

# Effects of Sarcopenia on Post-Operative Complications in Patients Undergoing Gastrectomy for Gastric Cancer: An Integrative Review

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## Abstract

The objective of this paper is to investigate the influence of sarcopenia on postoperative complications in patients undergoing gastrectomy for gastric cancer. PubMed, Cochrane, Science Direct and SciELO databases were used, with the search strategy: Sarcopenia and Stomach Neoplasms. The integrative review was structured with fifteen articles, published from 2015 to 2019. Data analysis was performed in a descriptive way. Twelve studies identified sarcopenia as a risk factor for postoperative complications in patients undergoing gastrectomy for gastric cancer. The reduction in skeletal muscle mass was associated with decreased intake or bioavailability of nutrients and metabolic changes, such as increased production of pro-inflammatory molecules resulting in weakening of the immune system and poor post-surgical healing. It was concluded that the presence of sarcopenia in these patients is related to a higher occurrence of postoperative complications.

## Keywords

Postoperative complications  
Gastrectomy  
Skeletal muscle  
Gastric neoplasms  
Sarcopenia

## 1. Introduction

Sarcopenia is a condition marked by a progressive and extensive decline in skeletal muscle mass and strength. It elevates the risk of falls and fractures whilst also reducing the capacity to engage in everyday tasks,

potentially causing disability and loss of independence, and resulting in a higher mortality rate. The impact of sarcopenia on postoperative morbidity may differ based on the type of complication observed<sup>[1,2]</sup>.

This condition can be classified as primary if it

relates solely to age, or secondary if one or more causes are present, such as inflammatory disease, malignancy, or malnutrition<sup>[3]</sup>. Sarcopenia is highly prevalent among cancer patients, with the rates ranging from 21% to 71% for both genders<sup>[4]</sup>.

Gastric cancer is the fourth most frequent neoplasm and the second primary reason for cancer-linked mortality globally. It is estimated that around one million new cases occur annually worldwide. Surgical resection is currently deemed the ultimate therapy for potentially treatable gastric cancer. Conversely, the procedure may entail numerous complications, including infection, leakage, hemorrhage, and dysfunction of organs. As a result, it can adversely affect the patient's post-operative recovery, leading to prolonged hospitalization, increased hospital expenses, and the squandering of medical resources<sup>[5]</sup>.

One way in which cancer can cause sarcopenia is through the generation of inflammatory cytokines by monocytes, leading to muscle atrophy, decreased walking speed, and reduced appetite<sup>[4,6]</sup>. Metabolic disruptions also contribute to the alterations in body composition. The liver diverts high levels of proteolysis and reduced muscle protein synthesis, leading to a decline in protein turnover and subsequent reduction of lean mass. Meanwhile, increased lipolysis results in significant mobilization of peripheral fat, thus depleting the adipose tissue reserves. There is an increase in gluconeogenesis from amino acids, and greater insulin resistance results in elevated circulating glucose levels, while reducing its accumulation in adipose tissue<sup>[7]</sup>.

These alterations ultimately lead to depletion of lean body mass and malnutrition. Symptoms including nausea, vomiting, loss of taste, fatigue, pain, early satiety, malabsorption, constipation, xerostomia, and dysphagia result from cancer treatment (surgery, chemotherapy, and radiotherapy) and are associated with negative impacts on body composition. These symptoms exacerbate sarcopenia and malnutrition, leading to reduced overall survival rates<sup>[4,8]</sup>.

In the post-operative period, a decrease in food

intake frequently occurs due to the stomach's reduced capacity, leading to a decline in body weight and quality of life in gastric cancer patients who have undergone resection. Consequently, developing sarcopenia may pose a higher risk in gastric cancer patients than in other cancer types<sup>[9]</sup>.

Tumor invasion heightens the vulnerability to malnutrition or cachexia, thereby elevating the chances of complications and mortality during the postoperative phase. Numerous risk factors, such as age, body mass index (BMI), preoperative serum albumin level, and comorbidities, have been suggested to prognosticate and formulate the therapeutic approach. Nevertheless, there is no universally accepted technique to precisely predict the clinical outcomes after gastrectomy<sup>[5]</sup>.

Therefore, given the significance of the impact of sarcopenia on the prognosis of cancer surgery, this study is warranted to establish the effect of sarcopenia on postoperative complications in patients who undergo gastrectomy for gastric cancer.

## **2. Materials and methods**

This study is an integrative literature review that follows the standards of rigor, clarity, and replication employed in primary studies<sup>[10,11]</sup>. The research was conducted using five closely linked stages:

- (1) Developing the guiding question: What effect does sarcopenia have on postsurgical complications in patients undergoing gastrectomy for gastric cancer?
- (2) Collecting data through a literature search
- (3) Critically analyzing data from the selected studies
- (4) Integrating the data and discussing results
- (5) Presenting the findings of the integrative review

The search strategy utilized the following descriptors from the Medical Subject Headings (MeSH) and Health Sciences Descriptors (DeCS): Sarcopenia and Stomach Neoplasms, which were combined using the Boolean operator "and." A systematic search

was conducted in the following databases: PubMed, Scientific Electronic Library Online (SciELO), Cochrane Library, and Science Direct.

The inclusion criteria were applied according to predefined guidelines: this study investigates the impact of sarcopenia on postoperative outcomes following gastrectomy for gastric cancer; the participants in the studies were adults and the elderly; articles and works published in Portuguese and English between 2009 and 2019, excluding theses, dissertations, literature reviews, notes, and editorials, as well as any duplicate articles. The results of this analysis are presented in **Figure 1**. Ultimately, 15 materials meeting our inclusion and exclusion criteria were analyzed descriptively to evaluate the relevant evidence.

### 3. Results

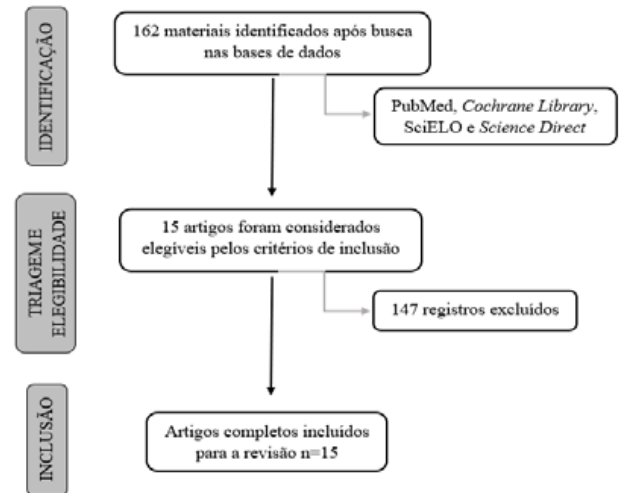
An initial assessment of the abstracts identified a total of 162 articles. However, 147 of them did not meet the time frame or the guiding question. As a result, 15 full-text articles were included in the integrative review. Publications between 2015 and 2019 were chosen, with the majority originating from China, followed by Japan. The majority of the studies were cohort studies, with sample sizes varying between 56 and 937 participants. Eleven studies were carried out with both adults and the elderly, whereas four were conducted exclusively with the elderly.

The instrument employed to extract the selected data was adjusted from the validated form by Ursi and Galvão<sup>[12]</sup> and included the following items: article title, year of publication, study method (including research type and sample size), primary outcomes, and conclusions.

A summary of the main aspects covered in each study and the corresponding outcomes can be seen in **Table 1**, which illustrates the inclusion of 15 articles.

### 4. Discussion

The term “gastric neoplasms” is commonly used in



**Figure 1.** Schematic representation of the record selection strategy

literature. Yamamoto *et al.*<sup>[13]</sup> reported that numerous studies have examined the correlation between sarcopenia and post-surgery outcomes among elderly patients who underwent gastrectomy. This integrative review identified 12 studies that identified sarcopenia as a risk factor for postoperative complications in patients with gastric cancer who underwent gastrectomy, emphasizing the significance of the investigation.

Yamamoto *et al.*<sup>[13]</sup> discovered that sarcopenia is a negative prognostic factor for overall survival following gastrectomy, as patients with sarcopenia are more susceptible to postoperative complications, which can result in prolonged inflammation, reduced tolerance to gastric cancer treatment, and diminished immunity. Sarcopenia is indicative of both poor nutritional status and physical disability, which leads to impaired postoperative recovery<sup>[14]</sup>.

Tamura *et al.*<sup>[15]</sup> found that sarcopenic patients do not have sufficient amino acids for the tissue repair needed during surgery such as gastrectomy, leading to delayed tissue healing and increased risk of infectious complications. Furthermore, Lutz and Quinn<sup>[24]</sup> noted that the decrease in skeletal muscle mass and increase in adipose tissue mass result in the increased production of pro-inflammatory molecules, which can weaken the immune system and negatively impact post-surgical healing.

**Table 1.** General characteristics and summary of relevant aspects of the articles included in the review

Author/Year	Article title	Methodological aspects		Results	Conclusions
		Research type	Sample/Location		
Yamamoto <i>et al.</i> , 2019 <sup>[13]</sup>	Sarcopenia is associated with impaired overall survival after gastrectomy for elderly gastric cancer	Retrospective cohort	90 elderly/Japan	Multivariate analysis indicated that sarcopenia was a risk factor independent for worse post-gastrectomy survival, together with disease stage, age $\geq 75$ years, and presence of severe postoperative complications	Sarcopenia is a risk factor independent for poor prognosis after gastrectomy in elderly patients with gastric cancer
Sierzega <i>et al.</i> , 2019 <sup>[14]</sup>	Prognostic and predictive implications of sarcopenia in Western patients undergoing gastric resections for carcinoma of the stomach	Retrospective cohort	138 adults and elderly/Poland	Sarcopenia has been associated with postoperative morbidity, important postoperative complications, and reoperations. Patients with sarcopenia also had prolonged postoperative period hospitalization	Sarcopenia is associated with an increased risk of postoperative morbidity and commitment of long-term survival
Tamura <i>et al.</i> , 2019 <sup>[15]</sup>	Adverse effects of preoperative sarcopenia on postoperative complications of patients with gastric cancer	Cohort	153 adults and elderly/Japan	Sarcopenia was significantly associated with age, body mass index, serum albumin, pulmonary disease due to comorbidities, operation time, surgical approach, and postoperative complications	Preoperative sarcopenia was considered a risk factor independent for infectious complications in the postoperative period in gastric cancer patients
Choi <i>et al.</i> , 2018 <sup>[16]</sup>	CT-quantified muscle and fat change in patients after surgery or endoscopic resection for early gastric cancer and its impact on long-term outcomes	Case control retrospective	6 adults and elderly/South Korea	The number of patients with sarcopenia has increased from 20 to 29 after surgery, and endoscopic resection group, decreased from 19 to 16. Overall survival was significantly correlated with sarcopenia after treatment	CT-based body composition analysis was useful to assess changes in fat areas and muscle after treatment of early gastric cancer
Zhang <i>et al.</i> , 2018 <sup>[17]</sup>	Computed tomography-quantified body composition predicts short-term outcomes after gastrectomy in gastric cancer	Prospective cohort	156 adults and elderly/China	The results showed that the overall rate of complications was significantly higher in the group with sarcopenia and in the group with myosteatosis. Patients with visceral obesity had a higher incidence of inflammatory complications	Sarcopenia, myosteatosis, and visceral obesity were significantly associated with increased postoperative complication rates and affected the nutritional and inflammatory status in the postoperative period of patients with gastric cancer
O'Brien <i>et al.</i> , 2018 <sup>[18]</sup>	Sarcopenia and post-operative morbidity and mortality in patients with gastric cancer	Retrospective cohort	56 adults and elderly/Ireland	There was a statistically significant difference between the two groups (sarcopenic and non-sarcopenic) in relation to severe postoperative complications, hospital mortality, and number of days in the ICU bed	There was a statistically significant difference between sarcopenia and decreased overall survival and severe postoperative complications, in patients undergoing gastrectomy
Kuwada <i>et al.</i> , 2018 <sup>[9]</sup>	Sarcopenia and comorbidity in gastric cancer surgery as a useful combined factor to predict eventual death from other causes	Retrospective cross-sectional	491 adults and elderly/Japan	Sarcopenic patients survived significantly worse overall. Sarcopenia is not a risk factor for complications in postoperative period, but it is an independent prognostic factor	For gastric cancer patients, sarcopenia increases the risk of death from other causes after surgery
Sakurai <i>et al.</i> , 2017 <sup>[19]</sup>	Adverse effects of low preoperative skeletal muscle mass in patients undergoing gastrectomy for gastric cancer	Retrospective cohort	569 adults and elderly/Japan	The mortality rate from stage I disease was significantly higher in the subgroup with low skeletal muscle index, and at all stages of gastric cancer, deaths related to recurrence were significantly more frequent in the group with low skeletal muscle index	The analysis showed no relationship between preoperative skeletal muscle index and post-operative complications
Huang <i>et al.</i> , 2017 <sup>[1]</sup>	Impact of different sarcopenia stages on the postoperative outcomes after radical gastrectomy for gastric cancer	Prospective cohort	470 adults and elderly/China	The incidence of pre-sarcopenia, sarcopenia, and severe sarcopenia was 20.6%, 10%, and 6.8%, respectively. The postoperative complications, duration of hospitalization, and hospital costs increased gradually with the advancement of stages of sarcopenia	Patients had worse post-operative outcomes with the advancement of sarcopenia stages. Severe sarcopenia was an independent risk factor for post-operative complications

**Table 1. (Continued)**

Author/Year	Article title	Methodological aspects		Results	Conclusions
		Research type	Sample/Location		
Zhou <i>et al.</i> , 2017 <sup>[20]</sup>	Sarcopenia: a new predictor of postoperative complications for elderly gastric cancer patients who underwent radical gastrectomy	Prospective cohort	240 elderly/China	Patients with sarcopenia were older; had lower BMI, albumin serum and hemoglobin; and higher scores of the Nutritional Risk Screening 2002. The postoperative complication rate was significantly higher in the sarcopenic group	Sarcopenia was a strong and independent risk factor for post-operative complications of patients with gastric cancer
Huang <i>et al.</i> , 2016 <sup>[21]</sup>	Sarcopenia predicts 1-year mortality in elderly patients undergoing curative gastrectomy for gastric cancer: a prospective study	Prospective cohort	173 elderly/China	Sarcopenia was an independent risk factor for 1-year mortality in the multivariate analysis and its effect did not depend on the postoperative complications. Furthermore, patients with sarcopenia had a higher tumor recurrence rate	Sarcopenia is predictive of mortality in 1 year in elderly patients undergoing gastric cancer surgery
Zhuang <i>et al.</i> , 2016 <sup>[3]</sup>	Sarcopenia is an independent predictor of severe postoperative complications and long-term survival after radical gastrectomy for gastric cancer	Retrospective cohort	937 adults and elderly/China	389 patients were sarcopenic. Sarcopenia was identified as an independent risk factor for serious complications	Sarcopenia, determined by abdominal CT, may be included in preoperative risk assessments of patients undergoing radical gastrectomy for cancer gastric
Wang <i>et al.</i> , 2015 <sup>[5]</sup>	Sarcopenia adversely impacts postoperative clinical outcomes following gastrectomy in patients with gastric cancer: a prospective study	Prospective cohort	255 adults and elderly/China	32 patients had sarcopenia. These presented a higher risk of postoperative complications, longer postoperative hospitalization, and more hospital costs	Sarcopenia is an independent predictor of postoperative complications in patients with gastric cancer after gastrectomy
Fukuda <i>et al.</i> , 2015 <sup>[22]</sup>	Sarcopenia is associated with severe postoperative complications in elderly gastric cancer patients undergoing gastrectomy	Retrospective cohort	99 elderly/Japan	BMI and lean body mass were smaller in the sarcopenic group, the loss of weight and the presence of serious complications were more frequently observed in sarcopenic group	Preoperative sarcopenia is a risk factor for severe post-operative complications in elderly patients with gastric cancer undergoing gastrectomy
Tegels <i>et al.</i> , 2015 <sup>[23]</sup>	Sarcopenia is highly prevalent in patients undergoing surgery for gastric cancer but not associated with worse outcomes	Retrospective cross-sectional	152 adults and elderly/Netherlands	86 of the patients were classified as sarcopenic. Sarcopenia was not a predictor of hospital mortality, severe complications, or mortality within 6 months	The prevalence of sarcopenia was high compared to other abdominal surgical oncology populations, however sarcopenia was not associated with post-operative morbidity and mortality

Abbreviations: CT, computed tomography; ICU, intensive care unit; BMI, body mass index

Research conducted by Choi *et al.*<sup>[16]</sup>, Zhang *et al.*<sup>[17]</sup>, and Sakurai *et al.*<sup>[19]</sup> revealed that the reduction in the intake or availability of nutrients and metabolic changes resulting from gastrectomy lead to a significant decline in fat and muscle areas.

Additionally, Zhou *et al.*<sup>[20]</sup> suggested that sarcopenia may heighten the risk of respiratory complications due to reduced cellular immune function, coupled with increased inflammatory activity, and impaired swallowing muscle function. Huang *et al.*<sup>[21]</sup> proposed that tumors with aggressive biological traits have raised

metabolic activity. This may cause intensified systemic inflammation, ultimately resulting in more severe muscle loss.

Huang *et al.*<sup>[1]</sup> emphasized the significance of categorizing sarcopenia to achieve improved risk stratification of postoperative complications. They also suggested that muscle function and physical performance should be evaluated prior to surgery and that these assessments should be included in regular surgical practice due to their simplicity and affordability. Furthermore, it was demonstrated that

tumors situated in the cardia presented an elevated nutritional risk as a result of the obstructed food intake caused by stenosis.

Early diagnosis and treatment of sarcopenia is crucial in this context. Various strategies must be employed to maintain muscle mass and improve post-operative outcomes [18,5].

Pharmacological agents have limited effectiveness in maintaining or increasing skeletal muscle mass or function. Thus, interventions, like exercise and nutritional support in the perioperative period, are fundamental to preventing or improving sarcopenia [9,2].

Among the possible complications that indicate the negative impact of sarcopenia in the postoperative period are: elevated postoperative inflammatory response, impaired innate and adaptive immunity, reduced tolerance to cancer treatment and other invasive procedures, and the discontinuation or reduction of chemotherapy [13,20]. Furthermore, frailty, low muscle quality, associated comorbidities, and decreased functional reserve are also factors that affect surgical outcomes [20]. It is worth noting that certain postoperative complications can lead to fatal outcomes, including intra-abdominal hemorrhage, heart failure, pneumonia after surgery, and subsequent sepsis [21]. Consequently, the results of this review support the notion that surgery is inherently an aggressive and inflammatory procedure, and its combination with gastric cancer and sarcopenia results in a higher incidence of negative prognosis.

To reduce the negative effects of sarcopenia during the postoperative period, it is advisable to perform a preoperative evaluation [21] to recognize high-risk cases in advance. Furthermore, a multi-professional follow-up should take place over a prolonged period. It is also

important to incorporate resistance training as it helps in the maintenance of functional muscle mass, along with regular physical activity and adequate dietary support. Nutritional supplementation including leucine and omega-3 polyunsaturated fatty acids must be prescribed by a specialist nutritionist [20].

There was a necessity to standardize the diagnostic criteria for sarcopenia, as some studies utilized only the muscle mass criterion, thereby neglecting the importance of function. Furthermore, adopting similar cut-off points for both the elderly and adults is not advisable as it can compromise the diagnosis, given the diverse body compositions of these populations. Lastly, it is crucial to establish and assess specific protocols for nutritional care in sarcopenic patients with gastric cancer.

## 5. Conclusion

Based on the data collected from this integrative review, it can be inferred that the presence of sarcopenia in patients undergoing gastrectomy for gastric cancer is associated with an increased incidence of complications in the postoperative period. Consequently, to achieve improved clinical outcomes, assessing sarcopenia in preoperative risk evaluations is essential.

Sarcopenia has been underdiagnosed in routine clinical practice, reflecting the lack of appropriate tests and assessment criteria. It has been verified that identifying sarcopenia should take into account not only the skeletal muscle mass, but also the muscle strength and physical performance. Therefore, it is important to conduct studies that analyze intervention strategies and therapeutic measures for sarcopenia in order to promote better post-operative outcomes.

### Disclosure statement

The authors declare no conflict of interest.



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