Osteosarcopenia May Be Associated with Complications after Colectomy for Diverticulitis

Saed Khalilieh MD[1,2], Mor Azhari MD[1,2], Ronny Maman MD[1,2], Ely Erez MD[1,2], Alon Israeli MD[1,2], Noa Avishay MD[1,2], Dan Assaf MD[1,2], Edward Ram MD[1,2], Nir Horesh MD[2,3]*, and Yaniv Zager MD[1,2,4]*

[1]Division of General Surgery, Sheba Medical Center, Tel Hashomer, Israel
[2]Gray Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel
[3]Shulman Digestive Disease Center, Cleveland Clinic, Florida, Weston, FL, USA
[4]Department of Colorectal Surgery, Adventhealth, Orlando, Florida, USA

*These authors contributed equally to this study.

ABSTRACT **Background:** Diverticulitis is a common cause of acute abdominal conditions, often requiring urgent or elective surgical intervention. Both psoas muscle area (PMA) and bone mineral density (BMD) have been linked to postoperative outcomes, but their role in diverticulitis remains unclear.

Objectives: To evaluate the relationship between PMA, BMD, and their combined effect on surgical outcomes in patients undergoing colectomy for diverticulitis.

Methods: In this retrospective, single-center study, we analyzed patients who underwent colectomy for diverticulitis. PMA and BMD were measured using preoperative computerized tomography. Statistical analysis assessed the association between postoperative outcomes and PMA, BMD, and their combined product (PMA × BMD).

Results: The cohort included 66 patients; median age 68.5 years (range 34–94); 41 (62.12%) females. Of the cases, 42 (63.63%) were urgent. Postoperative complications occurred in 38 patients (57.58%). Patients who developed major postoperative complications had lower PMA (1116.74 ± 716.31 mm² vs. 1948.01 ± 0.01 mm², $P = 0.02$). The area under the curve (AUC) for major postoperative complications was 0.94 for BMD. The AUC for postoperative ileus was 0.73, 0.69, and 0.76 for PMA, BMD, and PMA × BMD, respectively. The AUC for 30-day mortality was 0.66, 0.7, and 0.73. The AUC for ostomy reversal was 0.71, 0.71, and 0.76.

Conclusions: PMA and BMD were associated with postoperative complications after colectomy for diverticulitis. Their combined assessment may improve predictive accuracy. Current evidence regarding the impact of body composition on surgical outcomes in diverticulitis remains limited and inconsistent. Further research is warranted.

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KEY WORDS: colectomy, diverticulitis, osteopenia, postoperative complications, sarcopenia

Diverticulitis is an inflammatory condition of the sigmoid colon that presents with a wide range of severity in both acute and chronic settings. Its etiology is multifactorial, involving diet, microbiome, genetic predisposition, medications, and other co-morbidities. In the acute setting, patients who are hemodynamically unstable, exhibit generalized peritonitis, or have imaging-confirmed free perforation (typically on computerized tomography) require urgent surgical intervention. In contrast, the decision to perform elective sigmoidectomy in patients with recurrent or chronic diverticulitis is more nuanced, often based on the impact on the patient's quality of life, including the frequency, severity, and persistence of symptoms between episodes. Individualized risk assessment for postoperative complications, including life-threatening events is also considered. Traditionally, such assessments rely on patient age, functional status, and co-morbidities [1]. However, these factors can be difficult to quantify, highlighting the need for novel objective measures.

Sarcopenia has been associated with poor surgical outcomes across various benign and malignant conditions [2-5]. One commonly used measure for sarcopenia is the psoas muscle area (PMA), which is assessed via computed tomography (CT) or magnetic resonance imaging [6]. The relationship between sarcopenia and surgical outcomes in diverticulitis remains unclear, as existing literature on this topic is limited. While some studies support a link between sarcopenia and adverse postoperative outcomes [7], others have failed to establish a significant association [8,9].

Osteopenia, characterized by low bone mineral density (BMD), has also been linked to worse postoperative outcomes in malignancies, including pancreatectomy for pancreatic cancer [10], colectomy for colon cancer [11],

and gastrectomy for gastric cancer [12]. Osteosarcopenia, defined as the coexistence of both low skeletal muscle mass and low BMD [13], has recently been identified as a potential predictor of poor surgical outcomes in conditions such as extrahepatic bile duct cancer [14] and pancreatic ductal adenocarcinoma [15].

Given these emerging associations, we evaluate the relationship between PMA, BMD, and their combined effect on surgical outcomes in patients undergoing colectomy for diverticulitis.

PATIENTS AND METHODS

This retrospective, single-institution study was conducted in accordance with ethical standards outlined in the Declaration of Helsinki (Brazil 2013 revision) and received approval from the institutional review board (IRB #2036-15-SMC). All admissions for diverticulitis were identified through electronic medical records, and cases requiring surgical intervention were selected for further analysis. Collected data included patient demographics, co-morbidities, surgical details, postoperative outcomes, and follow-up information.

Postoperative complications were classified according to the Clavien-Dindo system with major complications defined as grade 3 or higher. Preoperative PMA was measured using available CT imaging obtained within 60 days prior to surgery. Measurements were performed using PACS software (Carestream Veu ver 11.3, Carestream Health, Rochester, NY), with PMA assessed in the transverse plane at the L5 vertebral level. The mean area of the right and left psoas muscles was used for statistical analysis.

BMD was quantified in Hounsfield units (HU) at the T11 vertebral level using a circular region of interest in the mid-vertebral core for all non-contrast-enhanced CT images. These measurements were conducted using PACS software (Carestream Veu ver 11.3, Carestream Health, Rochester, NY, USA) [16].

To quantify osteosarcopenia, we defined a composite metric as the product of PMA and bone mineral density (PMA × BMD). To the best of our knowledge, this represents a novel measure of osteosarcopenia.

STATISTICAL ANALYSIS

EZR software (version 1.61 by Y.Kanda [available from http://www.jichi.ac.jp/saitama-sct/SaitamaHP.files/statmed.html]) running on Statistical analyses were performed using R Statistical Software, version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria) was used for statistical processing. The area under the curve (AUC) analysis was used to find association between continuous variables and certain discrete conditions. A *t*-test was used to compare means. $P < 0.05$ is considered statistically significant.

RESULTS

Between January 2010 and May 2022, a total of 2131 hospital admissions for diverticulitis were recorded. Among these, 161 patients (7.56%) required surgical intervention. Sufficient data were available for the 66 patients who were included in our study. Of these, 41 (62.12%) were female, and the median age was 68.5 years (range 34–94). Baseline demographic and clinical characteristics are summarized in Table 1. The median interval between the preoperative CT scan used to assess PMA and BMD and the surgery was 13 days (range 0–60). Forty-two patients (63.64%) underwent surgery in an urgent setting. A minimally invasive approach was attempted in 28 cases (42.42%), but 10 (35.71%) required conversion to open surgery. Primary anastomosis was performed in 28 patients (42.42%), with protective ileostomy in 5 cases (17.86%). Details of surgical procedures and outcomes are presented in Table 2. Postoperative complications occurred in 38 patients (57.58%), with major complications (Clavien-Dindo ≥ 3) observed in 15 cases (22.73%). Notably, 14 patients (21.21%) developed surgical site infections, and 2 patients (7.14%) experienced an anastomotic leak (of 28 who underwent primary anastomosis). Reoperation within 30 days was necessary for 6 patients

Table 1. Basic demographic and clinical data (N=66)

Characteristic	Value
Female	41 (62.12%)
Median age in years	68.5 (34–94)
Median body mass index (kg/m²)	26.15 (15.6–42.2)
Hypertension	42 (63.63%)
Diabetes	13 (19.7%)
Atrial fibrillation	8 (12.12%)
Dyslipidemia	16 (24.24%)
Ischemic heart disease	3 (4.5%)
Cerebrovascular accident	5 (7.58%)
Active smoker	15 (22.73%)
Steroids usage	8 (12.12%)
Systematic lupus erythematosus	1 (1.52%)
Transplanted organ	2 (3.03%)

(9.09%). A total of 8 patients (12.12%) were readmitted within 30 days postoperatively, and 5 patients (7.36%) died within this period. A detailed breakdown of postoperative complications is provided in Table 3.

The mean PMA was 1764.62 ± 1270 mm², while the mean T11 BMD was 130.62 ± 29.58 HU. Patients who experienced major postoperative complications had significantly lower average PMA compared to those without major complications (1116.74 ± 716.31 mm² vs. 1948.01 ± 0.01 mm², $P = 0.02$).

Table 2. Procedure details and outcomes (N=66)

Procedure	Outcome
Urgent surgery	42 (63.63%)
Minimal invasive surgery	28 (42.42%)
Conversion (to open) rate	10 (35.71%)
Primary anastomosis	28 (42.42%)
Protective ileostomy	5 (17.85%)
Median length of stay	10 (3-51)
30-day readmission rate	8 (12.12%)
30-day mortality rates	5 (11.9%)
Recurrent diverticulitis after surgery	1 (2.38%)

Table 3. Postoperative complications (N=66)

Postoperative complications	Rate
Postoperative complications incidence	38 (57.58%)
Major postoperative complications incidence (Clavien-Dindo ≥ 3)	15 (22.73%)
Surgical site infection	14 (21.21%)
Ileus	5 (7.58%)
Anastomotic leak	2 (3.03%)
Intra-abdominal abscess	5(7.58%)
Pneumonia	4 (5.88%)
Urinary tract infection	0 (0%)
Reoperation within 30 days	6 (9.09%)

AREA UNDER THE CURVE

The AUC for major postoperative complications was 0.55, 0.94, and 0.55 for PMA, BMD, and PMA × BMD, respectively. For postoperative ileus, the AUC values were 0.73, 0.69, and 0.76 for PMA, BMD, and PMA × BMD, respectively. The AUC for 30-day mortality was 0.66, 0.70, and 0.73 for PMA, BMD, and PMA × BMD, respectively. Similarly, the AUC for ostomy closure was 0.71, 0.71, and 0.76 for PMA, BMD, and PMA × BMD, respectively. Additional AUC analyses are presented in Table 4.

DISCUSSION

Our findings indicate that PMA is associated with the occurrence of postoperative ileus, major postoperative complications, and 30-day mortality. Furthermore, this association is strengthened when PMA is combined (by multiplication) with BMD. Both measurements can be easily obtained from routine abdominal-pelvic CT scans at no additional cost. While previous studies have explored the relationship between sarcopenia or skeletal muscle mass and surgical outcomes in diverticulitis, the available evidence remains limited.

Matsushima et al. [7] reviewed a cohort of 89 patients who underwent urgent colectomy for diverticulitis. Their findings align with ours, demonstrating an association between low psoas muscle mass and major postoperative complications. However, they did not assess the role of low BMD in surgical outcomes.

Schaffler-Schaden and colleagues [8] conducted a retrospective study of 99 patients who underwent elective single-port surgery for diverticulitis. They evaluated the skeletal muscle index (SMI), defined as the skeletal muscle area divided by patient height, and Myosteatosis, a measure of skeletal muscle quality based on HU attenuation. Their study did not show a significant association between these muscle-related parameters and surgical outcomes.

Similarly, Krebs and colleagues [9] retrospectively analyzed 148 patients who underwent elective colectomy for diverticulitis. They assessed sarcopenia using both the SMI and the PMI. Other than an observed association between sarcopenia and prolonged length of hospital stay, no significant correlations were found between sarcopenia and other surgical outcomes.

Fukushima et al. [17] retrospectively reviewed 216 patients who underwent emergency surgery for gastrointestinal perforation, including 111 cases (51.39%) of colonic and rectal perforation. Their findings suggest a link between osteosarcopenia and postoperative complications, as well as in-hospital mortality. To the best of our knowledge, this study is the first to explore the association between osteosarcopenia and surgical outcomes in abdominal procedures for benign, non-malignant conditions (only 17.1% of the patients had malignancy). Although our cohort specifically included patients with diverticulitis, a condition characterized by micro- or macro-perforation of the colon, our results are consistent with those of Fukushima et al. [17], despite differences in patient populations and surgical settings.

Table 4. Area under the curve analysis (N=66)

	Psoas muscle area	Bone mineral density	PMA × BMD
Postoperative complications	0.552	0.563	0.561
Major postoperative complications	0.667	0.941	0.549
Ileus	0.731	0.689	0.757
Pneumonia	0.609	0.696	0.645
Intraabdominal abscess	0.692	0.671	0.671
Anastomotic leak among patients who underwent anastomosis (n=28)	Non-amenable for calculation		
Reoperation	0.644	0.604	0.672
30-day readmission	0.552	0.634	0.565
30-day mortality	0.659	0.703	0.734
Ostomy closure	0.712	0.712	0.755

PMA × BMD = psoas muscle area × bone mineral density

Osteopenia and sarcopenia are interconnected through complex cellular signaling pathways. Key cytokines implicated in these processes include insulin-like growth factor-1, myostatin, interleukin-6, interleukin-7, and vascular endothelial growth factor [18]. Contributing factors to both conditions include physical inactivity, vitamin D and calcium deficiencies, corticosteroid use, aging, chronic inflammation, hormonal imbalances, low protein intake, fat infiltration, and co-morbidities. Potential treatment strategies encompass progressive resistance and balance exercises, adequate nutritional support (including sufficient intake of protein, vitamin D, calcium, and creatine), and pharmacological interventions for osteopenia (such as antiresorptives, anabolics, antisclerostin agents, and hormonal treatments) [19].

One possible explanation for the negative impact of osteosarcopenia on postoperative outcomes is the role of 1,25(OH)2D in monocyte and macrophage activity, which may contribute to an increased susceptibility to bacterial invasion [17].

The primary limitations of our study are the small and heterogeneous cohort, which restricted our ability to perform subgroup analyses due to limited statistical power and also limited the capability to generalize our results. To the best of our knowledge, this study is the first that uses plain product of PMA and BMD to quantify osteosarcopenia. It is still unclear whether this method is a reliable and efficient way for osteosarcopenia quantification. In addition, this study was not aimed at determining the causality between sarcopenia, osteopenia, and osteosarcopenia and postoperative complications.

Our findings may influence surgical decision making regarding the timing of elective colectomy for diverticulitis. Patients with low muscle mass and low bone mineral density may benefit from preoperative nutritional optimization and prehabilitation [20].

In urgent cases, recognizing low PMA and BMD as risk factors may lead surgeons to consider a more conservative approach, such as lavage and drainage instead of colectomy, or opting against primary anastomosis when colectomy is necessary.

CONCLUSIONS

Although demonstrated in a relatively small and heterogenous cohort, PMA and bone mineral density were shown to be associated with postoperative complications in patients undergoing colectomy for diverticulitis. Combining them may enhance the association. In general, evidence about the association between body composition and outcomes of surgery for diverticulitis are low-volume and un-univocal. Further data should be gathered and analyzed for further understanding of this association. Further studies should be held to discuss plain product of PMA and bone mineral density as a reliable quantification for osteosarcopenia.

Correspondence

Dr. Y. Zager
Division of General Surgery, Sheba Medical Center, Tel Hashomer 5265601, Israel
Email: yaniv039@gmail.com

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Capsule

A modifier of Huntington's disease onset

Huntington's disease (HD) is an inherited neurodegenerative disorder caused by a mutated form of the huntingtin (HTT) protein. The mutated protein is toxic and forms aggregates in neurons. **Croce** and co-authors performed a genome-wide association study in a community of genetically related individuals in Venezuela and identified an association between a mutation in the *WDFY3* gene and age at HD onset. In individuals with this mutation, disease onset was delayed by up to 23 years. Inducing the equivalent mutation in a mouse model of HD increased the breakdown of HTT aggregates and prevented disease symptoms. The work identifies a potential therapeutic target for HD and is also relevant to other diseases caused by protein aggregates.

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Eitan Israeli

Capsule

Inhibition of CXCL10 and IFN-γ ameliorates myocarditis in preclinical models of SARS-CoV-2 mRNA vaccination

The highly effective SARS-CoV-2 mRNA vaccines were essential for limiting the COVID-19 pandemic. In very rare cases, myocarditis has been reported, mostly in young males and usually after booster doses of the vaccines. **Cao** et al. used in vitro and mouse models to better understand the potential mechanism behind this myocarditis. C-X-C motif chemokine ligand 10 (CXCL10) and interferon-γ (IFN-γ) were identified as drivers of inflammation, and their neutralization reduced cardiac injury in a mouse model of two-dose vaccine exposure. Neutralization similarly reduced markers of cardiac injury in human induced pluripotent stem cell (iPSC)-derived cardiac spheroids. Genistein, a compound with evidence for a role in reducing cardiovascular inflammation, similarly reduced cardiac injury markers and inflammation in mice exposed to CXCL10 and IFN-γ or to vaccines. Together, these data reveal a potential mechanism for the rare cases of myocarditis observed after SARS-CoV-2 mRNA vaccination

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Eitan Israeli