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Association between postoperative muscle wasting and survival in older patients undergoing surgery for non-metastatic colorectal cancer☆

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ABSTRACT

Background: Preoperative sarcopenia in older patients is a risk factor for adverse outcomes after colorectal cancer (CRC) surgery. Longitudinal changes in muscle mass in this group have not been studied previously although muscle wasting may have prognostic significance regarding survival. We aimed to determine the association between muscle wasting and overall survival (OS) in older patients who underwent surgery for CRC.
Methods: Patients ≥70 years who underwent surgery for non-metastatic CRC in Gelre hospitals, The Netherlands, between 2011 and 2015 were included. Cross-sectional area of skeletal muscle was measured at the level of the 3rd lumbar vertebra on preoperative and postoperative abdominal CT-scans. Patients who had >1 standard deviation decrease in muscle mass were considered to have muscle wasting. Cox regression analysis was used to evaluate associations between muscle wasting and OS.
Results: 233 patients were included (40% female, median age 76 years). Thirty-four patients had muscle wasting. After a median follow-up of 4.7 years, 53 (23%) patients died. The 3-year mortality rate was higher in patients with muscle wasting (27% vs 14%, $p = .05$). In multivariable analysis adjusted for age, recurrent disease and preoperative muscle mass, muscle wasting was associated with reduced OS (HR 2.8, 95% CI 1.5–5.4, $p = .002$).
Conclusion: Muscle wasting predicted poorer survival in older patients who underwent CRC surgery. Measuring changes in muscle mass may improve risk prediction in this patient group. Future studies should address the etiology of muscle wasting in older patients with CRC. Whether perioperative exercise interventions can prevent muscle wasting also warrants further study.

1. Introduction

An increasing number of older patients are undergoing surgery for colorectal cancer (CRC). While fast track surgery and minimally invasive techniques have been shown to reduce morbidity rates in older adults [1], many still experience life-threatening complications and decline in physical functioning. This physical decline can lead to loss of independence and even mortality [2].

Although physical functioning is a sum of many factors, skeletal muscle plays a pivotal role in the road to recovery. Readiness for discharge is determined by the patient's ability to care for themselves, which requires adequate muscle mass and strength. Amino acids derived from muscle tissue are used to repair surgery-induced trauma and to prevent infection [3,4]. Accordingly, insufficient muscle mass is associated with increased postoperative morbidity and mortality [5–7]. In the months and years following surgery, older patients are at risk for declining muscle mass due to age-related changes in muscle homeostasis, physical inactivity and nutritional deficiencies, and undergoing cancer treatment may further exacerbate this process [8]. Furthermore, it is becoming increasingly clear that skeletal muscle depletion outperforms traditional markers of body composition such as body mass index (BMI) or weight loss when it comes to predicting mortality in patients with cancer [9,10]. Loss of skeletal muscle can occur simultaneously with increase in adipose tissue and occult muscle depletion may go unnoticed [11].

Muscle mass is readily visualized on abdominal computed tomography (CT)-scans, and the cross-sectional area of abdominal muscles when measured on a CT-scan correlates well with total body muscle

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mass [12]. As patients with CRC often undergo diagnostic and surveillance CT-scans, it provides an opportunity to measure changes in muscle mass. If detected during follow-up, muscle wasting could serve as a red flag for physicians to initiate further work-up and appropriate interventions. Furthermore, changes in muscle mass could possibly be employed as a surrogate endpoint to study the effects interventions aimed at preventing physical decline.

Two studies have reported poorer survival outcomes in CRC patients with postoperative muscle wasting [13,14]. As both studies predominantly included patients under 70 years of age, postoperative changes in muscle mass have not been previously characterized exclusively in the older patient group. Even though older age is associated with progressive muscle loss [15], it is unclear whether muscle wasting can also be used as a prognostic marker for adverse long-term outcomes in this patient population. Therefore, the aim of this study was to determine whether postoperative muscle wasting is prognostic for survival in an older population of patients undergoing surgery for CRC.

2. Methods

2.1. Study population and design

For this retrospective cohort study, all patients who underwent surgical resection for primary CRC between 2011 and 2015 in Gelre Hospitals, Apeldoorn and Zutphen, The Netherlands were identified from the institutional database. Patients were eligible for inclusion if they were ≥ 70 years, had no evidence of metastatic disease at the time of surgery, survived for at least 6 months postoperatively and if muscle mass measurements were feasible on both preoperative scans and postoperative scans within 6–18 months after surgery. Informed consent was waived, and the study was approved by the local institutional review board of Gelre hospitals (2018_13). The study conforms to the principles of the Declaration of Helsinki.

2.2. Muscle mass measurements on CT-scans

For each patient, single axial images at the level of the 3rd lumbar vertebra (L3) were extracted from preoperative and postoperative CT-scans, resulting in two CT images per patient. Preoperatively, the scan closest to surgery was selected. Postoperatively, the scan closest to 12 months after surgery was selected. All CT images were extracted by one researcher (TA) who was trained by a radiologist (AvR) to identify the L3 region. Pre- and postoperative CT images of each patient were extracted side-to-side to ensure extraction at comparable levels (Fig. 1a-b).

Muscle mass was measured with *ImageJ* software as described by Gomez-Perez et al. [16,17] On each CT image, the cross-sectional area of skeletal muscles visible at the L3 level was delineated using the free-hand selection tool (Fig. 1c). Next, to allow for differentiation of skeletal muscle from other tissues such as intra-abdominal fat, Hounsfield unit (HU) thresholds were adjusted to −29 to +150 HU. The resulting cross-sectional area of the skeletal muscle (cm^2) was divided by the square of the patient's height (m^2) to obtain the skeletal muscle index (SMI). For assessment of inter-rater reliability, 10% of the measurements were performed by two independent researchers (TA and DS). The remaining measurements were performed by one researcher (TA). Both researchers were blinded to study outcomes at the time of the measurements.

2.3. Outcomes

The primary outcome of the study was OS, which was defined as the time interval between the date of surgery and the date of death. Patients were right-censored if they were alive five years after surgery or on study end date January 31, 2019, whichever occurred first. Information on survival was collected from hospital records with linkage to the Dutch municipal personal records database. The cause of death was determined from the electronic patient records.

2.4. Other variables in the study

The following patient information was retrieved from the medical records: age, sex, height, weight and BMI, Charlson Comorbidity Index (CCI) [18], American Society of Anesthesiologists (ASA) score, and preoperative anemia (hemoglobin <8.5 mmol/l for males, and < 7.5 mmol/l for females). Sarcopenia was present if the preoperative SMI was <38.5 cm^2/m^2 for females and < 52.4 cm^2/m^2 for males, as suggested by Prado et al. [19] Information was retrieved on urgency of surgery, type of surgery (laparoscopic/open (including conversions)), segment of resection, tumor stage (according to the 7th edition of the American Joint Committee on Cancer (AJCC) Tumor-Node-Metastasis (TNM) classification [20]), and administration of neoadjuvant or adjuvant therapies. Postoperative complications were classified using the Clavien-Dindo classification (CDC) [21], and the overall complication burden was assessed with the Comprehensive Complication Index [22]. Recurrent disease was present if evidence of metastases or local recurrence was present on the postoperative CT-scan.

2.5. Statistical analysis

Categorical variables were reported with number and percentage. Continuous variables were reported with mean (standard deviation (SD)) or median (interquartile range (IQR)). The relative percent

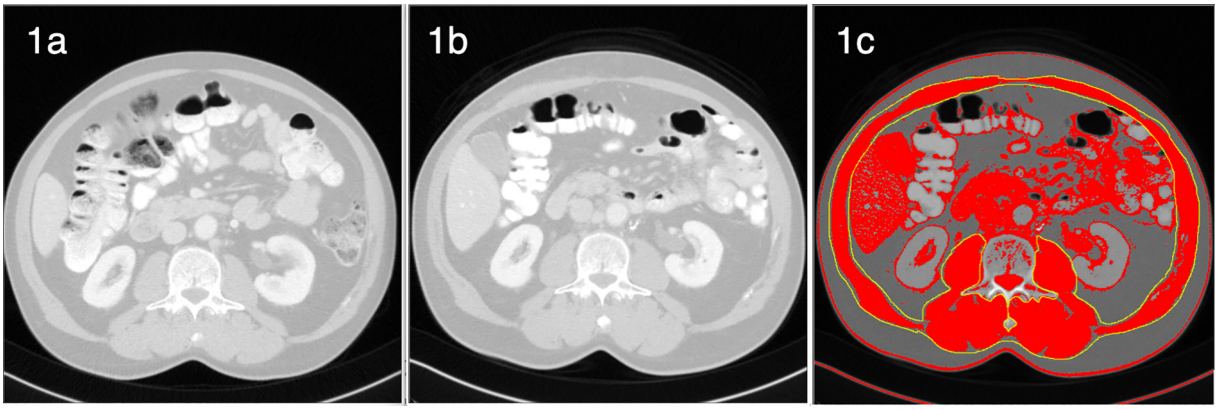

Fig. 1. Muscle mass measurements on abdominal CT scans; 1a preoperative axial CT-image at the L3 level; 1b postoperative axial CT-image at the L3 level of the same patient; 1c measurement of cross-sectional area of skeletal muscle at the L3 level by applying Hounsfield unit thresholds of −29 to +150 and delineating skeletal muscle (between yellow lines).

change in SMI between pre- and postoperative CT images was determined for each patient, and mean change and SD of change were calculated in the 5th to 95th percentiles. Patients were considered to have muscle wasting if they had >1SD decline in muscle mass, as suggested by Brown et al. [13] The inter-rater reliability for SMI measurements was assessed using a two-way mixed, absolute agreement, single measure intraclass correlation (ICC). The reliability of the measurements was considered good if the ICC was 0.75–0.90 and excellent if the ICC was 0.90 or greater [23].

Baseline patient and treatment characteristics and postoperative outcomes between groups were analyzed with parametric and non-parametric tests. Survival between included and excluded patients was compared with the log-rank test.

Cox regression analyses were performed to determine associations between muscle wasting and OS. Possible confounder variables were added to the multivariable model manually in a forward stepwise fashion starting with the variable that had the strongest association with the outcome. Variables were considered possible confounders if they were associated with both muscle wasting and OS in univariable analyses ($p < .20$). The variable was retained in the multivariable model if the beta coefficient of the central determinant (muscle wasting) changed by more than 10%. A subgroup analysis for OS was performed in patients without evidence of recurrence on the postoperative CT-scan.

Finally, four groups were created based on presence of baseline sarcopenia (present/absent) and subsequent muscle wasting (present/absent), and OS was compared between the reference group (absent sarcopenia and absent muscle wasting) and the other groups using Cox regression analysis adjusted for age and sex. Proportionality of hazards was confirmed with visual inspection of log-log plots. A two-tailed p-value <.05 was considered statistically significant for all analyses. SPSS version 25.0 for Windows (IBM Corp, Armonk, NY) was used for all analyses.

3. Results

3.1. Study cohort

During the study inclusion period, 1009 patients underwent surgery for CRC. After excluding patients based on the exclusion criteria, 233 patients remained in the study (Fig. 2).

3.2. Comparison between the study cohort and patients without a follow-up CT scan

Patients who survived at least six months but did not undergo a postoperative scan within 18 months of surgery ($N = 164$) were compared with the study cohort. Patients without a postoperative scan were older (median 80.3 vs 75.5 years, $p < .001$) and tended to be more often female (48.8% vs 39.9%, $p = .08$). They more often underwent open surgery (54.3% vs 30.9%, $p < .001$). Tumor stages (stage III 36.2% vs 33.5%, $p = .58$), preoperative ASA-scores (ASA III-IV 41.7% vs 34.8%, $p = .17$), prevalence of rectal cancer (20.7% vs 22.7%, $p = .63$) or acute operations (6.7% vs 7.7%, $p = .70$) did not differ between the groups. Excluded patients had a significantly shorter survival time (log-rank $p = .007$).

3.3. Timing of CT-scans

The median interval between pre- and postoperative scans was 12.3 months (IQR 10.0–14.3). The median interval between the preoperative scan and the operation was 27 days (IQR 19–35). Twenty-one patients (9%) had the scan before neoadjuvant therapy (86% radiotherapy only); for them, the interval between the scan and operation was longer with a median of 50 days (IQR 34–77), $p < .001$. The median interval between the operation and postoperative scan was 11.3 months (IQR 8.6–13.2); all patients had the scan at least six months after surgery and 73% of patients had the scan at least nine months after surgery. Of the 44 patients that received adjuvant therapy, eleven (25%) had the scan less than three months after the last chemotherapy. The interval between the operation and postoperative scan for these patients was shorter with a median of 8.7 months (IQR 7.6–10.0), $p = .02$.

3.4. Muscle wasting

The ICC and the corresponding 95% confidence interval (CI) for the muscle mass measurements was 0.99, 95% CI 0.99–1.00, $p < .001$, demonstrating excellent IRR between the measurements. The mean relative change in muscle mass in the whole cohort was +1.6% (±5.7%). There were 34 patients with muscle wasting (more than 1SD decline (−5.7%) in muscle mass). The median decline in muscle mass in this group was −8.1% (range − 28.2% to −5.8%).

3.5. Patient and treatment characteristics and short-term treatment outcomes

Baseline and treatment characteristics between patients with and without muscle wasting are shown in Table 1. Patients with muscle wasting tended to be female more often ($p = .19$) and had a higher SMI at baseline ($p = .03$). The prevalence of preoperative sarcopenia tended to be lower in the group with muscle wasting ($p = .08$). Patients who underwent rectum resections ($p = .06$) and who received neoadjuvant therapy after the preoperative scan ($p = .10$) tended to have muscle wasting more often.

Treatment outcomes for patients with and without muscle wasting are shown in Table 2. There was a trend towards a higher prevalence of severe complications ($p = .19$), ICU admissions ($p = .07$), and a longer LOS ($p = .11$) in the group with muscle wasting. The overall complication burden as measured with the Comprehensive Complication Index tended to be higher in the group with muscle wasting ($p = .14$). Although receipt of adjuvant chemotherapy was not different between the groups with and without muscle wasting ($p = .84$), patients who finished adjuvant chemotherapy less than three months before postoperative scan tended to have muscle wasting more often (12% vs 4%, $p = .06$). Twenty patients (8.6%) had evidence of recurrence at the time of postoperative CT-scan. Eighteen of them (90.0%) died during the study period. Patients with muscle wasting tended to have had recurrence more often ($p = .17$).

3.6. Muscle wasting and overall survival

The median follow-up time for the whole cohort was 4.7 (IQR 3.5–5.0) years. All surviving patients were followed for at least three years. A total of 53 patients (22.7%) died, and 34 patients (14.6%) died within three years. CRC was the cause of death in 22 cases (41.5%).

Muscle wasting was a predictor of OS in univariable Cox regression analysis (HR 2.1, 95% CI 1.1–3.8, $p = .02$). In multivariable Cox regression analysis adjusted for age, recurrence and baseline SMI, patients with muscle wasting had a 2.8-fold increased risk of dying from all causes (adjusted HR 2.8, 95% CI 1.5–5.4, $p = .002$) (Fig. 3a). Including rectal cancer or adjuvant therapy in the model did not significantly modify the relationship between muscle wasting and OS (adjusted HR 2.9, 95% CI 1.5–5.6, $p = .001$ and adjusted HR 2.8, 95% CI 1.5–5.4, $p = .002$, respectively). The addition of other possible confounder variables also did not modify the relationship between muscle wasting and survival.

We performed a subgroup analysis in patients who did not have evidence of recurrent cancer at the time of postoperative CT-scan ($N = 213$, 35 deaths). In multivariable analysis adjusted for age and preoperative SMI, muscle wasting was associated with increased mortality (adjusted HR 2.7, 95% CI 1.2–6.0, $p = .02$).

Finally, OS was compared between four groups of patients based on the presence of baseline sarcopenia and muscle wasting. The reference

group consisted of patients without baseline sarcopenia or muscle wasting ($N = 63$). Compared to the reference group, patients with baseline sarcopenia but without muscle wasting ($N = 136$) had significantly worse OS (adjusted HR 3.8, 95% CI 1.4–10.0, $p = .007$). Patients who had no baseline sarcopenia but who experienced muscle wasting ($N = 16$) also had poorer OS (adjusted HR 4.8, 95% CI 1.3–18.3, $p = .02$). Patients who had both baseline sarcopenia and subsequent muscle wasting ($N = 18$) had the highest mortality risk (adjusted HR 7.5, 95% CI 2.5–22.8, $p < .001$) (Fig. 3b).

4. Discussion

In this study, we showed that the risk of mortality was 2.8-fold higher in patients who had postoperative muscle wasting compared to those without, independent of baseline characteristics or postoperative outcomes. A subgroup analysis in patients without recurrence revealed a similar risk of mortality in the group with muscle wasting. Patients who had both sarcopenia at baseline and subsequent muscle wasting had the highest mortality risk. Although some decline in muscle mass can be expected in the older patient population as a result of age-related muscle loss [15], our results indicate that accelerated losses after CRC surgery are prognostic for poorer survival. Single preoperative measures of low muscle mass have been shown to predict OS in multiple studies [24]. Serial measurements take it a step further as they provide dynamic view on muscle homeostasis. Progressive muscle wasting may be a stronger prognostic factor than a single pre-treatment measurement. In a recent study in patients with metastatic CRC, continuing muscle loss but not pre-treatment sarcopenia was prognostic of worse OS [25].

Two recent studies have found an association between abdominal muscle wasting and poorer survival outcomes in patients with CRC. Brown et al. conducted a population-based cohort study in 1924 stage I-III CRC patients and found that muscle mass decline was a significant predictor of OS [13]. Similarly, Hopkins et al. showed that deteriorating muscle mass predicted OS in a cohort of 667 patients with non-metastatic CRC [14]. Our results add to the body of evidence linking postoperative muscle wasting to reduced survival. Importantly, as all patients in our study were older than 70 years (with a median age of 76), we have shown that muscle wasting is also a significant risk factor for reduced survival in an older population with CRC. This could have consequences for clinical practice, as quantifying changes in muscle mass could be used to improve risk prediction in this patient group.

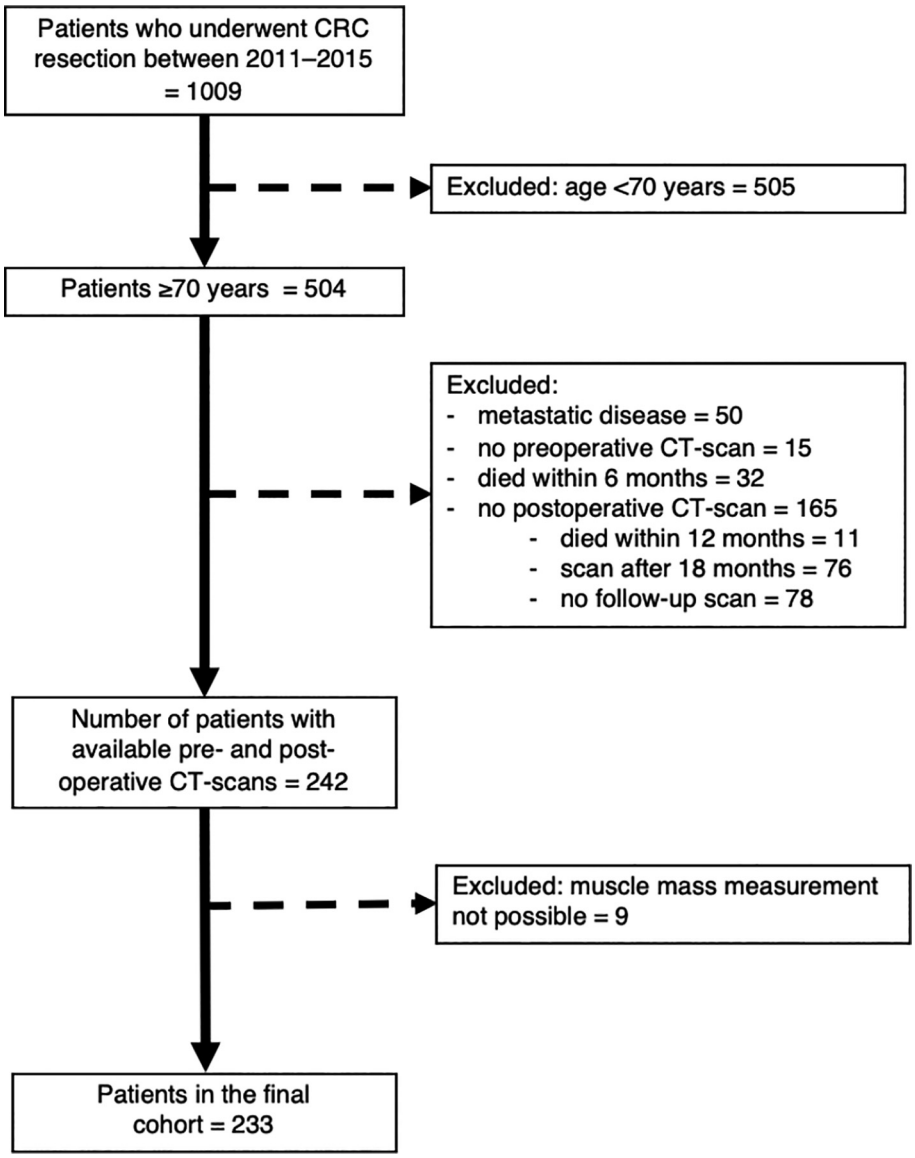

Fig. 2. Flow chart of patient inclusion in the study.

Table 1
Baseline and treatment characteristics of patients with non-metastatic CRC.

Characteristic	Total N = 233	No muscle wasting N = 199	Muscle wasting N = 34	p-value
Age, median (IQR), y	75.7 (72.9–79.2)	75.8 (73.0–79.2)	75.1 (72.6–78.9)	0.38
Female sex	93 (40)	76 (38)	17 (50)	0.19
BMI[a], median (IQR), kg/m^2	25.8 (24.1–29.4)	25.7 (24.1–29.0)	26.9 (23.4–30.9)	0.60
CCI				0.59
CCI 0	121 (52)	106 (53)	15 (44)	
CCI 1	56 (24)	46 (23)	10 (29)	
CCI ≥ 2	56 (24)	47 (24)	9 (27)	
ASA				0.65
ASA I-II	152 (65)	131 (66)	21 (62)	
ASA III-IV	81 (35)	68 (34)	13 (38)	
Preoperative anemia[b]	135 (58)	115 (58)	20 (59)	0.94
Preoperative SMI, mean (SD), cm^2/m^2	44.4 (7.7)	44.0 (7.6)	47.0 (7.5)	0.03
Preoperative sarcopenia	154 (66)	136 (68)	18 (53)	0.08
Pathological tumor stage				0.55
Stage 0-I	65 (28)	53 (27)	12 (35)	
Stage II	90 (39)	79 (34)	11 (32)	
Stage III	78 (34)	67 (34)	11 (32)	
Rectum resection	53 (23)	41 (21)	12 (35)	0.06
Urgent surgery	18 (8)	16 (8)	2 (6)	1.00
Open surgery	72 (31)	61 (31)	11 (32)	0.84
Neoadjuvant therapy after preoperative scan	21 (9.0)	15 (8)	6 (18)	0.07
Adjuvant therapy	44 (19)	38 (19)	6 (18)	0.84
<3 months before postoperative scan	11 (5)	7 (4)	4 (12)	0.06
Ostomy	61 (26)	49 (25)	12 (35)	0.19
Ostomy reversal[c]	24 (40)	18 (38)	6 (50)	0.43
Interval between CT-scans, median (IQR), m	12.1 (10.0–14.3)	12.2 (9.7–14.3)	12.5 (10.2–14.5)	0.76

Abbreviations: *ASA* American Society of Anesthesiologists; *BMI* body mass index; *CCI* Charlson Comorbidity Index; *CT* computed tomography; *IQR* interquartile range; *SD* standard deviation; *SMI* skeletal muscle index.
All values are reported as number (percentage) unless otherwise indicated.
[a] Missing n = 4.
[b] Missing n = 1.
[c] Taking into account patients who received an ostomy during primary surgery (N = 61).

Table 2
Postoperative outcomes and muscle wasting in patients with non-metastatic CRC.

Outcome	Total N = 233 (%)	No muscle wasting N = 199 (%)	Muscle wasting N = 34 (%)	p-value
Overall complications	108 (46)	89 (45)	19 (56)	0.23
Severe complications	55 (24)	44 (22)	11 (32)	0.19
ICU admission	37 (16)	28 (14)	9 (27)	0.07
Reoperation	30 (15)	23 (13)	7 (25)	0.30
30-day readmission	24 (10)	20 (10)	4 (12)	0.76
LOS[a], median (IQR), days	7 (5–15)	7 (5–15)	10 (6–20)	0.13
LOS > 14 days[a]	63 (27)	50 (25)	13 (38)	0.11
Comprehensive Complication Index, median (IQR)	0.0 (0.0–28.6)	0.0 (0.0–24.2)	20.9 (0.0–36.1)	0.14
Recurrence[b]	20 (8.6)	15 (7.5)	5 (14.7)	0.17
Overall mortality	53 (22.7)	40 (20.1)	13 (38.2)	0.02
CRC	22 (41.5)	17 (42.5)	5 (38.5)	0.70
Other	24 (45.3)	17 (42.5)	7 (53.8)	
Unknown	7 (13.2)	6 (15.9)	1 (7.7)	

Abbreviations: *CRC* colorectal cancer; *CT* computed tomography; *ICU* intensive care unit; *IQR* interquartile range; *LOS* length of stay.
All values are reported as number (percentage) unless otherwise indicated.
[a] Includes index admission and readmissions within 30 days.
[b] Evidence of recurrent CRC at the time of postoperative CT-scan.

Another interesting finding in our study was that patients with muscle wasting seemed to be more likely to have experienced severe complications and prolonged hospital admissions, although the results were not statistically significant. To our knowledge, the relationship between postoperative outcomes and muscle wasting has not been examined previously. Complications and prolonged bed rest are likely to lead to a net catabolic effect. Even in healthy older adults, ten days of bed rest led to a 3% decrease in muscle mass and significant reductions in physical capacity parameters [26,27]. However, as the second scan after surgery was performed at least six months later with no additional measurements in between, it is currently not possible to say what role postoperative complications may have played in muscle wasting.

Chemotherapy can have a significant negative impact on muscle homeostasis. In two studies in patients with colorectal liver metastases (mean age 56 to 68 years), neoadjuvant chemotherapy was associated with muscle depletion on serial abdominal CT-scans [28,29]. In another study in patients with metastatic CRC (mean age 66 years), muscle wasting during palliative chemotherapy was associated with worse survival [30]. In our cohort, muscle wasting tended to be more prevalent in patients who received neoadjuvant therapy (mostly radiotherapy) and patients with more recent adjuvant therapy (within three months of postoperative scan). (Neo)adjuvant therapy did not modify the relationship between muscle wasting and OS. As patients with non-metastatic CRC do not routinely undergo serial CT-scans during neoadjuvant or adjuvant treatment, it was not possible to measure the direct association between these therapies and muscle wasting. More studies are needed to elucidate the association between chemotherapy, muscle wasting and survival outcomes, especially in the older patient population.

Rectal cancer patients more often undergo neoadjuvant therapy and rectum resections frequently necessitate the construction of an ostomy. In our population, rectal cancer tended to be more prevalent in the group with muscle wasting. However, the inclusion of rectal cancer in the multivariable model did not modify the relationship between muscle wasting and OS. Due to the small number of patients and outcomes, we did not perform a separate subgroup analysis in patients with rectal cancer. It would be of interest to study the relationship between perioperative therapies and muscle wasting in a larger group of patients with rectal cancer.

Older patients with cancer often value their quality of life and the ability to remain functionally independent over the expected survival benefits [31]. Studies have shown that muscle strength declines 2–5 times faster than muscle mass [15]. Although we were not able to study the relationship between muscle wasting and functional outcomes, it is probable that patients with significant muscle mass decline also experienced functional impairment [32]. Changes in muscle mass could serve as an additional, objective endpoint for interventions aimed at preventing functional decline. Regarding possible interventions, there is high-quality evidence that resistance training is effective in increasing muscle strength and mass in the older population [33,34]. Specifically in patients undergoing abdominal surgery, multimodal prehabilitation programs (combining exercise and enhanced protein intake) aimed at improving the patients' functional capacity before surgery have reported short-term improvements in postoperative outcomes [35,36]. As the etiology of muscle wasting in older patients with CRC is multifactorial [8], relating to normal aging processes, cancer activity and treatment, comorbid conditions, physical activity, and nutritional deficiencies, it should be determined to what degree interventions can have a positive influence on muscle homeostasis. Specifically, it would be interesting to find out whether (p)rehabilitation programs can slow down or reverse muscle loss and improve physical functioning in older patients after CRC surgery.

This study has some limitations, all related to its retrospective design. Forty percent of older patients did not undergo a surveillance scan within the specified time period. In many cases, follow-up occurs

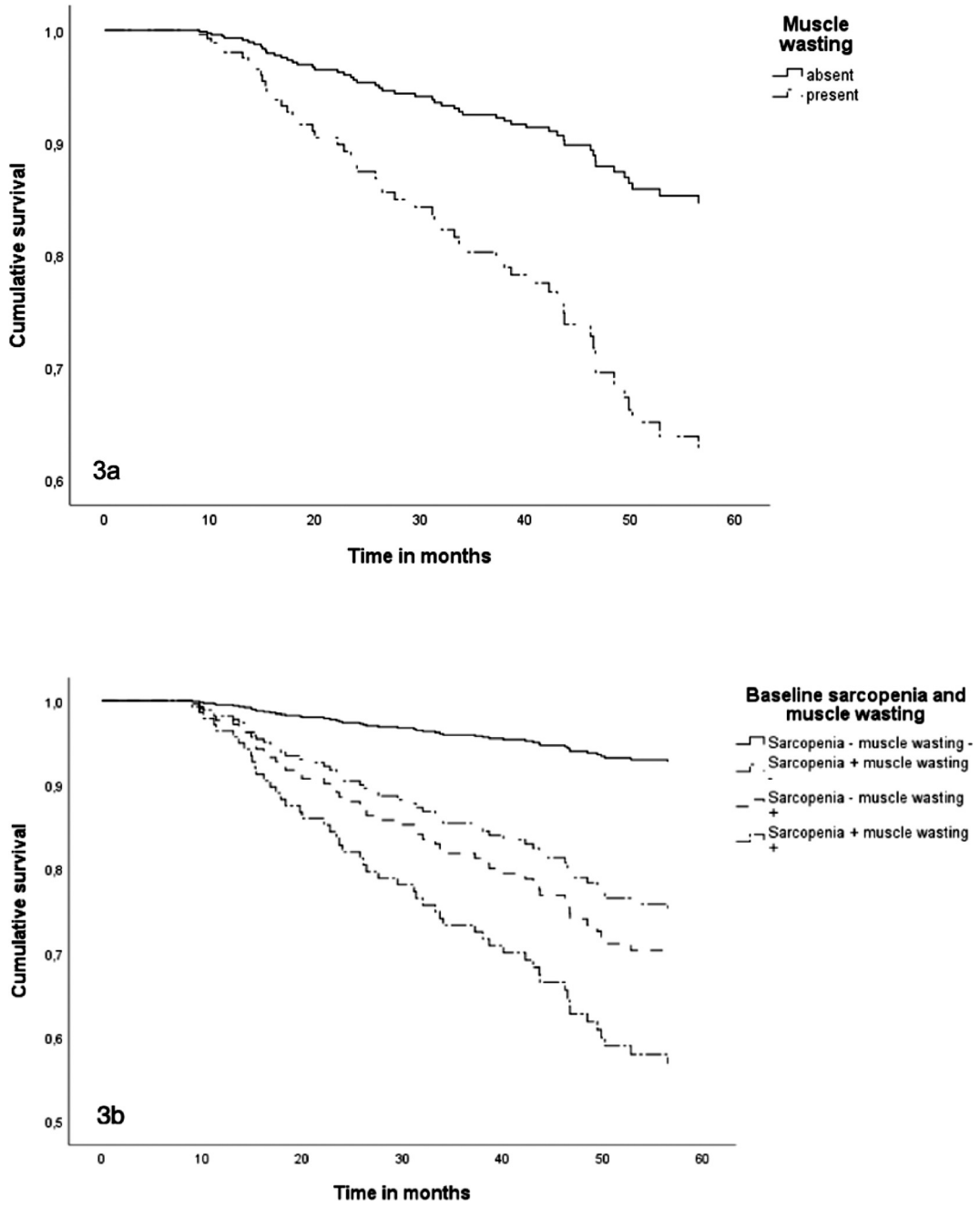

Fig. 3. a. Overall survival in patients with and without postoperative muscle wasting from multivariable Cox regression analysis adjusted for age, recurrence and preoperative muscle mass. b. Overall survival in four groups of patients according to baseline sarcopenia (+/−) and subsequent muscle wasting (+/−) from Cox regression analysis adjusted for age and sex.

by means of an ultrasound or by tracking carcinoembryonic antigen levels, and our results likely reflect standard practice. The excluded patients were older, more often female and had a shorter survival time. Patients with declining health were probably more likely to forgo surveillance scans. It is therefore plausible that the association between muscle wasting and survival would have been more pronounced had these patients also been included in the cohort.

A second limitation is that we were not able to quantify weight loss as weight measurements were unavailable at the time of postoperative CT-scan. However, in the study by Brown et al., muscle depletion occurred independently of weight loss [13]. Increasing adiposity can conceal muscle wasting while weight remains unchanged, meaning that tracking weight loss alone would not reveal important underlying changes in body composition [11].

Finally, we did not measure changes in muscle radiodensity which is a radiologic marker of muscle quality. Brown et al. showed that decreasing muscle radiodensity was prognostic of survival, although the association was less strong than for muscle mass [13]. For some patients in our cohort, there were differences in the level of contrast enhancement between pre- and postoperative scans (either no contrast or different phase of scan). The presence of intravenous contrast affects the radiodensity of muscle, and comparisons between pre- and postoperative muscle radiodensity measurements would have been unreliable [37].

5. Conclusion

Muscle wasting as measured on serial abdominal CT-scans was prognostic of poorer survival in patients ≥70 years undergoing surgery

for non-metastatic CRC. Measuring changes in muscle mass on follow-up CT-scans may improve risk prediction in this patient group. Future studies should address the etiology of muscle wasting in older CRC patients. Whether (p)rehabilitation can prevent muscle wasting and improve long-term functional and survival outcomes also warrants further study.

Category

Cohort study

Funding

None.

Author contributions

Conceptualization: T. Argillander, D. Spek, H.J. van der Zaag-Loonen, A.F. van Raamt, P. van Duijvendijk, B.C. van Munster; Methodology: T. Argillander, H.J. van der Zaag-Loonen, P. van Duijvendijk, B.C. van Munster; Data curation: T. Argillander, D. Spek, A.F. van Raamt, P. van Duijvendijk; Formal analysis: T. Argillander, D. Spek, H.J. van der Zaag-Loonen; Writing-original draft: T. Argillander, D. Spek, H.J. van der Zaag-Loonen, A.F. van Raamt, P. van Duijvendijk, B.C. van Munster. Writing-review and editing: T. Argillander, D. Spek, H.J. van der Zaag-Loonen, A.F. van Raamt, P. van Duijvendijk, B.C. van Munster

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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