X, et al. ESPEN guideline: Clinical nutrition in inflammatory bowel disease. *Clin Nutr* 2017;36:321–347.
5. Dong J, Chen Y, Tang Y, et al. Body Mass Index Is Associated with Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis. *PloS One* 2015;10:e0144872.
6. Schneider SM, Al-Jaouni R, Filippi J, et al. Sarcopenia is prevalent in patients with Crohn's disease in clinical remission. *Inflamm Bowel Dis* 2008;14:1562–1568.
7. Jahnsen J, Falch JA, Mowinckel P, et al. Body composition in patients with inflammatory bowel disease: a population-based study. *Am J Gastroenterol* 2003;98:1556–1562.
8. Adams DW, Gurwara S, Silver HJ, et al. Sarcopenia Is Common in Overweight Patients with Inflammatory Bowel Disease and May Predict Need for Surgery. *Inflamm Bowel Dis* 2017;23:1182–1186.
9. Sylvester FA, Leopold S, Lincoln M, et al. A two-year longitudinal study of persistent lean tissue deficits in children with Crohn's disease. *Clin Gastroenterol Hepatol* 2009;7:452–455.
10. Bin CM, Flores C, Alvares-da-Silva MR, et al. Comparison between handgrip strength, subjective global assessment, anthropometry, and biochemical markers in assessing nutritional status of patients with Crohn's disease in clinical remission. *Dig Dis Sci* 2010;55:137–144.
11. Wiskin AE, Wootton SA, Hunt TM, et al. Body composition in childhood inflammatory bowel disease. *Clin Nutr* 2011;30:112–115.
12. Cravo ML, Velho S, Torres J, et al. Lower skeletal muscle attenuation and high visceral fat index are associated with complicated disease in patients with Crohn's disease: An exploratory study. *Clin Nutr ESPEN* 2017;21:79–85.
13. Adams DW, Gurwara S, Silver HJ, et al. Sarcopenia Is Common in Overweight Patients with Inflammatory Bowel Disease and May Predict Need for Surgery. *Inflamm Bowel Dis* 2017;23:1182–1186.

- 355 14. Bryant RV, Trott MJ, Bartholomeusz FD, et al. Systematic review: body composition
356 in adults with inflammatory bowel disease. *Aliment Pharmacol Ther* 2013;38:213–225.
- 357 15. Bamba S, Sasaki M, Takaoka A, et al. Sarcopenia is a predictive factor for intestinal
358 resection in admitted patients with Crohn's disease. *PloS One* 2017;12:e0180036.
- 359 16. Holt DQ, Varma P, Strauss BJG, et al. Low muscle mass at initiation of anti-TNF
360 therapy for inflammatory bowel disease is associated with early treatment failure: a
361 retrospective analysis. *Eur J Clin Nutr* 2017;71:773–777.
- 362 17. Thiberge C, Charpentier C, Gillibert A, et al. Lower Subcutaneous or Visceral
363 Adiposity Assessed by Abdominal Computed Tomography Could Predict Adverse Outcome
364 in Patients With Crohn's Disease. *J Crohns Colitis* 2018;12:1429–1437.
- 365 18. Shen W, Punyanitya M, Wang Z, et al. Total body skeletal muscle and adipose tissue
366 volumes: estimation from a single abdominal cross-sectional image. *J Appl Physiol* 1985
367 2004;97:2333–2338.
- 368 19. Shen W, Punyanitya M, Chen J, et al. Visceral adipose tissue: relationships between
369 single slice areas at different locations and obesity-related health risks. *Int J Obes* 2005
370 2007;31:763–769.
- 371 20. Martin L, Birdsell L, Macdonald N, et al. Cancer cachexia in the age of obesity:
372 skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. *J*
373 *Clin Oncol* 2013;31:1539–1547.
- 374 21. Antoun S, Lanoy E, Iacovelli R, et al. Skeletal muscle density predicts prognosis in
375 patients with metastatic renal cell carcinoma treated with targeted therapies. *Cancer*
376 2013;119:3377–3384.
- 377 22. Prado CMM, Heymsfield SB. Lean tissue imaging: a new era for nutritional
378 assessment and intervention. *JPEN J Parenter Enteral Nutr* 2014;38:940–953.
- 379 23. Prado CMM. Body composition in chemotherapy: the promising role of CT scans.
380 *Curr Opin Clin Nutr Metab Care* 2013;16:525–533.
- 381 24. Holt DQ, Strauss BJG, Lau KK, et al. Body composition analysis using abdominal
382 scans from routine clinical care in patients with Crohn's Disease. *Scand J Gastroenterol*
383 2016;51:842–847.
- 384 25. Gomez-Perez SL, Haus JM, Sheean P, et al. Measuring Abdominal Circumference and
385 Skeletal Muscle From a Single Cross-Sectional Computed Tomography Image: A Step-by-
386 Step Guide for Clinicians Using National Institutes of Health ImageJ. *JPEN J Parenter Enteral*
387 *Nutr* 2016;40:308–318.
- 388 26. Silverberg MS, Satsangi J, Ahmad T, et al. Toward an integrated clinical, molecular
389 and serological classification of inflammatory bowel disease: report of a Working Party of the
390 2005 Montreal World Congress of Gastroenterology. *Can J Gastroenterol* 2005;19 Suppl

391 A:5A–36A.

392 27. Prado CMM, Lieffers JR, McCargar LJ, et al. Prevalence and clinical implications of
393 sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts:
394 a population-based study. *Lancet Oncol* 2008;9:629–635.

395 28. Kullberg J, Brandberg J, Angelhed J-E, et al. Whole-body adipose tissue analysis:
396 comparison of MRI, CT and dual energy X-ray absorptiometry. *Br J Radiol* 2009;82:123–
397 130.

398 29. Schneider SM, Al-Jaouni R, Filippi J, et al. Sarcopenia is prevalent in patients with
399 Crohn's disease in clinical remission. *Inflamm Bowel Dis* 2008;14:1562–1568.

400 30. Cederholm T, Jensen GL, Correia MITD, et al. GLIM criteria for the diagnosis of
401 malnutrition - A consensus report from the global clinical nutrition community. *Clin Nutr*
402 2019;38:1–9.

403 31. Janssen I, Baumgartner RN, Ross R, et al. Skeletal muscle cutpoints associated with
404 elevated physical disability risk in older men and women. *Am J Epidemiol* 2004;159:413–
405 421.

406 32. Woo J, Ho SC, Sham A. Longitudinal changes in body mass index and body
407 composition over 3 years and relationship to health outcomes in Hong Kong Chinese age 70
408 and older. *J Am Geriatr Soc* 2001;49:737–746.

409 33. Subramaniam K, Fallon K, Ruut T, et al. Infliximab reverses inflammatory muscle
410 wasting (sarcopenia) in Crohn's disease. *Aliment Pharmacol Ther* 2015;41:419–428.

411 34. Zhang T, Cao L, Cao T, et al. Prevalence of Sarcopenia and Its Impact on
412 Postoperative Outcome in Patients With Crohn's Disease Undergoing Bowel Resection. *JPEN*
413 *J Parenter Enteral Nutr* 2017;41:592–600.

414 35. Tsujinaka S, Konishi F, Kawamura YJ, et al. Visceral obesity predicts surgical
415 outcomes after laparoscopic colectomy for sigmoid colon cancer. *Dis Colon Rectum*
416 2008;51:1757–1765.

417 36. Shimizu A, Tani M, Kawai M, et al. Influence of visceral obesity for postoperative
418 pulmonary complications after pancreaticoduodenectomy. *J Gastrointest Surg* 2011;15:1401–
419 1410.

420 37. Ding Z, Wu X-R, Remer EM, et al. Association between high visceral fat area and
421 postoperative complications in patients with Crohn's disease following primary surgery.
422 *Colorectal Dis* 2016;18:163–172.

423 38. Erhayiem B, Dhingsa R, Hawkey CJ, et al. Ratio of visceral to subcutaneous fat area
424 is a biomarker of complicated Crohn's disease. *Clin Gastroenterol Hepatol* 2011;9:684–687.

425 39. Holt DQ, Moore GT, Strauss BJG, et al. Visceral adiposity predicts post-operative
426 Crohn's disease recurrence. *Aliment Pharmacol Ther* 2017;45:1255–1264.

40. Peyrin-Biroulet L, Chamaillard M, Gonzalez F, et al. Mesenteric fat in Crohn's disease: a pathogenetic hallmark or an innocent bystander? Gut 2007;56:577–583.

41. Ward LC, Müller MJ. Bioelectrical impedance analysis. Eur J Clin Nutr 2013;67 Suppl 1:S1.

Figure 1: Evaluation of the body composition using a third lumbar computed tomography scan slice.

Red: Adipose Tissue, subcutaneous and visceral

Green: Skeletal muscle

Tables

442 **Table 1:** Baseline and follow-up Crohn's disease patients' characteristics.

Baseline	n= 88
Demographic and disease data	
Age (years), mean \pm sd	35.4 \pm 12.4
Male gender, n (%)	44 (50)
Current Smokers, n (%)	44 (50)
Disease duration (months), mean \pm sd	170.2 \pm 290.5
Location*, n (%)	L1 30 (34.1), L2 11 (12.5), L3 47 (53.4)
Behaviour*, n (%)	B1 20 (22.7), B2 38 (43.2), B3 30 (34.1)
Perianal Disease, n (%)	24 (27.3)
Cause of hospital admissions, n (%)	Abdominal pain 52 (59.1), Abdominal pain and diarrhoea 27 (30.7), Diarrhoea 5 (5.7), Fever 4 (4.6)
HBI, mean \pm sd	7.4 \pm 4.4
Biological data	
CRP (mg/L), mean \pm sd	63.5 \pm 69.3
Serum Albumin (g/L), mean \pm sd	28.7 \pm 6.4
Anthropometric and radiological data	
BMI (kg/m ²), mean \pm sd	22.7 \pm 4.6
Malnutrition	
BMI < 18.5kg/m ² , n (%)	19 (21.6)
Normal BMI	
BMI 18.5-25kg/m ² , n (%)	41 (46.6)
Overweight	
BMI 25-30kg/m ² , n (%)	20 (22.7)
Obese	
BMI \geq 30kg/m ² , n (%)	8 (9.1)
Serum albumine <30g/L and/or BMI <18.5kg/m ² , n (%)	55 (62.5)
SMI (cm ² /m ²), mean \pm sd	43 \pm 9.1
VFA (cm ²), mean \pm sd	79.1 \pm 70.2
SFA (cm ²), mean \pm sd	153.8 \pm 114.4
Sarcopenia‡, n (%)	51 (58)
Visceral obesity#, n (%)	17 (19.3)
Treatments during hospitalization	
Corticosteroids, n (%)	Total 39 (44.3) IV 26 (29.5), oral 23 (26.1), budesonide 10 (11.4)
Thiopurine, n (%)	19 (21.6)
Anti-TNF, n (%)	39 (44.3)
Surgery, [perianal + intestinal] n (%)	6 [2 + 4] (6.8)
Antibiotics, n (%)	53 (60.2)
Nutritional supplementation	
Modulen®, n (%)	44 (50)
Oral supplements, n (%)	12 (13.6)
Enteral nutrition, n (%)	9 (10.2)
Parenteral nutrition, n (%)	0 (0)

Follow-up	n= 85
Follow-up (months), mean \pm sd	22.2 \pm 20.1
Abscess (perineal or enteral), n (%)	31 (36.5)
New hospitalization, n (%)	43 (50.6)
Surgery, [perianal + intestinal] n (%)	41 [9 +32] (48.2)
Start of an anti-TNF, n (%)	42 (48.8)
Switch of anti-TNF, n (%)	20 (23.5)
Optimization of anti-TNF, n (%)	36 (42.9)

443
444 * according to the Montreal classification: L1, ileal; L2, colonic; L3, ileocolonic; B1, non-stricturing non-penetrating; B2,
445 stricturing; B3, penetrating.
446 ‡ Skeletal Muscle Index < 38.5cm²/m² in women and < 52.4cm²/m² in men
447 # VFA \geq 130cm²
448 BMI, Body Mass Index ; CRP, C Reactive Protein; HBI, Harvey Bradshaw Index; IV, Intravenous; SFA, Subcutaneous Fat
449 Area; SMI, Skeletal Muscle Index; TNF, Tumour Necrosis Factor; VFA, Visceral Fat Area

Table 2: Crohn's disease patients' characteristics, at baseline and after follow-up, according to their body composition and nutritional status.

	Sarcopenia‡	No Sarcopenia	P Value	Malnutrition †	No malnutrition	P Value
	n=51	n=37		n=19	n=69	
Demographic and disease data						
Age (years), mean ± sd	36.6 ± 13.7	33.8 ± 10.3	0.29	32.2 ± 12.1	36.3 ± 12.4	0.78
Male Gender, n (%)	30 (58.8)	14 (37.8)	0.052	12 (63.2)	32 (46.4)	0.19
Disease duration (months), median [IQR]	116 [19 - 198.5]	46 [17.25 - 856]	0.2835	49 [1 - 327]	74.5 [1 - 1265]	0.31
Current Smokers, n (%)	27 (52.9)	17 (46)	0.517	11 (57.9)	33 (47.8)	0.43
Location*, n (%)						
L1	18 (35.3)	12 (32.4)	0.95	5 (26.3)	25 (36.2)	0.71
L2	6 (11.8)	5 (13.5)		2 (10.5)	9 (13.0)	
L3	27 (52.9)	20 (54.1)		12 (63.7)	35 (50.7)	
Behaviour*, n (%)						
B1	9 (17.7)	11 (29.7)	0.09	5 (26.3)	15 (21.7)	0.21
B2	20 (39.2)	18 (48.7)		5 (26.3)	33 (47.8)	
B3	22 (43.1)	8 (21.6)		9 (47.4)	21 (30.4)	
Perianal Disease, n (%)	15 (29.4)	9 (24.3)	0.6	9 (47.4)	15 (21.7)	0.03
HBI, mean ± sd	8.2 ± 4.3	6.4 ± 4.4	0.052	8.1 ± 4.6	7.2 ± 4.4	0.36
Biological data						
Serum Albumin (g/L), mean ± sd	27 ± 6.3	30.9 ± 6	0.004	27.3 ± 7.1	29.1 ± 6.2	0.323
CRP (mg/L), median [IQR]	48.1 [12.8 - 109]	22.9 [10.8 - 61.3]	0.12	73.1 [1 - 289]	28.6 [1.6 - 314]	0.0008
Anthropometric and radiological data						
BMI (kg/m ²) mean ± sd	20.6 ± 4	25.6 ± 3.7	<0.0001	16.8 ± 1.2	24.4 ± 3.8	<0.0001
Normal BMI (18.5-25kg/m ²), n (%)	25 (49.2)	16 (43.2)	0.017		41 (59.4)	
Overweight (25-30kg/m ²), n (%)	7 (13.7)	13 (35.1)			20 (29)	
Obese (BMI ≥ 30kg/m ²), n (%)	1 (2)	7 (18.9)			8 (11.6)	
Malnutrition†, n (%)	18 (35.3)	1 (2.7)	0.0002			
VFA (cm ²), mean ± sd	75.5 ± 69.3	92.6 ± 60.5	0.11	21.3 ± 21	95 ± 70.6	<0.0001
SFA (cm ²), mean ± sd	112.4 ± 97.7	211.2 ± 112.2	<0.0001	48.8 ± 36.9	183.5 ± 111.4	<0.0001
Visceral Obesity, n (%)	8 (15.7)	9 (24.3)	0.31	0	17 (24.6)	0.365
Sarcopenia‡, n (%)				18 (94.7)	33 (47.8)	0.0002
Treatments during hospitalization						
Corticosteroids, n (%)	22 (43.1)	17 (46)	0.79	11 (57.9)	28 (40.6)	0.18
Thiopurine, n (%)	7 (13.7)	12 (32.4)	0.03	5 (26.3)	14 (20.3)	0.55
Anti-TNF, n (%)	20 (39.2)	19 (51.4)	0.26	11 (57.9)	28 (40.6)	0.18

Surgery, [perianal + intestinal] n (%)	6 (11.7)	0	0.04	1 (5.3)	5 (7.3)	1
Antibiotics, n (%)	35 (68.6)	18 (48.7)	0.06	15 (79)	38 (55.1)	0.06
Modulen, n (%)	33 (64.7)	11 (29.7)	0.001	13 (68.4)	31 (44.9)	0.07
Oral supplementation, n (%)	7 (13.7)	5 (13.5)	0.98	4 (21.1)	8 (11.6)	0.28
Enteral nutrition, n (%)	8 (15.7)	1 (2.7)	0.07	4 (21.1)	5 (7.25)	0.1
Parenteral nutrition, n (%)	0	0		0	0	
Follow-up n= 85	n=49	n=36		n=19	n=66	
Follow-up duration (months), mean ± sd	25.2 ± 21.6	18 ± 17.2	0.08	24 ± 17.3	21.7 ± 20.9	0.29
Abscess, n (%)	25 (51.0)	6 (16.7)	0.001	10 (52.6)	21 (31.8)	0.09
Hospitalization, n (%)	30 (61.2)	13 (36.1)	0.022	10 (52.6)	33 (50)	0.84
Surgery, n (%)	31 (63.3)	10 (27.8)	0.001	10 (52.6)	31 (47)	0.66
Start of anti-TNF, n (%)	27 (54)	15 (41.7)	0.259	13 (68.4)	29 (43.3)	0.053
Switch of anti-TNF, n (%)	8 (16.3)	12 (33.3)	0.067	1 (5.3)	19 (28.8)	0.03
Optimisation of anti-TNF, n (%)	22 (45.8)	14 (38.9)	0.524	7 (36.8)	29 (44.6)	0.54

* according to the Montreal classification: L1, ileal; L2, colonic; L3, ileocolonic; B1, non-stricturing non-penetrating; B2, stricturing; B3, penetrating

† albuminemia <30g/L and/or Body mass index <18.5kg/m²

‡ Skeletal Muscle Index < 38.5cm²/m² in women and < 52.4cm²/m² in men; # VFA ≥ 130cm²

BMI, Body mass index; CRP, C Reactive Protein; HBI, Harvey Bradshaw Index; IQR, interquartile range; sd, standard deviation; SFA, subcutaneous fat area; TNF, tumor necrosis factor; VFA, visceral fat area.

Table 3: Comparison of Crohn's disease patients according to their surgical status during the follow-up.

	Surgery n=41	No surgery n=44	P Value
Demographic data			
Age (years), mean \pm sd	38.2 \pm 13.4	33.1 \pm 10.9	0.059
Male gender, n (%)	26 (63.4)	16 (36.4)	0.012
Current Smokers, n (%)	23 (56.1)	20 (45.5)	0.326
Location*, n (%)			0.446
L1	17 (41.5)	13 (29.6)	
L2	4 (9.8)	7 (15.9)	
L3	20 (48.8)	24 (54.6)	
Perianal disease, n (%)	13 (31.7)	11 (25)	0.492
Behaviour*, n (%)			0.013
B1	4 (9.8)	15 (34.1)	
B2	19 (46.3)	19 (43.2)	
B3	18 (29.3)	10 (22.7)	
HBI, mean \pm sd	7.2 \pm 3.8	7.8 \pm 5	0.98
Body composition and nutritional characteristics			
Serum albumin (g/L), mean \pm sd	26,8 \pm 5,4	30,2 \pm 7	0.014
CRP (mg/L), mean \pm sd	80.5 \pm 67.3	63.1 \pm 58.5	0.79
BMI, mean \pm sd	22.3 \pm 4.9	23.2 \pm 4.5	0.38
Malnutrition†, n (%)	10 (24.4)	9 (20.4)	0.66
VFA (cm ²), mean \pm sd	92.3 \pm 85.5	66.1 \pm 49.3	0.09
SFA (cm ²), mean \pm sd	139.4 \pm 118.5	167.9 \pm 111.1	0.26
Sarcopenia‡, n (%)	31 (75.6)	18 (40.9)	0.0021
Visceral adiposity#, n (%)	12 (29.3)	4 (9.1)	0.0357

* according to the Montreal classification, L1, ileal; L2, colonic; L3, ileocolonic; B1, non-stricturing, non-penetrating; B2, stricturing; B3, penetrating.

† body mass index <18.5kg/m²

‡ Skeletal Muscle Index < 38.5cm²/m² in women and < 52.4cm²/m² in men

VFA \geq 130cm²

BMI, Body mass index; CRP, C Reactive Protein; HBI, Harvey Bradshaw Index; sd, standard deviation; SFA, subcutaneous fat area; VFA, visceral fat area;

Table 4: Univariate and Multivariate analysis of risk factors for surgery during the follow-up

Variable	Univariate analysis			Multivariate analysis		
	Odds Ratio	95% CI	P value	Odds Ratio	95% CI	P value
Age (continuous variable)	1.04	(1;1.07)	0.055			
Male Gender	3.03	(1.25;7.34)	0.012			
Behaviour (B1) *			0.011			
B2	3.75	(1.05;13.39)				
B3	6.75	(1.76;25.96)				
Serum Albumin (continuous variable)	0.92	(0.85;0.99)	0.014	0.94	(0.87;1.02)	0,13
Malnutrition†	1.25	(0.45;3.49)	0.663			
Sarcopenia‡	4.48	(1.76;11.38)	0.001	5.04	(1.72;14.79)	0.002
Visceral obesity #	4.14	(1.21;14.13)	0.016	6.42	(1.58;26.01)	0.005

* according to the Montreal classification, L1, ileal; L2, colonic; L3, ileocolonic; B1, non-stricturing, non-penetrating; B2, stricturing; B3, penetrating.

† body mass index <18.5kg/m²

‡ Skeletal Muscle Index < 38.5cm²/m² in women and < 52.4cm²/m² in men

Visceral fat area ≥ 130cm²

Authors' Contributions:

Guarantor of the article: Lucine Vuitton, MD, PhD

JG was involved in the design of the study, the conception of the case report form (CRF), patients' recruitment, data collection and drafting of the manuscript. LV supervised the study design and drafting. LV, SB and GP contributed to data interpretation and manuscript preparation. JG and ALP contributed to statistical analysis and interpretation of data. CDE, SK, CG, DC, MdB recruited patients and recorded clinical data. All authors contributed to the critical revising and the final approval of the manuscript.

Conflict of interest statement:

J Grillot has received lecture fees from Baxter, Pfizer and MSD.

S Koch has received lecture fees from Abbvie, Mayoli, MSD, FujiFilm.

C Gay has received lecture fees from Abbvie, MSD and Takeda.

L Vuitton has received lecture fees from Abbvie, Ferring, MSD, Pfizer, Janssen and Takeda, consulting fees from Abbvie, Ferring and Gilead and research grants from MSD, Pfizer and Takeda.

CDE, ALP, DC, GP, MdB, ZL and SB declare no conflict of interest.

Funding source: none

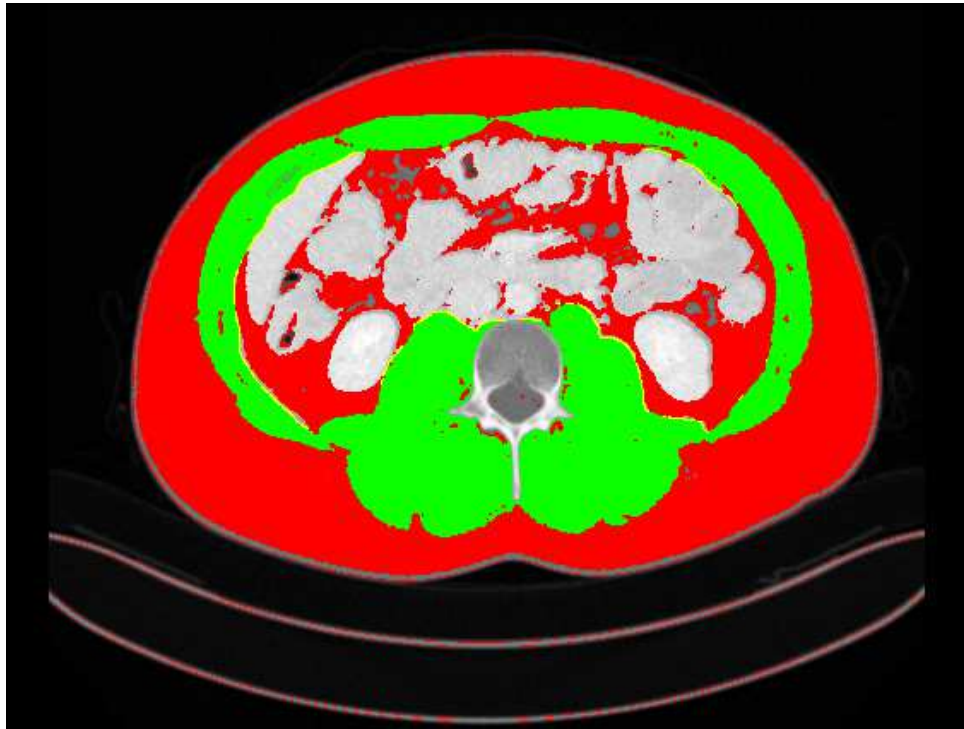


Figure 1: Evaluation of the body composition using a third lumbar CT scan slice.

Red: Adipose Tissue, subcutaneous and visceral

Green: Skeletal muscle