

# Prognostic Significance of Sarcopenia in Colorectal Cancer: A Review of Clinical Evidence

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**Background:** Colorectal cancer (CRC) is one of the most common and deadly malignancies worldwide. Sarcopenia, defined as a progressive loss of skeletal muscle mass and function, has recently been recognized as an important prognostic factor in CRC, influencing both postoperative complications and long-term survival.

**Methods:** We conducted a descriptive review of 18 clinical studies investigating the association between sarcopenia and CRC across stages I–IV. Sarcopenia was primarily assessed using computed tomography-derived skeletal muscle index (SMI) or psoas index (PI) at the lumbar vertebrae (L3/L4), with some studies additionally incorporating muscle strength and performance.

**Results:** The prevalence of sarcopenia among CRC patients ranged from 12% to 60%. Most studies reported higher risks of postoperative complications in sarcopenic patients. For instance, Peng et al demonstrated an increased risk of complications in stage IV CRC patients with sarcopenia (OR: 3.12, 95% CI: 1.14–8.49). Regarding survival, sarcopenia was consistently associated with worse overall survival (OS), disease-free survival (DFS), and recurrence-free survival (RFS). Brown et al (2018) showed that deterioration in muscle mass and radiodensity significantly predicted poorer OS in 1,924 stage I–III CRC patients (HR: 2.15, 95% CI: 1.59–2.92). However, several studies reported no significant associations.

**Conclusion:** Sarcopenia is prevalent in CRC patients and strongly correlates with both short-term surgical outcomes and long-term prognosis. However, current evidence is mainly derived from heterogeneous observational studies, and further prospective studies are needed before sarcopenia assessment can be translated into routine clinical practice.

**Keywords:** colorectal cancer, sarcopenia, skeletal muscle index, prognosis, postoperative complications, survival

## Introduction

Colorectal cancer (CRC) is one of the most common malignancies worldwide, ranking third in global cancer incidence and second in cancer-related mortality.<sup>1</sup> In 2020, nearly 2 million new CRC cases and approximately 1 million CRC-related deaths were reported globally, accounting for 10.7% of all newly diagnosed cancers and 9.5% of all cancer deaths.<sup>2</sup> The prognosis of CRC patients is primarily determined by tumor stage and the feasibility of curative surgery. However, progressive loss of skeletal muscle mass has also been shown to strongly correlate with increased risk of postoperative complications and mortality.<sup>3,4</sup> Sarcopenia, together with cancer-associated cachexia, represents the two major etiologies of muscle loss in patients with malignancies, including CRC.<sup>5,6</sup>

The concept of sarcopenia was first introduced by Rosenberg in 1989, initially referring to age-related decline in muscle mass.<sup>7</sup> The term itself derives from Greek, in which sarx means “flesh” and penia denotes “loss.” Accumulating evidence suggests that sarcopenia may contribute to higher rates of perioperative complications, enhanced susceptibility to chemotherapy- and radiotherapy-related toxicities, and unfavorable survival outcomes among CRC patients.<sup>8–10</sup>

Despite the growing body of literature on sarcopenia in colorectal cancer, including several systematic reviews and meta-analyses,<sup>11,12</sup> substantial heterogeneity remains across published studies. In particular, variability has been reported in diagnostic cut-off values, CT-based assessment approaches, and in the prognostic effects observed across different tumor stages and clinical endpoints.<sup>3,4,12–14</sup> As a result, the interpretation and clinical relevance of sarcopenia in CRC remain incompletely clarified.

Therefore, rather than providing another quantitative synthesis, the aim of this review is to offer a descriptive overview of the existing clinical evidence and to discuss potential sources of heterogeneity reported in the literature. We sought to summarize the associations between sarcopenia and postoperative outcomes as well as long-term survival in CRC, while highlighting areas where current evidence appears inconsistent or limited.

## Definition and Diagnostic Criteria of Sarcopenia

Since its introduction by Rosenberg, sarcopenia has progressively evolved to be defined as an age-related decline in skeletal muscle mass accompanied by a reduction in muscle strength.<sup>15</sup> The first operational consensus was proposed by the European Working Group on Sarcopenia in Older People (EWGSOP) in 2010. This consensus emphasized that sarcopenia should be diagnosed based on the coexistence of low muscle mass and low muscle function (strength or performance), and it provided a diagnostic algorithm centered on gait speed, handgrip strength, and muscle mass assessment.<sup>16</sup> In 2018, the group reconvened (EWGSOP2) and revised the definition by placing low muscle strength at the core of sarcopenia diagnosis. According to this updated framework, reduced muscle strength alone is sufficient to indicate “probable sarcopenia.” Confirmation requires evidence of low muscle quantity or quality, while the presence of both these features plus impaired physical performance establishes a diagnosis of severe sarcopenia.<sup>17</sup>

The etiology of sarcopenia is multifactorial. Based on underlying causes, sarcopenia can be broadly categorized into two types: primary sarcopenia, which is predominantly age-related and occurs in the absence of other apparent causes; and secondary sarcopenia, which results from other conditions such as physical inactivity, malignancy, organ failure, chronic inflammatory diseases, or malnutrition.<sup>14,16</sup>

These consensus definitions provide important context for understanding sarcopenia; however, in clinical oncology practice, sarcopenia is most commonly assessed using imaging-based measures.

## Methods

A literature search was performed using PubMed to identify relevant studies published up to December 2024. The search terms included combinations of “colorectal cancer”, “colon cancer”, “rectal cancer”, and “sarcopenia.” Reference lists of relevant reviews and original articles were also screened to identify additional eligible studies.

Studies were considered for inclusion if they met the following criteria: (1) involved adult patients diagnosed with colorectal cancer; (2) evaluated sarcopenia using imaging-based measures, most commonly computed tomography-derived skeletal muscle indices; and (3) reported clinical outcomes, including postoperative complications and/or survival outcomes such as overall survival, disease-free survival, or recurrence-free survival. Reviews, conference abstracts, case reports, and studies lacking relevant outcome data were excluded.

A total of 18 studies met these criteria and were included in the present review.<sup>8,9,13,18–32</sup> Given the heterogeneity in study design, sarcopenia definitions, and outcome measures, no formal meta-analysis was performed, and the findings were synthesized descriptively.

## Results

To investigate the current progress in sarcopenia research within CRC, we conducted a descriptive review of 18 published studies examining the relationship between sarcopenia and CRC (Table 1). We found that the majority of CRC patients with concurrent sarcopenia were elderly individuals. In most studies, sarcopenia was diagnosed based on the skeletal muscle index (SMI) at the level of the third or fourth lumbar vertebra, whereas a minority of studies employed the psoas muscle index at the same anatomical level for diagnosis.

Based on an analysis of 15 previously published studies (Table 2), we observed substantial variability in the reported prevalence of sarcopenia among patients with CRC. For instance, in a 2015 study by Huang et al, 142 resectable CRC patients were evaluated, and the prevalence of sarcopenia was reported to be only 12%. In contrast, Broughman et al (2020) investigated 87 patients with stage I–III CRC and reported a markedly higher prevalence of 57.4%. Taken together, these findings suggest that the prevalence of sarcopenia in CRC patients varies widely across studies, ranging from approximately 12% to 60%.

**Table 1** Basic Information of the Included Studies

Author	Time	Sample	Age (Years)	Tumor Staging	Diagnostic Criteria for Sarcopenia
Peng <sup>18</sup>	2011	259	Median: 58	IV	L3 PI
Lieffers <sup>19</sup>	2012	234	Mean: 63	II–IV	L3 SMI
Van Vledder <sup>20</sup>	2012	196	Median: 64.5	IV	L3 SMI
Sabel <sup>19</sup>	2013	302	Mean: 67.9	I–IV	L4 PI
Huang <sup>22</sup>	2015	142	≥75 (15%)	Resectable CRC	L3 SMI
Miyamoto <sup>23</sup>	2015	220	Mean: 70	I–III	L3 SMI
Jung <sup>9</sup>	2015	229	Median: 61	III	L4 PI
Reisinger <sup>8</sup>	2015	310	>70 (51.3%)	CRC after surgery	L3 SMI
Broughman <sup>24</sup>	2015	87	Median: 77	I–III	L3 SMI
Dolan <sup>25</sup>	2018	650	>65 (64%)	I–III	L3 SMI
Sueda <sup>26</sup>	2018	211	Mean: 65	I–III	L3 SMI
Brown <sup>27</sup>	2018	1924	Mean: 61.1	I–III	L3 SMI
Ojima <sup>28</sup>	2019	142	Median: 80.5	I–III	L3 PI
Hopkins <sup>29</sup>	2019	968	Mean: 65.8	I–III	L3 SMI
Oh <sup>13</sup>	2020	423	≥65 (59.6%)	I–III	L3 SMI
Shirdel <sup>30</sup>	2020	974	Mean: 67.7	I–IV	L3 SMI
Olmez <sup>31</sup>	2020	209	Mean: 61.2	CRC after surgery	L3 SMI
Argillander <sup>32</sup>	2021	233	Mean: 75.7	I–III	L3 SMI

**Abbreviations:** L3 SMI: Third lumbar skeletal muscle index; L3 PI: Third lumbar psoas index; L4 PI: Fourth lumbar psoas index.

**Table 2** Prevalence of Sarcopenia in Patients with CRC

Author	Sample	Age (Years)	Tumor Staging	Incidence Rate
Peng <sup>18</sup>	259	Median: 58	IV	17.0%
Lieffers <sup>19</sup>	234	Mean: 63	II–IV	38.9%
Van Vledder <sup>20</sup>	196	Median: 64.5	IV	19.4%
Huang <sup>22</sup>	142	≥75 (15%)	Resectable CRC	12.0%
Jung <sup>9</sup>	229	Median: 61	III	25.3%
Reisinger <sup>8</sup>	310	>70 (51.3%)	CRC after surgery	47.7%
Broughman <sup>24</sup>	87	Median: 77	I–III	57.4%
Dolan <sup>25</sup>	650	>65 (64%)	I–III	43.5%
Sueda <sup>26</sup>	211	Mean: 65	I–III	49.8%
Ojima <sup>28</sup>	142	Median: 80.5	I–III	24.6%
Hopkins <sup>29</sup>	968	Mean: 65.8	I–III	27.5%
Oh <sup>13</sup>	423	≥65 (59.6%)	I–III	12.8%
Shirdel <sup>30</sup>	974	Mean: 67.7	I–IV	32.0%
Olmez <sup>31</sup>	209	Mean: 61.2	CRC after surgery	46.4%
Argillander <sup>32</sup>	233	Mean: 75.7	I–III	14.6%

Subsequently, our focus shifted to the impact of sarcopenia on postoperative complications in CRC. A total of eight studies were included in this analysis (Table 3). The majority of these reports consistently demonstrated that CRC patients with sarcopenia had a higher likelihood of developing postoperative complications. For example, Peng et al investigated 259 patients with stage IV CRC and found that those with sarcopenia exhibited significantly higher rates of overall postoperative complications and infections compared with their non-sarcopenic counterparts. Similarly, a meta-analysis conducted by Levolger et al<sup>33</sup> identified sarcopenia as an independent risk factor for both postoperative complications and postoperative mortality in CRC patients. Another meta-analysis by Su et al<sup>11</sup> confirmed that preoperative sarcopenia was associated with an increased risk of overall postoperative morbidity.

However, a minority of studies reported conflicting results. For instance, Olmez et al observed no significant difference in postoperative infection rates between CRC patients with and without sarcopenia. Likewise, Argillander et al reported no

**Table 3** Impact of Sarcopenia on Postoperative Complications in Patients with CRC

Author	Sample	Age (Years)	Tumor Staging	Postoperative Complication
Peng <sup>18</sup>	259	Median: 58	IV	Overall: OR: 3.12 (95% CI: 1.14–8.49) Infection: 23.1% vs 12.6%, p = 0.036 Length of stay: 15.9 days vs 12.3 days, p = 0.038
Lieffers <sup>19</sup>	234	Mean: 63	II–IV	
Sabel <sup>21</sup>	302	Mean: 67.9	I–IV	Psoas muscle density: Overall: OR: 0.96 (95% CI: 0.94–0.99) Infection: OR: 0.95 (95% CI: 0.93–0.98)
Huang <sup>22</sup>	142	≥75 (15%)	Resectable CRC	Overall: 59% vs 24% (p = 0.007)
Reisinger <sup>8</sup>	310	>70 (51.3%)	CRC after surgery	Death occurred within 30 days of surgery: OR: 43.30 (95% CI: 2.74–685.2)
Oh <sup>13</sup>	423	≥65 (59.6%)	I–III	Overall: 27.8% vs 12.5% (p = 0.006)
Olmez <sup>31</sup>	209	Mean: 61.2	CRC after surgery	Infection: 20.6% vs 23.2%, p = 0.65
Argillander <sup>32</sup>	233	Mean: 75.7	I–III	Overall: 56% vs 45% (p = 0.23) Admitted to ICU: 27% vs 14% (p = 0.07) Length of stay: 10 days vs 7 days (p = 0.13)

**Table 4** Impact of Sarcopenia on Overall Survival in Patients with CRC

Author	Sample	Age (Years)	Tumor Staging	Overall Survival (OS)
Peng <sup>18</sup>	259	Median: 58	IV	30 months vs 46 months (p = 0.05)
Van Vledder <sup>20</sup>	196	Median: 64.5	IV	23.8 months vs 59.8 months (p = 0.001)
Sabel <sup>21</sup>	302	Mean: 67.9	I–IV	HR: 1.01 (95% CI: 1.00–1.03)
Miyamoto <sup>23</sup>	220	Mean: 70	I–III	HR: 2.27 (95% CI: 1.147–4.494)
Jung <sup>9</sup>	229	Median: 61	III	HR: 1.85 (95% CI: 1.10–3.13)
Dolan <sup>25</sup>	650	>65 (64%)	I–III	HR: 1.50 (95% CI: 1.04–2.18)
Sueda <sup>26</sup>	211	Mean: 65	I–III	HR: 2.94 (95% CI: 1.32–7.17)
Brown <sup>27</sup>	1924	Mean: 61.1	I–III	HR: 2.15 (95% CI: 1.59–2.92)
Ojima <sup>28</sup>	142	Median: 80.5	I–III	Five-year OS: 61% vs 87% (p = 0.0007)
Hopkins <sup>29</sup>	968	Mean: 65.8	I–III	HR: 1.45 (95% CI: 1.15–1.84)
Oh <sup>13</sup>	423	≥65 (59.6%)	I–III	HR: 1.38 (95% CI: 0.79–2.41)
Shirdeh <sup>30</sup>	974	Mean: 67.7	I–IV	HR: 1.77 (95% CI: 1.33–2.36)
Argillander <sup>32</sup>	233	Mean: 75.7	I–III	HR: 3.8 (95% CI: 1.4–10.0)

significant differences in overall postoperative complication rates or length of hospital stay between sarcopenic and non-sarcopenic CRC patients.

To further explore the impact of sarcopenia on the prognosis of CRC, we analyzed 13 studies that reported overall survival (OS) outcomes in CRC patients (Table 4). The majority of these studies demonstrated that CRC patients with sarcopenia had shorter OS compared with those without sarcopenia. For example, a meta-analysis conducted by Leveloger et al<sup>33</sup> identified sarcopenia as an independent risk factor for reduced OS in CRC patients. Similarly, Su et al<sup>11</sup> also reported that preoperative sarcopenia was associated with inferior OS in CRC.

Nevertheless, conflicting evidence exists. For instance, a study by Oh et al showed no significant difference in OS between CRC patients with and without sarcopenia.

In addition, we reviewed four studies that reported disease-free survival (DFS) outcomes in patients with CRC (Table 5). Most of these studies indicated that CRC patients with sarcopenia had shorter DFS compared with those without sarcopenia. A meta-analysis by Su et al<sup>11</sup> further confirmed that preoperative sarcopenia was a significant risk factor for reduced DFS in CRC patients. However, consistent with the findings for overall survival, Oh et al reported contradictory results, showing no significant difference in DFS between CRC patients with and without sarcopenia.

We further summarized three studies that reported recurrence-free survival (RFS) outcomes in patients with CRC (Table 6). These studies consistently demonstrated that CRC patients with sarcopenia had shorter RFS compared with those without sarcopenia.

**Table 5** Impact of Sarcopenia on Disease-Free Survival in Patients with CRC

Author	Sample	Age (Years)	Tumor Staging	Disease-Free Survival (DFS)
Van Vledder <sup>20</sup>	196	Median: 64.5	IV	8.7 months vs 15.1 months ( $p = 0.002$ )
Sabel <sup>21</sup>	302	Mean: 67.9	I–IV	HR: 1.01 (95% CI: 1.00–1.03)
Sueda <sup>26</sup>	211	Mean: 65	I–III	HR: 2.87 (95% CI: 1.48–5.87)
Oh <sup>13</sup>	423	≥65 (59.6%)	I–III	HR: 1.55 (95% CI: 0.70–3.48)

**Table 6** Impact of Sarcopenia on Recurrence-Free Survival in Patients with CRC

Author	Sample	Age (Years)	Tumor Staging	Recurrence-Free Survival (RFS)
Miyamoto <sup>23</sup>	220	Mean: 70	I–III	HR: 2.176 (95% CI: 1.200–3.943)
Ojima <sup>28</sup>	142	Median: 80.5	I–III	5-year RFS: 51% vs 78% ( $p = 0.0014$ )
Hopkins <sup>29</sup>	968	Mean: 65.8	I–III	HR: 1.36 (95% CI: 1.05–1.78)

## Discussion

This review summarizes the existing clinical evidence regarding the prognostic significance of sarcopenia in patients with colorectal cancer. Across the majority of included studies, sarcopenia was associated with increased postoperative complications and poorer long-term outcomes, including overall survival, disease-free survival, and recurrence-free survival.<sup>3,11,14,27</sup> These findings suggest that reduced skeletal muscle mass and quality may reflect a vulnerable physiological state that adversely affects both short-term recovery and long-term oncologic outcomes in CRC.<sup>4,25</sup>

Several biological and clinical mechanisms may underlie the observed associations between sarcopenia and adverse outcomes. Sarcopenia often reflects impaired nutritional reserve, chronic systemic inflammation, and reduced physical resilience, which may limit tolerance to major surgery and systemic anticancer therapies.<sup>34–36</sup> In addition, sarcopenic patients may be more susceptible to postoperative infections, delayed recovery, and treatment-related toxicity, thereby contributing to inferior survival outcomes.<sup>9,19</sup>

Importantly, the strength and consistency of the reported associations varied across studies. While many investigations demonstrated a clear relationship between sarcopenia and adverse outcomes,<sup>8,9,18–23,25–30</sup> several studies reported no significant associations.<sup>13,31,32</sup> This heterogeneity may be attributable to differences in study populations, tumor stages, clinical endpoints, and CT-based assessment approaches. Variability in the CT diagnostic cut-off values of sarcopenia may further limit the comparability of results across studies. For instance, Olmez et al<sup>31</sup> defined sarcopenia as an L3 SMI of  $<545 \text{ mm}^2/\text{m}^2$  for men and  $<385 \text{ mm}^2/\text{m}^2$  for women. In contrast, Oh et al<sup>13</sup> defined it as an L3 SMI of  $<41 \text{ cm}^2/\text{m}^2$  for women and  $<43 \text{ cm}^2/\text{m}^2$  for men with a body mass index (BMI) of  $<25 \text{ kg}/\text{m}^2$ , and  $<53 \text{ cm}^2/\text{m}^2$  for men with a BMI of  $\geq 25 \text{ kg}/\text{m}^2$ .

Differences in tumor stage and treatment context may also contribute to inconsistent findings. In earlier-stage disease, sarcopenia may primarily reflect baseline frailty and physiological reserve, whereas in advanced or metastatic CRC, muscle loss may be more strongly influenced by tumor burden and systemic disease.<sup>18,20,30</sup> Furthermore, postoperative outcomes and long-term survival represent distinct clinical endpoints that may be differentially influenced by sarcopenia. With respect to short-term postoperative outcomes, sarcopenia may reflect limited physiological and nutritional reserve, which can impair tolerance to surgical stress and delay recovery. Reduced skeletal muscle mass has been associated with a higher risk of postoperative complications, including infectious events and prolonged hospitalization, suggesting that muscle depletion may compromise perioperative resilience.<sup>11</sup> In contrast, the impact of sarcopenia on long-term survival outcomes may be mediated through different mechanisms. Low muscle mass and adverse body composition profiles have been linked to systemic inflammatory responses and metabolic vulnerability, which are known to adversely affect oncologic outcomes and overall survival.<sup>25</sup> In addition, sarcopenic patients may experience reduced tolerance to systemic anticancer therapies, leading to increased treatment-related toxicity, dose reductions, or early discontinuation of therapy. Such treatment limitations could, in turn, contribute to inferior disease control and survival outcomes.<sup>9</sup> Taken together, these observations suggest that the associations between sarcopenia and adverse outcomes in colorectal cancer may arise

through partially distinct pathways depending on the clinical endpoint considered, which could help explain discrepancies among studies evaluating postoperative complications versus long-term survival.

Several limitations of this review should be acknowledged. As a narrative review, no formal systematic search strategy or meta-analysis was performed, and the selection of included studies may be subject to selection bias. In addition, substantial heterogeneity in sarcopenia assessment methods and study design limits direct comparison across studies. Therefore, the findings of this review should be interpreted with caution. Future research should focus on standardized diagnostic criteria and prospective studies to clarify the clinical utility of sarcopenia assessment in colorectal cancer.

## Conclusions

Sarcopenia is a common condition among patients with colorectal cancer and has been frequently associated with adverse postoperative outcomes and poorer long-term prognosis, including overall survival, disease-free survival, and recurrence-free survival. The available evidence suggests that reduced skeletal muscle mass and quality may reflect diminished physiological reserve and increased vulnerability in CRC patients. However, the existing literature is predominantly based on heterogeneous observational studies, with substantial variability in sarcopenia assessment methods, diagnostic cut-off values, patient populations, tumor stages, and clinical endpoints. As a result, the prognostic impact of sarcopenia in CRC cannot be interpreted uniformly across all clinical contexts. Therefore, while sarcopenia assessment may offer useful prognostic information and contribute to risk stratification in colorectal cancer, its routine application in clinical practice requires caution. Future studies employing standardized diagnostic criteria and well-designed prospective designs are needed to clarify the clinical utility of sarcopenia assessment and to determine whether targeted interventions can improve outcomes in patients with CRC.

## Data Sharing Statement

Data sharing is not applicable to this article as no new data were created or analyzed.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

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