



# Evaluating the role of sarcopenia in adverse clinical outcomes for Crohn's disease patients: a systematic review and meta-analysis

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## Abstract

**Background** Sarcopenia is an age-related condition marked by muscle loss and weakened muscular strength. It is a new predictor of poor clinical outcomes in several illnesses. The association between sarcopenia and poor outcomes in Crohn's disease is still debated. Our main objective is to evaluate the impact of sarcopenia vs non-sarcopenia on the development of adverse outcomes in patients with Crohn's disease.

**Methods** We conducted a systematic review and meta-analysis synthesizing observational studies, which were retrieved by systematically searching PubMed, Web of Science, SCOPUS, EMBASE, and Cochrane until October 1, 2024. The odd ratio (OR) for dichotomous outcomes with the corresponding 95% confidence interval (CI) was used.

**Results** There were fourteen studies with a total of 2334 patients. The sarcopenia group was associated with a higher risk of hospitalization (OR, 1.87 with 95% CI [1.19–2.93],  $P=0.006$ ) and developing abscess (OR, 5.03 with 95% CI [2.05–12.38],  $P=0.0004$ ). However, there was no statistically significant difference between sarcopenia and non-sarcopenia groups, regarding the need for surgery (OR, 1.12 with 95% CI [0.5–2.5],  $P=0.79$ ), loss of biological response (OR, 1.11 with 95% CI [0.34–3.66],  $P=0.86$ ), need for biological therapy (OR, 0.77 with 95% CI [0.43–1.36],  $P=0.36$ ), and surgical site leak (OR, 2.01 with 95% CI [0.66–6.18],  $P=0.22$ ).

**Conclusion** Our study showed that sarcopenia is associated with an increased risk of hospitalization and abscess formation in patients with Crohn's. However, sarcopenia does not significantly affect the need for surgery, loss of biological response, need for biological therapy, or the occurrence of surgical site leaks. Further studies are required to explore the mechanisms underlying these associations.

**Keywords** Systematic review · Sarcopenia · Muscle loss · Crohn's disease · Inflammatory bowel disease · Meta-analysis

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## Background

Crohn's disease (CD) is a chronic inflammatory bowel disease, relapsing–remitting characterized by recurrent gastrointestinal tract inflammation. This disease can lead to complications such as strictures, fistulas, abscesses, and malnutrition. It also increases the risk of hospitalization and surgery as well as impacts patient quality of life. Identifying predictors of poor clinical outcomes is essential for improving disease management and patient prognosis in CD [1–3].

Sarcopenia is an age-related condition marked by the progressive loss of skeletal muscle mass, strength, and function [4]. Studies have shown that sarcopenic adults have an 87% increased risk for overall mortality compared with non-sarcopenic adults [5]. Sarcopenia is increasingly recognized as an important factor influencing prognosis and outcomes in many chronic diseases, including cancer, chronic kidney disease, and cirrhosis [6–8]. In a previous systematic review, it has been reported that 52.1% of CD patients suffered from sarcopenia [9]. It is attributed to the fact that CD is associated with chronic inflammation, malabsorption, altered metabolic pathways, and physical inactivity, all of which contribute to the deterioration of muscle tissue [10, 11].

Current clinical predictors used in CD primarily rely on various factors such as age at diagnosis, disease phenotype, initial use of steroids, and laboratory markers like C-reactive protein (CRP) and fecal calprotectin (FC). Despite these advancements, reliable prognostic factors for predicting long-term outcomes remain limited, highlighting the need for improved indicators [12–14]. Recently, the role of sarcopenia as a prognostic factor has been gaining attention due to its potential association with poor patient outcomes.

The relationship between sarcopenia and specific outcomes in CD patients remains inconclusive. While some studies indicate that sarcopenia may increase the risk of complications such as infections, surgical complications, and prolonged hospitalization, others find no significant differences when compared to non-sarcopenic patients. Hence, due to these inconsistent findings, we aim to assess the impact of sarcopenia vs non-sarcopenia on the development of adverse outcomes in patients with CD [15].

## Methodology

### Protocol registration

This systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16] and the Cochrane Handbook of Systematic Reviews and Meta-Analysis [17].

## Data sources and search strategy

Five databases (PubMed, Cochrane, WOS, SCOPUS, EMBASE) were systematically searched by O.S. and S.A. until September 28, 2024, without search limits. The search strategy included the following: (“Sarcopenia” OR “muscle wasting” OR “muscle loss” OR “muscle atrophy”) AND (“Crohn's disease” OR “Crohn's Disease” OR “Inflammatory Bowel Disease” OR “IBD” OR “Ileitis” OR “Regional Enteritis”) (Table S1).

## Eligibility criteria

We used the following PICOS criteria to include:

1. Population (P): sarcopenic patients with Crohn's disease.
2. Intervention (I): magnetic resonance enterography (MRE), magnetic resonance imaging (MRI), or computed tomography (CT).
3. Control (C): placebo (non-sarcopenic patients).
4. Outcome (O): the primary outcome of this review—need for any surgery, hospitalization, and abscess. Secondary outcomes were a leak from the surgical site, loss of biological response, and need for biological therapy.
5. Study design (S): non-randomized controlled trials (non-RCTs).

## Study selection

Three reviewers (M.A., S.S., and M.A.) individually screened the titles and abstracts of the retrieved records via (Covidence) online software after excluding duplicates. Then, full-text screening was conducted by the same three reviewers using the previously stated eligibility criteria. Any conflicts were solved via discussion.

## Data extraction

Two reviewers (M.A. and M.A.) pilot-tested and drafted an extraction sheet for the following data: summary characteristics (study design, country, total participants, imaging type, sarcopenia definition, main inclusion criteria, primary outcome, and follow-up duration) and baseline characteristics (a number of patients in each group, age, gender, body mass index (BMI), smoking, C-reactive protein (CRP), hemoglobin, albumin, subcutaneous fat areas (SFA), skeletal muscle areas (SMA), skeletal muscle index (SMI), visceral fat areas (VFA), SMA/SFA, SMA/VFA, age of diagnosis, location of the disease, disease phenotype, current treatments use, previous surgery). Disagreements were resolved through discussion.

## Risk of bias and certainty of evidence

Two independent investigators (O.A. and D.A.) implemented the Newcastle–Ottawa scale for assessing the quality of non-randomized studies (NOS) [18], considering eight domains grouped into three main clusters: (1) the selection of the study groups, (2) the comparability of the groups, and (3) the ascertainment of the outcome of interest. Each of the eight domains may be given an asterisk, except for the comparability criterion which may be given two, meaning that the highest quality studies can achieve a maximum of nine asterisks. Any disagreement was resolved through discussion or by a third reviewer (O.S.).

## Statistical analysis

We performed the meta-analysis using Revman software version 5.4 [19] to pool dichotomous outcomes using risk ratio (RR) and continuous outcomes using mean difference (MD), along with the corresponding 95% confidence interval (CI). We conducted the pooled analysis using the random-effects model. In case of significant heterogeneity, the random-effects model was implemented. We evaluated heterogeneity, using the chi-square test, and it was measured by the *I*-square test. On an alpha level below 0.1, the chi-square test was considered significant, and heterogeneity was considered significant if the *I*-square was > 50%. To investigate the source of heterogeneity, sensitivity analysis was conducted by excluding one study at a time and rerunning the analysis.

## Results

### Search results and study selection

Our search yielded 1495 results across the different databases, with 905 records remaining for abstract screening after omitting 590 duplicates. After screening abstracts and titles, 794 records were excluded, leaving 111 studies retrieved for full-text review. Of them, 97 were excluded, and 14 were included in our review. The flow diagram records search and selection are depicted in Fig. 1.

### Characteristics of included studies

The summary characteristics of the 14 included studies are presented in Table 1. Twelve studies used CT scans as an imaging tool to assess sarcopenia [11, 20] and two studies used both MRI and CT scans to assess sarcopenia. A total of 2334 patients (males = 1490; sarcopenic group = 788, non-sarcopenic group = 702) were enrolled, with the mean age of the sarcopenic group being 35.54 years old (SD = 15.32) and the non-sarcopenic group is 36.85 years old (SD = 13.54).

Characteristics of studies' participants are presented in Table 2.

## Risk of bias and quality of evidence

The 14 included studies had a retrospective cohort design and were assessed for quality using the Newcastle–Ottawa Scale (NOS) for cohort studies. The detailed quality assessment results are available in Table S2. Overall, most studies were classified as having good quality. Two studies (Grova 2023 and Nam 2023) were assessed as having fair quality, and three studies (Carvalho 2019, Lee 2020, and Ouni 2022) were classified as poor quality.

## Efficacy outcomes

### Primary outcomes

The non-sarcopenia group was associated with a higher risk of hospitalization (OR, 1.87 with 95% CI [1.19–2.93],  $P=0.006$ ) (Fig. 2A) and developing abscess (OR, 5.03 with 95% CI [2.05–12.38],  $P=0.0004$ ) (Fig. 2B). However, there was no statistically significant difference between the sarcopenia and non-sarcopenia groups, regarding the need for surgery (OR, 1.12 with 95% CI [0.5–2.5],  $P=0.79$ ) (Fig. 2C).

Studies were homogenous in hospitalization ( $P=0.29$ ,  $I^2=19\%$ ) and developing abscess ( $P=0.75$ ,  $I^2=0\%$ ). However, the result was heterogeneous regarding the need for surgery ( $P=0.00001$ ,  $I^2=81\%$ ).

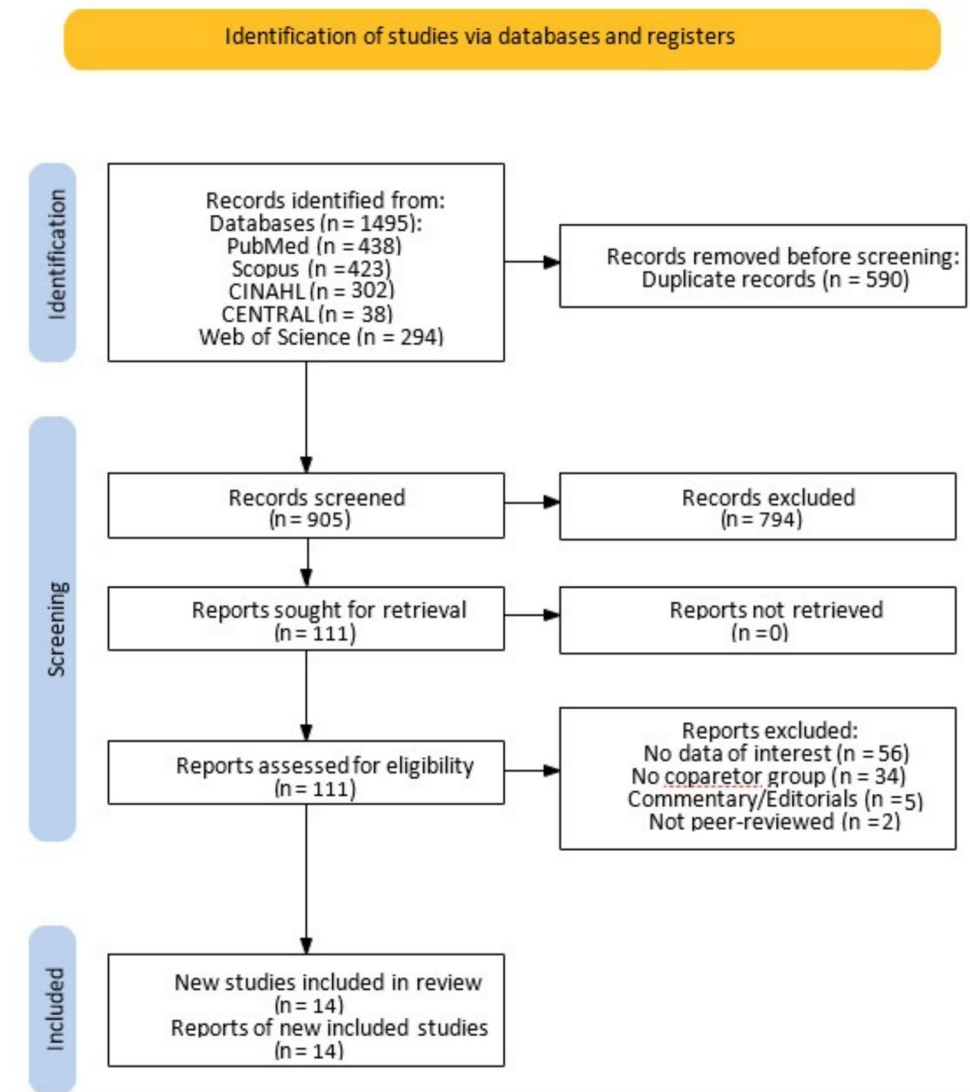
### Secondary outcomes

There was no statistically significant difference between sarcopenia and non-sarcopenia groups, regarding the loss of biological response (OR, 1.11 with 95% CI [0.34–3.66],  $P=0.86$ ) (Fig. 3A), need for biological therapy (OR, 0.77 with 95% CI [0.43–1.36],  $P=0.36$ ) (Fig. 3B), and surgical site leak (OR, 2.01 with 95% CI [0.66–6.18],  $P=0.22$ ) (Fig. 3C).

Studies were homogenous in the need for biological therapy ( $P=0.34$ ,  $I^2=7\%$ ) and surgical site leak ( $P=0.75$ ,  $I^2=0\%$ ). However, the result was heterogeneous regarding the loss of biological response ( $P=0.03$ ,  $I^2=73\%$ ).

## Discussion

Sarcopenia plays a significant role in shaping the clinical outcomes of CD. Our study highlights the critical impact of sarcopenia, particularly its association with adverse outcomes, such as hospitalization and abscess formation. These findings are supported by existing literature, which consistently identifies sarcopenia as a prevalent and

**Fig. 1** PRISMA flow chart of the screening process

clinically impactful condition among patients with CD. For instance, [35] identified sarcopenia as an independent risk factor for loss of response (LOR) to infliximab, with a threefold increased risk in patients with sarcopenia. While our analysis found no significant difference in LOR between the sarcopenic and non-sarcopenic, this discrepancy may reflect heterogeneity in treatment timelines, patient demographics, and disease severity.

The postoperative outcomes underscore the effect of sarcopenia in patients with CD. Previous studies have demonstrated that reduced skeletal muscle area correlates with increased rates of infectious complications, anastomotic leakage, and endoscopic recurrence within 1 year of surgery. [36, 37] further report associations with venous thromboembolism and wound infections, necessitating targeted preoperative assessments. Although our findings did not reveal significant differences in surgical site, the increased risk of abscess development in sarcopenic

patients underscores the role of muscle wasting in shaping CD-related complications.

The broader effect of sarcopenia in CD is mirrored in other chronic diseases, such as cancer, chronic liver disease, and cardiovascular conditions, where it predicts therapy resistance, increased complications, and poor survival outcomes [31, 38]. For instance, sarcopenic CD patients have up to a fivefold higher likelihood of failing to achieve endoscopic remission after 12 months of biological therapy [31]. This aligns with our findings, as sarcopenia significantly impacted hospitalization rates, but did not affect remission rates or the need for biologic therapy.

The mechanisms underlying sarcopenia in patients with CD are complex and multifactorial. Chronic inflammation plays a central role with cytokines such as TNF- $\alpha$  and IL-6, which drive muscle catabolism via the ubiquitin–proteasome system and autophagy pathways [15]. This persistent inflammation exacerbates gut dysbiosis and disrupts nutrient

**Table 1** Summary characteristics

Authors (year)	Study design	Country	Sample size	Imaging type	Follow-up duration (months)	Definition of sarcopenia	Main inclusion criteria	Primary outcome
Zhang et al. (2015) [21]	Prospective cohort study, single center	China	114	CT scan	13.96 ± 22.52	SMI < 55 cm <sup>2</sup> /m <sup>2</sup> for men and < 39 cm <sup>2</sup> /m <sup>2</sup> for women	All patients who underwent bowel resection for CD at the Department of General Surgery in Jinling Hospital from May 2011 to March 201	The prevalence of sarcopenia in patients with CD undergoing bowel resection and to evaluate the impact of sarcopenia on postoperative outcomes
Carvalho et al. (2019) [22]	Retrospective cohort study, single center	Portugal	58	CT scan	NA	SMI values less than 38.5 cm <sup>2</sup> /m <sup>2</sup> in women and less than 52.4 cm <sup>2</sup> /m <sup>2</sup> in men	From 1 January 2009 to 31 December 2017, Patients with histological diagnosis of Crohn's disease and patients who underwent EnterocT with complete visibility of the muscle area at the L3 level	To evaluate the prevalence of sarcopenia and its impact on morbidity and prognosis in patients with Crohn's disease
Lee et al. (2020) [23]	Retrospective cohort study, single center	South Korea	79	CT scan	Median of 34.8	SMI < 49 cm <sup>2</sup> /m <sup>2</sup> for men and < 31 cm <sup>2</sup> /m <sup>2</sup> for women	≥ 18 years old; diagnosis of CD based on clinical, endoscopic, and radiological examination; availability of accurate height, weight, and CT data within 3 months after diagnosis	The prevalence of sarcopenia among CD patients reveals the predictive values of sarcopenia in impacts on prognostic outcomes
Grillot et al. (2020) [24]	Retrospective cohort study, single center	France	88	CT scan	22.2 ± 20.1	SMI < 38.5 cm <sup>2</sup> /m <sup>2</sup> in women and < 52.4 cm <sup>2</sup> /m <sup>2</sup> in men	A confirmed diagnosis of CD and follow-up at Besançon University Hospital, those aged 18–65 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 201	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

**Table 1** (continued)

Authors (year)	Study design	Country	Sample size	Imaging type	Follow-up duration (months)	Definition of sarcopenia	Main inclusion criteria	Primary outcome
Zhang et al. (2021)[25]	Retrospective cohort study, single center	China	124	CT scan	NA	SMI < 41 cm <sup>2</sup> /m <sup>2</sup> in women, < 43 cm <sup>2</sup> /m <sup>2</sup> in men with BMI < 25 kg/m <sup>2</sup> , and < 53 cm <sup>2</sup> /m <sup>2</sup> in men with BMI ≥ 25 kg/m	Patients who underwent CD-related bowel surgery from January 2013 to October 2019	To assess (1) the prevalence of sarcopenia in patients with CD undergoing bowel resection and (2) evaluate the influence of sarcopenia as a risk factor for postoperative complications on these patients
Boparai et al. (2021)[26]	Retrospective cohort study, single center	India	44	CT scan	32.53 ± 31.8	SMI < 36.54 cm <sup>2</sup> /m <sup>2</sup> and 30.21 cm <sup>2</sup> /m <sup>2</sup> for males and females, respectively	Patients with CD (aged 18–65 years) under follow-up at the IBD clinic, All India Institute of Medical Sciences, New Delhi, with available CT images < 1 mm in thickness from the archiving system (PACS) were included	To evaluate the prevalence of sarcopenia and visceral fat parameters in patients with CD, correlate sarcopenia and visceral fat with disease severity, location, and behavior and assess the impact of sarcopenia and visceral fat on clinical outcomes
Yasueda et al. (2022) [27]	Retrospective cohort study, single center	Japan	56	CT scan	NA	SMI < 6.36 cm <sup>2</sup> /m <sup>2</sup> for men and < 3.92 cm <sup>2</sup> /m <sup>2</sup> for women	Patients with CD who underwent surgery, including intestinal resections, at Osaka University Hospital from 2000 to 2018	Investigating the effects of preoperative sarcopenia on postoperative disease activity
Nardone et al. (2022) [28]	Retrospective cohort study, single center	Italy	63	CTE	12	SMI < 38.5 cm <sup>2</sup> /m <sup>2</sup> in women and < 52.4 cm <sup>2</sup> /m <sup>2</sup> in men	All CD patients between 2005 and 2018 who underwent CTE performed in an emergency setting	Investigating the effects of preoperative sarcopenia on postoperative disease activity
Ouni et al. (2022)[29]	Retrospective cohort study, single center	Texas, USA	40	CT scan	NA	SMI < 38.5 cm <sup>2</sup> /m <sup>2</sup> in women and < 52.4 cm <sup>2</sup> /m <sup>2</sup> in men	NA	Investigate the impact of sarcopenia on disease phenotype, biological therapy failure



**Table 1** (continued)

Authors (year)	Study design	Country	Sample size	Imaging type	Follow-up duration (months)	Definition of sarcopenia	Main inclusion criteria	Primary outcome
Lee et al. (2022) [30]	Retrospective cohort study, single center	South Korea	71	CT scan	138.7 ± 60.2	SMI < 38.5 cm <sup>2</sup> /m <sup>2</sup> in women and < 52.4 cm <sup>2</sup> /m <sup>2</sup> in men	All patients diagnosed with CD between January 2000 and December 2009 were followed up until August 2020. In the Kyung Hee University Hospital	To analyze serial changes in body composition and investigate the association between body composition changes and disease activity in Crohn's disease
Grova et al. (2023)[31]	Retrospective cohort study, single center	Italy	358	MRI, CT	12	SMI < 38.5 cm <sup>2</sup> /m <sup>2</sup> in women and < 52.4 cm <sup>2</sup> /m <sup>2</sup> in men	All patients diagnosed with CD between January 2000 and December 2009 were followed up until August 2020. In the Kyung Hee University Hospital	To analyze serial changes in body composition and investigate the association between body composition changes and disease activity in Crohn's disease
Nam et al. (2023)[32]	Retrospective cohort study, single center	South Korea	854	CT scan	Median of 80	SMI < 49 cm <sup>2</sup> /m <sup>2</sup> for male and < 31 cm <sup>2</sup> /m <sup>2</sup> for female	All patients who were included in the Asan IBD registry between June 1989 and December 2016 and underwent abdominal-pelvic CT	To evaluate the association between sarcopenia at diagnosis and the need for medical and surgical treatment during follow-up
Cankurtaran et al. (2023)[33]	Retrospective cohort study, single center	Turkey	116	MRI, CT	12 (12–79)	SMI < 38.5 cm <sup>2</sup> /m <sup>2</sup> in women and < 52.4 cm <sup>2</sup> /m <sup>2</sup> in men	Crohn's disease patients who underwent magnetic resonance enterography between January 2015 and August 2021	To evaluate the association between sarcopenia at diagnosis and the need for medical and surgical treatment during follow-up
Fang et al. (2024) [34]	Retrospective cohort study, single center	China	269	CT scan	8–26	SMI < 28.4 cm <sup>2</sup> /m <sup>2</sup> in women and < 39.8 cm <sup>2</sup> /m <sup>2</sup> in men	Crohn's disease patients who underwent magnetic resonance enterography between January 2015 and August 2021	The association between sarcopenia at diagnosis and the need for medical and surgical treatment during follow-up

**Table 2** Baseline characteristics of the participants

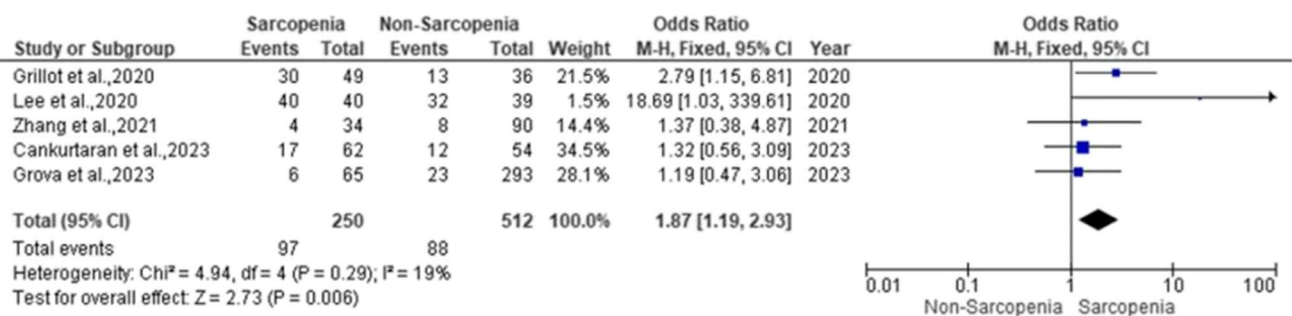
	Total CD patients ( <i>n</i> = 2242)	
	Non-sarcopenia ( <i>n</i> = 1220)	Sarcopenia ( <i>n</i> = 1022)
<b>Demographic features</b>		
Age (years), mean $\pm$ SD	<i>n</i> = 857 36.85 $\pm$ 13.54	<i>n</i> = 531 35.54 $\pm$ 15.32
Male gender, <i>n</i> (%)	702 (57)	798 (78)
Disease duration (years), mean $\pm$ SD	<i>n</i> = 608 9.12 $\pm$ 16.3	<i>n</i> = 320 8.89 $\pm$ 11.75
BMI (kg/m <sup>2</sup> ), mean $\pm$ SD	<i>n</i> = 1155 21.44 $\pm$ 4.39	<i>n</i> = 960 20.02 $\pm$ 3.81
Smokers, <i>n</i> (%)	<i>n</i> = 620 197 (31.8)	<i>n</i> = 310 106 (34.2)
HBI, mean $\pm$ SD	<i>n</i> = 588 5.53 $\pm$ 3.81	<i>n</i> = 227 6.84 $\pm$ 3.75
<b>Montreal classification, <i>n</i> (%)</b>		
<b>Age of diagnosis</b>		
A1	<i>n</i> = 593 89 (15)	<i>n</i> = 636 81 (12.7)
A2	416 (70.1)	492 (77.3)
A3	88 (14.8)	63 (10)
<b>Location</b>		
L1	<i>n</i> = 1057 561 (53.1)	<i>n</i> = 860 502 (58.3)
L2	81 (7)	61 (7)
L3	441 (41.7)	304 (35.3)
<b>Behavior</b>		
B1	<i>n</i> = 1086 484 (44.6)	<i>n</i> = 871 424 (48.6)
B2	395 (36.3)	228 (26.2)
B3	261 (24)	247 (28.4)
Perianal disease	<i>n</i> = 656 179 (27.3)	<i>n</i> = 328 103 (31.4)
<b>Lab parameters, mean <math>\pm</math> SD</b>		
Serum albumin (g/dL)	<i>n</i> = 394 3.66 $\pm$ 0.97	<i>n</i> = 344 3.57 $\pm$ 1.02
CRP (mg/L)	<i>n</i> = 187 2.45 $\pm$ 4.19	<i>n</i> = 213 3.83 $\pm$ 5.78
Hemoglobin (g/dL)	<i>n</i> = 274 12.1 $\pm$ 2.5	<i>n</i> = 215 11.76 $\pm$ 2.44
<b>Body composition parameters, mean <math>\pm</math> SD</b>		
VFA (cm <sup>2</sup> )	<i>n</i> = 528 57.67 $\pm$ 49.8	<i>n</i> = 714 42.38 $\pm$ 38.74
SFA (cm <sup>2</sup> )	<i>n</i> = 528 106.3 $\pm$ 80.42	<i>n</i> = 714 77.11 $\pm$ 63.07
SMA (cm <sup>2</sup> )	<i>n</i> = 563 143.12 $\pm$ 42.56	<i>n</i> = 698 115.1 $\pm$ 44.34
SMI (cm <sup>2</sup> /m <sup>2</sup> )	<i>n</i> = 942 49.89 $\pm$ 11.45	<i>n</i> = 805 38.38 $\pm$ 8.06
SMA\SFA	<i>n</i> = 446 3.96 $\pm$ 7.91	<i>n</i> = 601 4.64 $\pm$ 10.59
<b>Treatment history, <i>n</i> (%)</b>		
Corticosteroids	<i>n</i> = 611 243 (39.7)	<i>n</i> = 690 280 (40.5)



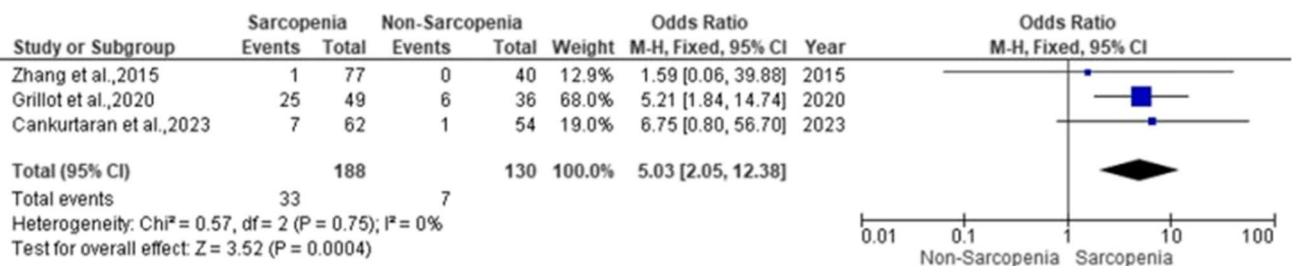
**Table 2** (continued)

	Total CD patients (n = 2242)	
	Non-sarcopenia (n = 1220)	Sarcopenia (n = 1022)
Thiopurine	n = 420	n = 585
	342 (81.4)	459 (78.4)
Biological treatment	n = 725	n = 755
	360 (49.6)	309 (40.9)
ASA	n = 137	n = 43
	50 (36.4)	14 (32.5)
Previous surgeries (intestinal, anal)	n = 843	n = 732
	327 (38.7)	405 (55.3)

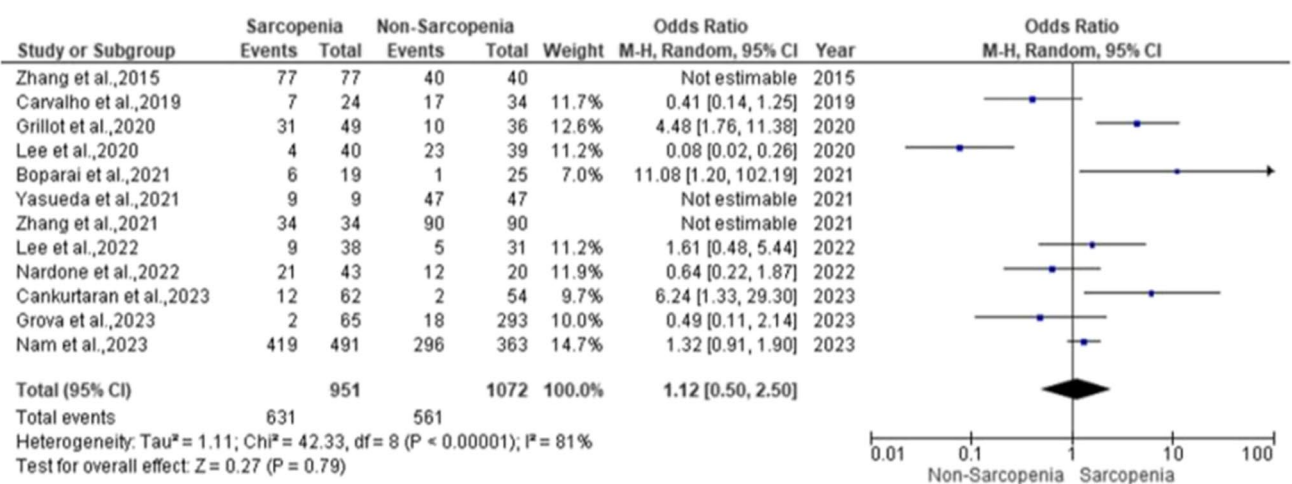
## A Hospitalization



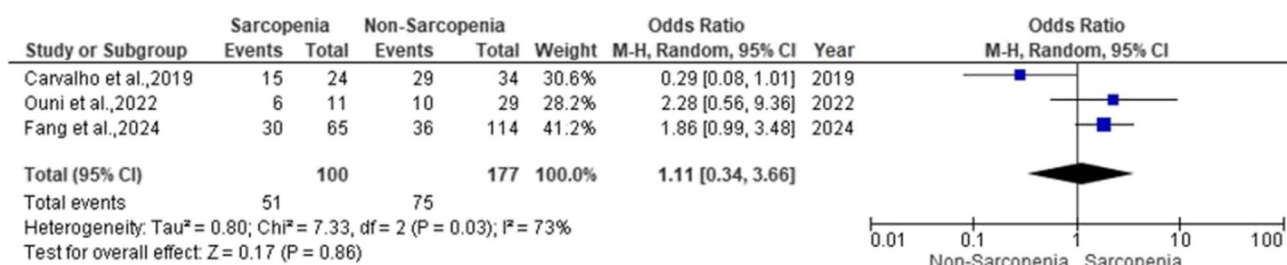
## B Abscess



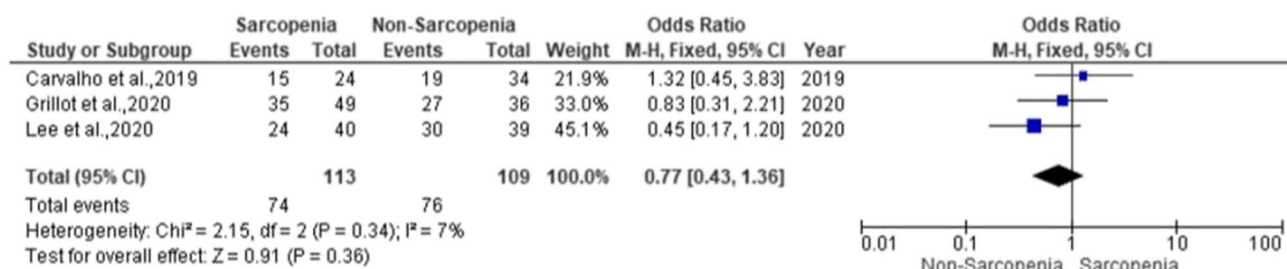
## C Need for surgery

**Fig. 2** Forest plot of the primary outcomes (**A** hospitalization, **B** abscess, **C** need for surgery). RR, risk ratio; CI, confidence interval

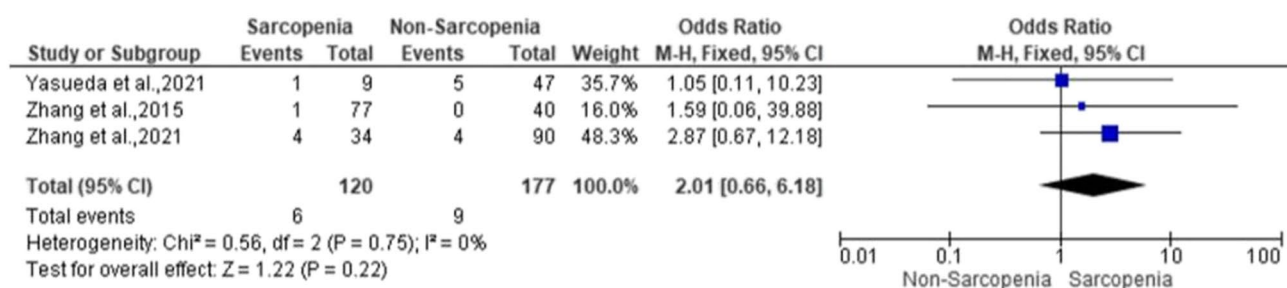
## A Loss of biological response



## B Need for biological therapy



## C Surgical site leak



**Fig. 3** Forest plot of the secondary outcomes (**A** loss of biological response, **B** need for biological therapy, **C** surgical site leak). RR, risk ratio; CI, confidence interval

absorption, thereby creating a bidirectional relationship between inflammation and muscle wasting [39]. Our findings, particularly the increased risk of abscess formation in sarcopenic patients, reinforce the role of systemic inflammation in amplifying the clinical impact of sarcopenia. Furthermore, mesenteric fat, which is often expanded in CD, acts as an endocrine organ, secreting pro-inflammatory mediators that worsen muscle breakdown [40].

Vitamin and mineral deficiencies, particularly vitamin D deficiencies, are also critical contributors to sarcopenia in patients with CD. Vitamin D deficiency impairs muscle function by disrupting calcium metabolism and mitochondrial activity [11]. Additionally, insulin resistance, a common consequence of chronic inflammation, interferes with anabolic signaling pathways, such as PI3K-AKT-mTOR, further inhibiting muscle repair and growth. Collectively, these mechanisms highlight the need for comprehensive, multi-faceted strategies to address sarcopenia in CD, including

anti-inflammatory therapies, nutritional supplementation, and resistance training.

Imaging tools, particularly computed tomography (CT) and magnetic resonance imaging (MRI), are invaluable for assessing sarcopenia in CD patients. The skeletal muscle area (SMA) at the L3 vertebra is a reliable proxy for the total body muscle mass and correlates well with clinical outcomes [41]. MRI offers advantages in pediatric and recurrent CD cases as it avoids radiation exposure while concurrently assessing disease activity. Our study aligns with these findings, with CT and MRI being the primary tools used for identifying sarcopenia in the included studies. These imaging modalities not only aid in early detection but also facilitate disease monitoring and personalized treatment strategies.

Systematic reviews and meta-analyses, such as ours, play a pivotal role in consolidating the evidence on the prevalence and impact of sarcopenia in CD. [42] reported that

sarcopenia doubles the risk of surgical complications, a finding partially reflected in our results, where abscess formation was significantly higher in sarcopenic patients. However, the lack of significant differences in surgery rates and heterogeneity in these results ( $I^2 = 81\%$ ) highlights the challenges of standardizing diagnostic criteria and accounting for confounding variables. [43] emphasize the need for consistent definitions and methodologies to enhance the comparability and reliability of sarcopenia research.

Intervention studies targeting sarcopenia in CD have emphasized nutritional and physical rehabilitation as key strategies for improving outcomes. High-protein diets, vitamin D supplementation, and omega-3 fatty acids have shown promise for mitigating muscle loss and enhancing muscle strength [44]. Resistance training further complements these dietary strategies, improves functional outcomes, and reduces inflammation by enhancing muscle anabolism. Our findings align with these recommendations, as prehabilitation programs integrating nutrition and exercise are increasingly recognized to reduce hospitalization costs, shorten recovery times, and improve the quality of life [45].

Despite these advances, observational studies of sarcopenia in CD face challenges such as selection bias, variability in diagnostic criteria, and outcome heterogeneity [33]. The discrepancies in sarcopenia's prevalence and its association with clinical outcomes across studies highlight the need for prospective multicenter research to improve the reliability of evidence. For example, while Schneider et al. [45] reported significant associations with increased mortality and hospital stay, our findings showed no clear correlation with surgery rates, likely due to differences in population characteristics and study designs.

Finally, machine learning models integrating clinical and imaging data offer a promising avenue for predicting sarcopenia and enabling the proactive management of high-risk CD patients [46]. These models, combined with personalized care plans that incorporate sarcopenia assessments, have the potential to optimize therapeutic decisions, enhance disease monitoring, and improve long-term outcomes for CD patients with CD.

## Conclusion

Our meta-analysis underscores sarcopenia as a significant predictor of adverse outcomes in Crohn's disease, notably higher hospitalization rates, and increased risk of abscess formation. However, sarcopenia did not significantly influence the need for surgery, loss of biological response, or surgical site leaks, highlighting the heterogeneous nature of its effect on CD. These findings necessitate further research to elucidate the underlying mechanisms and to develop targeted interventions. Future strategies should focus on

integrating sarcopenia management into the holistic care of patients with CD to enhance outcomes and improve the quality of life. Comprehensive studies are essential to refine our understanding of this complex interrelation, ensuring better patient care and optimized treatment pathways.

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**Author contribution** O.S. conceived the idea. O.S. and S.A. designed the research workflow. O.S. and S.A. searched the databases. M.A., S.S., D.A., and O.A. screened the retrieved records, extracted relevant data, assessed the quality of evidence, and O.S. resolved the conflicts. S.A. performed the analysis. S.A., O.S., H.H, M.H., and M.A. wrote the final manuscript. O.S. supervised the project. All authors have read and agreed to the final version of the manuscript.

**Data availability** Data is provided within the manuscript or supplementary information files.

## Declarations

**Ethics approval and consent to participate** Not applicable.

**Consent for publication** Not applicable.

**Competing interests** The authors declare no competing interests.

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