ORIGINAL ARTICLE

*JCSM Clinical Reports* 2022; **7**: 65–76
Published online 27 June 2022 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/crt2.54

# The combination of computed tomography-derived muscle mass and muscle density and relationship with clinicopathological characteristics and survival in patients undergoing potentially curative surgery for colorectal cancer

Josh McGovern*, Allan M. Golder, Ross D. Dolan, Campbell S.D. Roxburgh, Paul G. Horgan & Donald C. McMillan

*Academic Unit of Surgery, School of Medicine, University of Glasgow, New Lister, Building, Royal Infirmary, Glasgow, UK*

## Abstract

**Background** Sarcopenia has been defined as a loss of muscle mass and function. CT-derived muscle measurements, skeletal muscle index (SMI) and density (SMD), taken together may provide an objective measure of sarcopenia. The aim of the present study was to examine the relationship between CT-derived sarcopenia (low SMI and SMD), clinicopathological characteristics, systemic inflammation and survival in patients undergoing surgery for colorectal cancer.

**Methods** Consecutive patients who underwent resections for colorectal cancer (TNM I–III) at our institution, between April 2008 and 2018, were identified from a prospectively maintained database. CT-derived muscle mass (SMI) and density (SMD) measurements were combined to form the CT-Sarcopenia score (CT-SS). Thresholds for low SMI and SMD reported by Martin and co-workers and Caan/Xiao and co-workers were combined to form two iterations of the CT-SS. Patients were categorized as normal/high SMI (irrespective of SMD) = 0, low SMI and normal/high SMD = 1 and low SMI and low SMD = 2. The Pearson Chi square test was used to examine the associations between categorical variables and the Chi square test for linear trend was used for ordered variables with multiple categories. Survival data were analysed using univariate and multivariate Cox regression.

**Results** One thousand and two patients met the study inclusion criteria. Fifty-five per cent ($n = 554$) of patients were male and 66% ($n = 657$) were aged 65 years or older. Twenty-four per cent ($n = 240$) of patients had TNM stage I disease, 40% ($n = 404$) stage II and 36% ($n = 358$) stage III. Eighteen per cent ($n = 174$) of patients were at risk of malnutrition. Forty-eight per cent ($n = 479$) of patients had an NLR ≥ 3 and 27% ($n = 271$) had an mGPS ≥ 1. Similar numbers of patients defined as CT-SS 0, 1 and 2 irrespective of thresholds applied (49%/12%/39% vs. 43%/19%/38%, respectively). Eight hundred and thirty four ($n = 834$) patients who underwent surgical resection for non-metastatic colorectal cancer with curative intent were alive at 3 years. On univariate analysis, both the CT-SS (Martin/Martin) and CT-SS (Caan/Xaio) were significantly associated with age ($P < 0.001$ and $P < 0.001$, respectively), ASA ($P < 0.01$ and $P < 0.001$, respectively), MUST ($P < 0.001$ and $P < 0.005$, respectively), mGPS ($P < 0.001$ and $P < 0.001$, respectively), NLR ($P < 0.001$ and $P < 0.001$, respectively), and overall survival ($P < 0.001$ and $P < 0.001$, respectively). CT-SS (Caan/Xaio) was significantly associated with TNM stage ($P < 0.05$), but not CT-SS (Martin/Martin, $P = 0.221$).

**Conclusions** The objective CT-SS was significantly associated with older age, co-morbidity, nutritional risk, systemic inflammation and poorer survival, irrespective of thresholds used. However, the relationship between CT-SS and TNM stage was inconsistent and threshold dependent.

**Keywords** sarcopenia; skeletal muscle index; density; cancer; outcomes

*Received: 23 February 2022; Revised: 6 June 2022; Accepted: 14 June 2022*
**Correspondence to: Josh McGovern, Academic Unit of Surgery, University of Glasgow, Level 2, New Lister Building, Glasgow Royal Infirmary, Glasgow G31 2ER, UK. Email: josh.mcgovern@glasgow.ac.uk*

## Introduction

The second European Working Group on Sarcopenia in Older People (EWGSOP2) revised operational definition of sarcopenia highlighted the importance of assessing muscle strength, in addition to muscle mass, for defining sarcopenia and its impact on the individual.[1] In patients with cancer, a variety of approaches have been used to determine muscle strength including subjective assessments such as performance status to objective assessments such as hand grip strength.[2,3] However, to date, there has been no widely accepted objective assessment to supplement performance status in patients with cancer. Therefore, there is a continued interest in identifying objective assessments of sarcopenia and to determine its impact on clinical outcome in patients with cancer.

CT-derived body composition analysis has facilitated the assessment of skeletal muscle in patients with cancer. Specifically, the quantification of muscle mass and density as part of routine clinical investigations.[4,5] Skeletal muscle mass is most often calculated from the cumulative volume of the intra-abdominal musculature on a CT image slice, generally at the level of the third lumbar vertebra, normalized by the square of the patient's height in metres (skeletal muscle index, SMI), analogous to that of BMI.[6] Indeed, CT-derived muscle mass measurements have been shown to be consistent with measurements of other modalities,[7] specifically bioelectrical impedance analysis[8] and dual-energy X-ray absorptiometry.[9] Skeletal muscle density (SMD) on the other hand is an assessment of muscle quality, with striated skeletal muscle, free from fat infiltration, having a greater density on CT analysis compared against that with fat deposition.[10,11] While subject to confounding factors,[12] there is now consistent evidence that SMD is associated with physical function in patients with cancer, across a range of cancer subtypes and disease stages.[13–15] Therefore, taken together, SMI and SMD, may provide a routine clinical methodology by which sarcopenia and its clinical impact can be characterized.

In isolation, a low SMI and SMD have been negatively associated with clinical outcomes in colorectal cancer.[16–18] Furthermore, they have also been associated with prognostic host factors including malnutrition[19] and systemic inflammation.[20] However, the relationship between CT-derived sarcopenia, malnutrition, systemic inflammation and clinical outcomes in colorectal cancer has yet to be examined. Specifically, whether these measurements together, if carried out using standardized methodology,[12] may have complementary prognostic value. Therefore, the aim of the present study was to examine the relationship between CT-derived sarcopenia and clinicopathological characteristics and the relationship with survival in patients undergoing potentially curative surgery for colorectal cancer.

## Patients and methods

### *Patients*

Consecutive patients who underwent potentially curative resections for colorectal cancer, within NHS Greater Glasgow and Clyde (NHSGGC), between April 2008 and April 2018, were identified from a prospectively maintained database. Those patients with a pre-operative CT scan, recorded height and weight, pre-operative assessment of the systemic inflammatory response and had TNM stage I–III disease were assessed for inclusion. Exclusion criteria were as follows; patients without satisfactory pre-operative CT imaging, without a recorded height and weight, had no pre-operative assessment of the systemic inflammatory response or had TNM stage IV disease.

### *Clinicopathological characteristics*

Routine demographic details included age, sex and BMI. Age categories were grouped into $<64$, 65–74, and $>74$ years. BMI was categorized as $<20$, 20–24.9, 25–29.9, and $\geq 30$ kg/m$^2$. The Malnutrition Universal Screening Tool (MUST) was used to determine the overall risk of malnutrition. MUST is a three-component score consisting of the patient's current weight status using BMI, unintentional weight loss, and the acute disease effect. Scores were identified retrospectively from patient's medical records. Assessment was made by clinical nursing staff, using a dedicated proforma, within 24 h of admission. Patients were categorized as into low risk (MUST score = 0), medium risk (MUST score = 1), and high risk (score $\geq 2$) of malnutrition, as previously described.[21] Patient co-morbidity was classified using the American Society of Anesthesiologists (ASA) grading system: ASA 1, a normal healthy patient; ASA 2, a patient with mild systemic disease; ASA 3, a patient with severe systemic disease that is not incapacitating; and ASA 4, a patient with incapacitating severe systemic disease that is a constant threat to life.[22]

Tumour site was identified from pre-operative CT imaging, endoscopic and pathology reports. Tumours were staged using the fifth edition of the TNM classification, consistent

with practice current in the United Kingdom during the study period.[23] Patients were followed-up for a minimum of 3 years following surgery. The date and cause of death were confirmed using hospital electronic case records. Date of last recorded follow-up or last review of electronic case records (1 October 2021), which served as the censor date. Ethical approval was granted by the West of Scotland Research Ethics Committee, Glasgow.

## Computed tomography body composition

CT images were obtained at the level of the third lumbar vertebra as previously described.[24] Patients with CT imaging taken 3 months or more prior to their surgery were excluded from the study. Furthermore, Scans with significant movement artefact or missing region of interest were not considered for inclusion. Each image was analysed using a free-ware program (NIH Image J version 1.47, http://rsbweb.nih.gov/ij/) shown to provide reliable measurements.[25]

Region of interest (ROI) measurements were made of subcutaneous fat (SFA), visceral fat (VFA) and skeletal muscle area (SMA) ($cm^2$) using standard Hounsfield Unit (HU) ranges (adipose tissue −190 to −30, and skeletal muscle −29 to +150). These were then normalized for height$^2$ to create indices; subcutaneous fat index (SFI, $cm^2/m^2$), and skeletal muscle index (SMI, $cm^2/m^2$). Skeletal muscle radiodensity (SMD, HU) was measured from the same ROI used to calculate SMI, as its mean HU.

A high SFI was defined as ≥50.0 $cm^2/m^2$ in men and ≥42.0 $cm^2/m^2$ in women.[26] Visceral obesity was defined as VFA > 160 $cm^2$ for male patients and >80 $cm^2$ for female patients.[27] A low SMI was defined as described by Martin *et al*. as an SMI < 43 $cm^2/m^2$ if BMI < 25 $kg/m^2$ and SMI < 53 $cm^2/m^2$ if BMI ≥ 25 $kg/m^2$ in male patients and an SMI < 41 $cm^2/m^2$ in female patients.[4] A low SMI was also described by Caan et al. as an SMI < 52.3 $cm^2/m^2$ if BMI < 30 $kg/m^2$ and SMI < 54.3 $cm^2/m^2$ if BMI ≥ 30 $kg/m^2$ in male patients and an SMI < 38.6 $cm^2/m^2$ if BMI < 30 $kg/m^2$ and SMI < 46.6 $cm^2/m^2$ if BMI ≥ 30 $kg/m^2$ in female patients.[28] A low SMD was defined by Martin et al. as an SMD < 41 HU in patients with BMI < 25 $kg/m^2$ and <33 HU in patients with BMI > 25 $kg/m^2$.[4] A low SMD was also defined by Xiao et al. as <35.5 HU in men and <32.5 HU in women.[29]

CT-derived muscle measurements (SMI and SMD) were combined to form the CT-sarcopenia score (CT-SS). Patients were categorized as normal/high SMI (irrespective of SMD) = 0, low SMI and normal/high SMD = 1 and low SMI and low SMD = 2. The thresholds for low SMI and SMD reported by Martin and co-workers were combined to form the first iteration of the CT-SS (Martin). Thresholds derived from cohorts of patients with colorectal cancer were also used to calculate a second iteration of the CT-SS for comparison (Caan/Xiao).

## Systemic inflammation

Pre-operative haematological and biochemical results were identified from medical records and prospectively recorded. Blood samples were either obtained at pre-operative assessment, within 30 days of surgery, for elective patients or on admission for patients undergoing emergency surgery. An autoanalyser was used to measure serum CRP (mg/L) and albumin (g/L) concentrations (Architect; Abbot Diagnostics, Maidenhead, UK).

Systemic inflammatory status was retrospectively assessed by calculating the neutrophil/lymphocyte ratio (NLR) and modified Glasgow Prognostic Score (mGPS) for each patient, using pre-operative blood results. The NLR was calculated by division of the neutrophil count by the lymphocyte count, obtained from the patient's full blood count (FBC). NLR values were grouped as <3 (considered normal), 3–5 (considered moderate), and >5 (considered raised), as previously described.[25] The mGPS was derived as the following: patients with a normal CRP (<10 mg/L) scored 0, those with an elevated CRP (>10 mg/L) alone were scored 1, and those with an elevated CRP (>10 mg/L) and hypoalbuminaemia (<35 g/L) were scored 2, as previously described.[30]

## Statistical analysis

Demographic data, clinicopathological variables, MUST, BMI, CT-SS, SFI, VFA, NLR, and mGPS were presented as categorical variables. The Pearson $\chi^2$ test was used to examine the associations between categorical variables, and the $\chi^2$ test for linear trend was used for ordered variables with multiple categories.

The relationship between the CT-SS (Martin and Caan/Xiao), clinicopathological characteristics, CT-derived adipose measurements and systemic inflammation were examined using univariate and multivariate binary logistic regression, to calculate OR and 95% CI. Clinicopathological factors that had a *P*-value <0.1 were taken into a multivariate model using a backward conditional model to identify independently significant factors.

The primary end point was overall survival (OS) at 3 years post operatively. Patients who died within 30-days of surgery were excluded from subsequent survival analysis. The time between the date of surgery and the date of death of any cause was used to define overall survival. Survival data were analysed using univariate and multivariate Cox regression. Those variables associated with a degree of $P < 0.1$ were entered into a backward conditional multivariate model.

Missing data were excluded from analysis on a variable-by-variable basis. Two-tailed *P*-values $<0.05$ were considered statistically significant. Statistical analysis was performed using SPSS software version 25.0. (SPSS Inc., Chicago, IL, USA).

# Results

## *Patient inclusion*

The clinicopathological characteristics of the included patients are shown in *Table* 1 (*n* = 1002). 55.3% (*n* = 554) of patients were male and 65.6% (*n* = 657) were aged 65 years or older. 24% (*n* = 240) of patients had TNM stage I disease, 40.3% (*n* = 404) stage II and 35.7% (*n* = 358) stage III. 17.7% (*n* = 174) of those with a pre-operative MUST were at risk of malnutrition. The median BMI of the cohort was 27 kg/m$^2$ and 65.1% (*n* = 652) of patients had a BMI $\geq$ 25 kg/m$^2$. A high VFA was present in 73% (*n* = 731) of patients and 80.1% (*n* = 803) had a high SFI. 47.8% (*n* = 479) of patients had an NLR $\geq$ 3 and 27% (*n* = 271) had an mGPS $\geq$ 1. In the whole cohort, 83.2% (*n* = 834) patients who underwent surgical resection for non-metastatic colorectal cancer with curative intent were alive at 3 years. When stratified by site of tumour, 82% (*n* = 491) of patients with colonic tumours were alive at 3 years post-operatively and 86% (*n* = 343) of those with rectal tumours.

A low SMI and SMD were present in 51% (*n* = 507) and 67% of patients (*n* = 668), respectively, using the Martin thresholds. A low SMI was present in 57% (*n* = 570) of patients using the Caan thresholds and a low SMD in 58% (*n* = 584) of patients using the Xiao thresholds. The median (IQR) of SMI for patients categorized as having a low SMI using Martin threshold was 39.1 cm$^2$/m$^2$ (35.5–44.6). The median (IQR) of SMI for patients categorized as having a normal/high SMI using Martin threshold was 51.1 cm$^2$/m$^2$ (45.3–57.6). The median (IQR) of SMI for patients categorized as having a low SMI using Caan threshold was 41.5 cm$^2$/m$^2$ (36.0–47.1). The median (IQR) of SMI for patients categorized as having a normal/high SMI using Caan threshold was 53.4 cm$^2$/m$^2$ (44.5–59.7).

The relationship between SMI, SMD and 3 year survival in patients undergoing potentially curative surgery for CRC using thresholds of Martin and co-workers is shown in *Table* 2a. In patients with a low SMI, a low SMD was significantly associated with 3 year survival ($P < 0.01$). The relationship between SMI, SMD and 3 year overall survival in patients undergoing potentially curative surgery, using thresholds of Caan/Xiao and co-workers is shown in *Table* 2b. In patients with a low SMI, a low SMD was significantly associated with 3 year overall survival ($P < 0.001$).

The prevalence of CT-derived sarcopenia scores using thresholds of Martin and co-workers and Caan/Xiao is shown in *Table* 3. A similar prevalence was observed irrespective of threshold combination used (49%/12%/39% vs. 43%/19%/38%).

**Table 1** Clinicopathological characteristics of included patients (*n* = 1002)

| Clinicopathological characteristic | *n* = 1002 (%) |
|---|---|
| **Age** | |
| <65 | 345 (34.4) |
| 65–74 | 367 (36.6) |
| >74 | 290 (28.9) |
| **Sex** | |
| Female | 448 (44.7) |
| Male | 554 (55.3) |
| **ASA** | |
| 1 | 196 (19.6) |
| 2 | 456 (45.5) |
| 3 | 316 (31.5) |
| 4 | 34 (3.4) |
| **MUST** | |
| Low risk | 810 (80.8) |
| Medium risk | 91 (9.1) |
| High risk | 83 (8.3) |
| Missing | 18 (1.8) |
| **Tumour site** | |
| Colon | 602 (60.1) |
| Rectum | 400 (39.9) |
| **TNM stage** | |
| I | 240 (24.0) |
| II | 404 (40.3) |
| III | 358 (35.7) |
| **BMI** | |
| <20 | 58 (5.8) |
| 20–24.9 | 292 (29.1) |
| 25–29.9 | 337 (33.6) |
| ≥30 | 315 (31.4) |
| **High SFI** | |
| No | 199 (19.9) |
| Yes | 803 (80.1) |
| **High VFA** | |
| No | 271 (27.0) |
| Yes | 731 (73.0) |
| **Low SMI** | |
| No | 495 (49.4) |
| Yes | 507 (50.6) |
| **Low SMD** | |
| No | 334 (33.3) |
| Yes | 668 (66.7) |
| **mGPS** | |
| 0 | 731 (73.0) |
| 1 | 109 (10.9) |
| 2 | 162 (16.2) |
| **NLR** | |
| <3 | 532 (52.2) |
| 3–5 | 310 (30.9) |
| >5 | 169 (16.9) |
| **3 year survival** | |
| Yes | 834 (83.2) |
| No | 168 (16.8) |

The Kaplan–Meier curve in *Figure* 1A shows the relationship between the CT-SS (Martin) and overall survival in patients undergoing potentially curative surgery for CRC (log rank $P < 0.001$). The Kaplan–Meier curve in *Figure* 1B shows the relationship between CT-SS (Caan/Xiao) and overall survival in patients undergoing potentially curative surgery for CRC (log rank $P < 0.001$).

**Table 2a** The relationship between SMI, SMD, and 3 year survival in patients undergoing potentially curative surgery for CRC using thresholds of Martin and co-workers ($n$ = 1002)

| | Normal SMI ($n$ = 495) | Low SMI ($n$ = 507) | Total ($n$ = 1002) | $P$-value |
|---|---|---|---|---|
| Normal SMD ($n$ = 334) | 190 (88.4%) | 106 (89.1%) | 296 (88.6%) | 0.864 |
| Low SMD ($n$ = 668) | 238 (85.0%) | 300 (77.3%) | 538 (80.5%) | 0.013 |
| Total ($n$ = 1002) | 428 (86.5%) | 406 (80.1%) | 834 (83.2%) | 0.007 |
| $P$-value | 0.277 | 0.005 | 0.001 | |

**Table 2b** The relationship between SMI, SMD, and 3 year survival in patients undergoing potentially curative surgery for CRC using thresholds of Caan/Xiao and co-workers ($n$ = 1002)

| | Normal SMI ($n$ = 432) | Low SMI ($n$ = 570) | Total ($n$ = 1002) | $P$-value |
|---|---|---|---|---|
| Normal SMD ($n$ = 418) | 202 (86.7%) | 165 (89.2%) | 367 (87.8%) | 0.439 |
| Low SMD ($n$ = 584) | 171 (85.9%) | 296 (76.9%) | 467 (80.0%) | 0.010 |
| Total ($n$ = 1002) | 373 (86.3%) | 461 (80.9%) | 834 (83.2%) | 0.022 |
| $P$-value | 0.817 | <0.001 | 0.001 | |

**Table 3** The prevalence of CT-derived sarcopenia scores using thresholds of Martin and co-workers and Caan/Xiao and co-workers in patients undergoing potentially curative surgery for CRC ($n$ = 1002)

| | CT-SS 0 ($n$ = %) | CT-SS 1 ($n$ = %) | CT-SS 2 ($n$ = %) |
|---|---|---|---|
| Martin et al. | 495 (49%) | 119 (12%) | 388 (39%) |
| Caan/Xiao et al. | 432 (43%) | 185 (19%) | 296 (38%) |

The relationship between the CT-SS (Martin and Caan/Xiao), clinicopathological characteristics, CT-derived adipose measurements, systemic inflammation and overall survival in patients undergoing potentially curative surgery for CRC, is shown in *Tables* 4a and 4b, respectively. On univariate analysis, the CT-SS (Martin) was significantly associated with age ($P < 0.001$), ASA ($P < 0.01$), MUST ($P < 0.001$), tumour site ($P < 0.05$), BMI ($P < 0.001$), high SFI ($P < 0.05$), mGPS ($P < 0.001$), NLR ($P < 0.001$), and overall survival ($P < 0.001$, *Table* 4a). On univariate analysis, the CT-SS (Caan/Xaio) was significantly associated with age ($P < 0.001$), sex ($P < 0.001$), ASA ($P < 0.001$), MUST ($P < 0.05$), tumour site ($P < 0.05$), TNM stage ($P < 0.05$), BMI ($P < 0.001$), high SFI ($P < 0.05$), mGPS ($P < 0.001$), NLR ($P < 0.001$), and overall survival ($P < 0.001$, *Table* 4b).

The relationship between the CT-SS (Martin and Caan/Xiao), clinicopathological characteristics, CT-derived adipose measurements, and systemic inflammation in patients undergoing potentially curative surgery for CRC is also shown in *Tables* 5a and 5b, respectively. On univariate analysis, the CT-SS (Martin) was significantly associated with age ($P < 0.001$), ASA ($P < 0.001$), MUST ($P < 0.001$), tumour site ($P < 0.05$), BMI ($P < 0.001$), mGPS ($P < 0.001$), and NLR ($P < 0.001$). Age ($P < 0.001$), BMI ($P < 0.001$), and mGPS ($P < 0.001$) remained significantly associated with CT-SS (Martin) on multivariate analysis. On univariate analysis, the CT-SS (Caan/Xiao) was significantly associated with age ($P < 0.001$), sex ($P < 0.001$), ASA ($P < 0.001$), tumour site ($P < 0.001$), TNM stage ($P < 0.05$), mGPS ($P < 0.001$), and NLR ($P < 0.001$). Age ($P < 0.001$), sex ($P < 0.001$), and mGPS ($P < 0.001$) remained significantly associated with CT-SS (Caan/Xiao) on multivariate analysis.

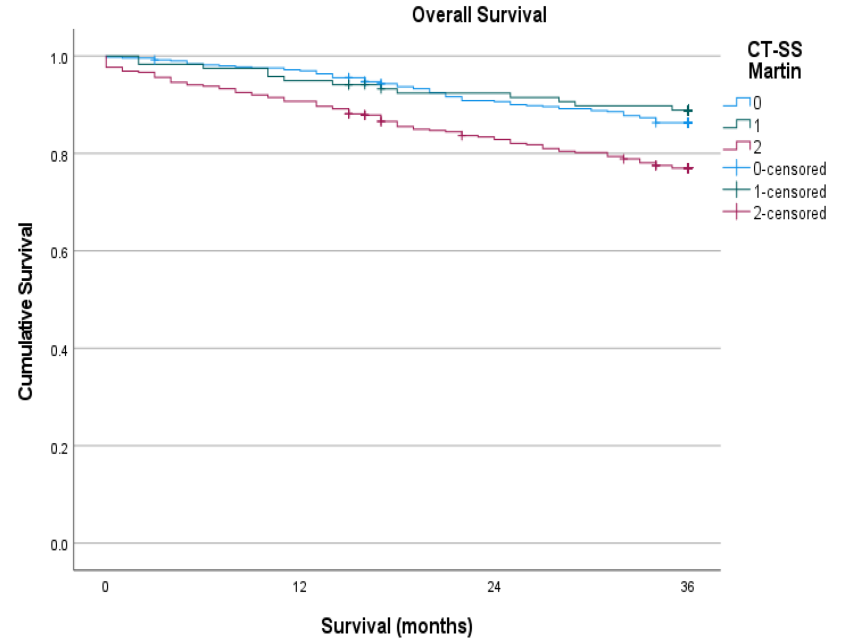
The relationship between clinicopathological characteristics, BMI, CT-derived adipose measurements, CT sarcopenia score (CT-SS Martin), systemic inflammation and overall survival in patients undergoing potentially curative surgery for CRC is shown in *Table* 6a. On univariate analysis, age ($P < 0.001$), ASA ($P < 0.001$), MUST ($P < 0.001$), TNM stage ($P < 0.001$), BMI ($P < 0.001$), CT-SS ($P < 0.001$), mGPS ($P < 0.001$), and NLR ($P < 0.001$) were significantly associated with overall survival. On multivariate analysis, ASA ($P < 0.001$), MUST ($P < 0.001$), TNM stage ($P < 0.001$), mGPS ($P < 0.05$), and NLR ($P < 0.05$) remained significantly associated with overall survival (see *Table* 6a).

The relationship between clinicopathological characteristics, CT-derived adipose measurements, CT sarcopenia score (CT-SS Martin), systemic inflammation and overall survival in patients undergoing potentially curative surgery for CRC, without the inclusion of BMI, is shown in *Table* 6b. On univariate analysis, age ($P < 0.001$), ASA ($P < 0.001$), MUST ($P < 0.001$), TNM stage ($P < 0.001$), CT-SS ($P < 0.001$), mGPS ($P < 0.001$), and NLR ($P < 0.001$) were significantly associated with overall survival. On multivariate analysis, ASA ($P < 0.05$), MUST ($P < 0.001$), TNM stage ($P < 0.001$), mGPS ($P < 0.05$), and NLR ($P < 0.05$) remained significantly associated with overall survival (see *Table* 6b).

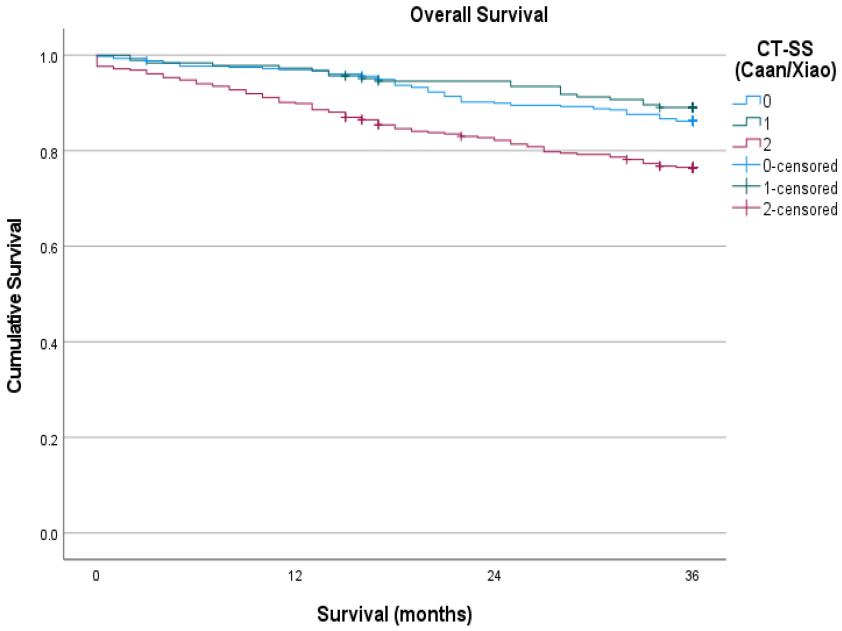
The relationship between clinicopathological characteristics, BMI, CT-derived adipose measurements, CT sarcopenia score (CT-SS Cann/Xiao), systemic inflammation and overall survival in patients undergoing potentially curative surgery for CRC is shown in *Table* 7a. On univariate analysis, CT-SS


DOI: 10.1002/crt2.54

**Figure 1** (A) Kaplan–Meier curve of the relationship between the CT-SS (Martin) and overall survival in patients undergoing potentially curative surgery for CRC (log rank $P < 0.001$). (B) Kaplan–Meier curve of the relationship between the CT-SS (Caan/Xiao) and overall survival in patients undergoing potentially curative surgery for CRC (log rank $P < 0.001$).




(A)




(B)

was significantly associated with overall survival ($P < 0.001$). On multivariate analysis, ASA ($P < 0.001$), MUST ($P < 0.001$), TNM stage ($P < 0.001$), and mGPS ($P < 0.05$) remained significantly associated with overall survival (See *Table* 7a).

The relationship between clinicopathological characteristics, CT-derived adipose measurements, CT sarcopenia score (CT-SS Caan/Xiao), systemic inflammation and overall survival in patients undergoing potentially curative surgery for CRC,


DOI: 10.1002/crt2.54

**Table 4a** The relationship between clinicopathological characteristic, systemic inflammation, CT-derived adipose measurements and overall survival in patients undergoing potentially curative surgery for CRC, stratified by CT sarcopenia score (Martin, *n* = 1002)

| | CT-SS 0 (*n* = 495) | CT-SS 1 (*n* = 119) | CT-SS 2 (*n* = 388) | *P*-value[a] |
|---|---|---|---|---|
| **Age** | | | | <0.001 |
| <65 | 217 (43.8) | 46 (38.7) | 82 (21.1) | |
| 65–74 | 174 (35.2) | 55 (46.2) | 138 (35.6) | |
| >74 | 104 (21.0) | 18 (15.1) | 168 (43.3) | |
| **Sex** | | | | 0.626 |
| Female | 222 (44.8) | 59 (49.6) | 167 (43.0) | |
| Male | 273 (55.2) | 60 (50.4) | 221 (57.0) | |
| **ASA** | | | | 0.003 |
| 1 | 103 (20.8) | 35 (29.4) | 58 (14.9) | |
| 2 | 227 (45.9) | 55 (46.2) | 174 (44.8) | |
| 3 | 155 (31/3) | 27 (22.7) | 134 (34.5) | |
| 4 | 10 (2.0) | 2 (11.9) | 22 (5.7) | |
| **MUST** | | | | <0.001 |
| Low risk | 433 (88.2) | 377 (76.5) | 286 (75.1) | |
| Medium risk | 29 (5.9) | 62 (12.6) | 51 (13.4) | |
| High risk | 29 (5.9) | 54 (11.0) | 44 (11.5) | |
| Missing | 4 | 7 | 7 | |
| **Tumour site** | | | | 0.015 |
| Colon | 281 (56.8) | 69 (58.0) | 252 (64.9) | |
| Rectum | 214 (43.2) | 50 (42.0) | 136 (35.1) | |
| **TNM stage** | | | | 0.221 |
| I | 143 (28.9) | 26 (21.8) | 71 (18.3) | |
| II | 171 (34.5) | 40 (33.6) | 193 (47.9) | |
| III | 181 (36.6) | 53 (44.5) | 124 (32.0) | |
| **BMI** | | | | <0.001 |
| <20 | 17 (3.4) | 7 (5.9) | 34 (8.8) | |
| 20–24.9 | 128 (25.9) | 26 (21.8) | 138 (35.6) | |
| 25–29.9 | 129 (26.1) | 69 (58.0) | 139 (35.8) | |
| ≥30 | 221 (44.6) | 17 (14.3) | 77 (19.8) | |
| **High SFI** | | | | 0.261 |
| No | 87 (17.6) | 33 (27.7) | 79 (20.4) | |
| Yes | 408 (82.4) | 86 (72.3) | 309 (79.6) | |
| **High VFA** | | | | 0.449 |
| No | 124 (25.1) | 42 (35.3) | 105 (27.1) | |
| Yes | 371 (74.9) | 77 (64.7) | 283 (72.9) | |
| **mGPS** | | | | <0.001 |
| 0 | 394 (79.6) | 89 (74.8) | 248 (63.9) | |
| 1 | 56 (11.3) | 17 (14.3) | 36 (9.3) | |
| 2 | 45 (9.1) | 13 (10.9) | 104 (26.8) | |
| **NLR** | | | | <0.001 |
| <3 | 227 (56.0) | 74 (62.2) | 172 (44.3) | |
| 3–5 | 147 (29.7) | 32 (62.9) | 131 (33.8) | |
| >5 | 71 (14.3) | 13 (10.9) | 85 (21.9) | |
| **3 year survival** | | | | <0.001 |
| Yes | 428 (86.5) | 106 (89.1) | 300 (77.3) | |
| No | 67 (13.5) | 13 (10.9) | 88 (22.7) | |

Each cell is presented as *n* = (%).
[a]*P*-value is from $\chi^2$ analysis.

without the inclusion of BMI, is shown in *Table* 7b. On multivariate analysis, ASA ($P < 0.001$), MUST ($P < 0.001$), TNM stage ($P < 0.001$), and mGPS ($P < 0.05$) remained significantly associated with overall survival (see *Table* 7b).

## Discussion

The results of the present study showed that in a large cohort of patients with operable colorectal cancer, the combination of a low muscle mass and density (CT-sarcopenia score, CT-SS) was significantly associated with older age, greater co-morbidity and nutritional risk, systemic inflammation and poorer survival, irrespective of threshold used to define a low SMI or SMD. Therefore, this simple objective score has clinical utility to inform on likely outcome and may be useful in the investigation of the underlying mechanisms of sarcopenia in patients with cancer.

CT-derived skeletal muscle mass and density measurements have been shown to have independent prognostic value in patients with cancer.[31,32] However, the present study found that patients with both a low skeletal muscle mass and density had significantly reduced overall survival compared to patients with a normal muscle mass or density. These results


DOI: 10.1002/crt2.54

**Table 4b** The relationship between clinicopathological characteristic, systemic inflammation, CT-derived adipose measurements and overall survival in patients undergoing potentially curative surgery for CRC, stratified by CT sarcopenia score (Caan/Xiao, *n* = 1002)

| | CT-SS 0 (*n* = 432) | CT-SS 1 (*n* = 185) | CT-SS 2 (*n* = 385) | *P*-value[a] |
|---|---|---|---|---|
| **Age** | | | | <0.001 |
| <65 | 203 (47.0) | 69 (37.3) | 73 (19.0) | |
| 65–74 | 152 (35.2) | 77 (42.6) | 138 (35.8) | |
| >74 | 77 (17.8) | 39 (21.1) | 174 (45.2) | |
| **Sex** | | | | <0.001 |
| Female | 237 (54.9) | 83 (44.9) | 128 (33.2) | |
| Male | 195 (45.1) | 102 (55.1) | 257 (66.8) | |
| **ASA** | | | | <0.001 |
| 1 | 96 (22.2) | 47 (25.4) | 53 (13.8) | |
| 2 | 203 (47.0) | 86 (46.5) | 167 (43.4) | |
| 3 | 123 (28.5) | 49 (26.5) | 144 (37.4) | |
| 4 | 10 (2.3) | 3 (1.6) | 21 (5.5) | |
| **MUST** | | | | 0.036 |
| Low risk | 372 (87.1) | 130 (70.3) | 308 (80.0) | |
| Medium risk | 29 (6.8) | 24 (13.0) | 38 (9.9) | |
| High risk | 26 (6.1) | 26 (14.1) | 31 (2.1) | |
| Missing | 5 | 5 | 8 | |
| **Tumour site** | | | | 0.001 |
| Colon | 242 (56.0) | 101 (54.6) | 259 (67.3) | |
| Rectum | 190 (44.0) | 84 (45.4) | 126 (32.7) | |
| **TNM stage** | | | | 0.033 |
| I | 126 (29.2) | 42 (22.7) | 72 (18.7) | |
| II | 152 (35.2) | 80 (43.2) | 172 (44.7) | |
| III | 154 (35.6) | 63 (34.1) | 141 (36.6) | |
| **BMI** | | | | <0.001 |
| <20 | 17 (3.9) | 20 (10.8) | 21 (5.5) | |
| 20–24.9 | 84 (19.4) | 95 (51.4) | 113 (29.4) | |
| 25–29.9 | 151 (35.0) | 47 (25.4) | 139 (36.1) | |
| ≥30 | 180 (41.7) | 23 (12.4) | 112 (29.1) | |
| **High SFI** | | | 73 (19.0) | 0.008 |
| No | 52 (12.0) | 74 (40.0) | 73 (19.0) | |
| Yes | 380 (88.0) | 111 (60.0) | 312 (81.0) | |
| **High VFA** | | | | 0.566 |
| No | 98 (22.7) | 95 (51.4) | 78 (20.3) | |
| Yes | 334 (77.3) | 90 (48.6) | 307 (79.7) | |
| **mGPS** | | | | <0.001 |
| 0 | 345 (79.9) | 134 (72.4) | 252 (65.5) | |
| 1 | 46 (10.6) | 25 (13.5) | 38 (9.9) | |
| 2 | 41 (9.5) | 26 (14.1) | 95 (24.7) | |
| **NLR** | | | | <0.001 |
| <3 | 254 (58.8) | 89 (48.1) | 180 (46.8) | |
| 3–5 | 128 (29.6) | 64 (34.6) | 118 (30.6) | |
| >5 | 50 (11.6) | 32 (17.3) | 87 (22.6) | |
| **3 year survival** | | | | <0.001 |
| Yes | 373 (86.3) | 165 (89.2) | 296 (76.9) | |
| No | 59 (13.7) | 20 (10.8) | 89 (23.1) | |

Each cell is presented as *n* = (%).
[a]*P*-value is from $\chi^2$ analysis.

**Table 5a** The relationship between clinicopathological characteristics, BMI, systemic inflammation, and the CT sarcopenia score (CT-SS Martin 0/1 vs. 2) in patients undergoing potentially curative surgery for CRC (*n* = 1002)

| | OR (univariate) | *P*-value[a] | OR (multivariate) | *P*-value[a] |
|---|---|---|---|---|
| Age (<55/65–74/>74) | 2.11 (1.78–2.50) | <0.001 | 1.99 (1.66–2.38) | <0.001 |
| Sex (male/female) | 1.12 (0.86–1.44) | 0.389 | - | - |
| ASA (1/2/3/4) | 1.37 (1.14–1.64) | <0.001 | - | 0.228 |
| MUST (Low/medium/high risk) | 1.58 (1.28–1.95) | <0.001 | - | 0.716 |
| Tumour site (Colon/rectum) | 0.72 (0.55–0.93) | 0.012 | - | 0.762 |
| BMI (<20/20–24.9/35–29.9/>30 kg/m$^2$) | 0.62 (0.54–0.71) | <0.001 | 0.67 (0.57–0.78) | <0.001 |
| mGPS (0/1/2) | 1.74 (1.47–2.10) | <0.001 | 1.60 (1.33–1.93) | <0.001 |
| NLR (<3/3–5/>5) | 1.45 (1.22–1.71) | <0.001 | - | 0.082 |

[a]*P*-value is from binary logistics regression analysis.

**Table 5b** The relationship between clinicopathological characteristics, BMI, systemic inflammation and the CT sarcopenia score (CT-SS Caan/Xiao 0/1 vs. 2) in patients undergoing potentially curative surgery for CRC ($n$ = 1002)

| | OR (univariate) | $P$-value[a] | OR (multivariate) | $P$-value[a] |
|---|---|---|---|---|
| Age (<55/65–74/>74) | 2.37 (1.99–2.82) | <0.001 | 2.38 (1.99–2.86) | <0.001 |
| Sex (male/female) | 2.16 (1.66–2.82) | <0.001 | 2.32 (1.75–3.10) | <0.001 |
| ASA (1/2/3/4) | 1.53 (1.30–1.81) | <0.001 | - | 0.220 |
| MUST (Low/medium/high risk) | 1.02 (0.82–1.26) | 0.867 | - | - |
| Tumour site (colon/rectum) | 0.61 (0.47–0.79) | <0.001 | - | 0.164 |
| TNM stage (I/II/III) | 1.19 (1.00–1.41) | 0.044 | - | 0.056 |
| BMI (<20/20–24.9/35–29.9/>30 kg/m$^2$) | 0.96 (0.84–1.11) | 0.604 | - | - |
| High SFI (yes/no) | 1.10 (0.80–1.51) | 0.573 | - | - |
| mGPS (0/1/2) | 1.56 (1.32–1.85) | <0.001 | 1.42 (1.18–1.71) | <0.001 |
| NLR (<3/3–5/>5) | 1.37 (1.16–1.63) | <0.001 | - | 0.079 |

[a]$P$-value is from binary logistics regression analysis.

**Table 6a** The relationship between clinicopathological characteristics, BMI, CT-derived adipose measurements, CT sarcopenia score (CT-SS Martin), systemic inflammation, and overall survival in patients undergoing potentially curative surgery for CRC ($n$ = 1002)

| | HR (univariate) | $P$-value[a] | HR (multivariate) | $P$-value[a] |
|---|---|---|---|---|
| Age | 1.46 (1.19–1.77) | <0.001 | - | 0.291 |
| Sex | 1.21 (0.89–1.64) | 0.232 | - | - |
| ASA | 1.68 (1.37–2.05) | <0.001 | 1.56 (1.27–2.13) | <0.001 |
| MUST | 2.07 (1.72–2.48) | <0.001 | 1.43 (1.24–1.64) | <0.001 |
| Tumour site | 0.75 (0.55–1.04) | 0.080 | - | 0.445 |
| TNM stage | 1.65 (1.33–2.04) | <0.001 | 1.55 (1.24–1.95) | <0.001 |
| BMI | 0.71 (0.60–8.34) | <0.001 | - | 0.342 |
| High SFI | 0.77 (0.54–1.10) | 0.148 | - | - |
| High VFA | 0.85 (0.61–1.19) | 0.346 | - | - |
| CT sarcopenia score (0/1/2) | 1.36 (1.15–1.60) | <0.001 | - | 0.334 |
| mGPS | 1.55 (1.30–1.84) | <0.001 | 1.26 (1.05–1.52) | 0.015 |
| NLR | 1.46 (1.21–1.77) | <0.001 | 1.24 (1.02–1.51) | 0.035 |

[a]$P$-value is from univariate and multivariate Cox regression analysis.

**Table 6b** The relationship between clinicopathological characteristics, CT-derived adipose measurements, CT sarcopenia score (CT-SS Martin), systemic inflammation, and overall survival in patients undergoing potentially curative surgery for CRC, excluding BMI ($n$ = 1002)

| | HR (univariate) | $P$-value[a] | HR (multivariate) | $P$-value[a] |
|---|---|---|---|---|
| Age | 1.46 (1.19–1.77) | <0.001 | - | 0.194 |
| Sex | 1.21 (0.89–1.64) | 0.232 | - | - |
| ASA | 1.68 (1.37–2.05) | <0.001 | 1.48 (1.17–1.86) | 0.001 |
| MUST | 2.07 (1.72–2.48) | <0.001 | 1.79 (1.48–2.17) | <0.001 |
| Tumour site | 0.75 (0.55–1.04) | 0.080 | - | 0.809 |
| TNM stage | 1.65 (1.33–2.04) | <0.001 | 1.54 (1.23–1.93) | <0.001 |
| High SFI | 0.77 (0.54–1.10) | 0.148 | - | - |
| High VFA | 0.85 (0.61–1.19) | 0.346 | - | - |
| CT sarcopenia score (0/1/2) | 1.36 (1.15–1.60) | <0.001 | - | 0.227 |
| mGPS | 1.55 (1.30–1.84) | <0.001 | 1.26 (1.05–1.52) | 0.014 |
| NLR | 1.46 (1.21–1.77) | <0.001 | 1.25 (1.03–1.53) | 0.027 |

[a]$P$-value is from univariate and multivariate cox regression analysis.

suggest that the prognostic value of CT-derived muscle measurements is likely to be greatest when used in combination, such as the proposed CT-SS. Combining CT-derived muscle measurements has previously been proposed in the literature in the form of the unvalidated skeletal muscle gauge (SMG), the product of SMI × SMD. However, the methodology used did not account for the relative importance and accuracy of the individual components. In contrast, the proposed CT-SS is based on the measurement of SMI using standardized thresholds and methodology validated against other techniques.[7] Furthermore, the CT-SS utilizes standardized thresholds for SMD and accounts for potential confounding factors in the methodology, such as the phase of the contrast enhanced CT scan.[12,33] Therefore, the CT-SS reflects an incremental approach to defining sarcopenia and the impact on clinical outcomes.

The association between CT-derived sarcopenia and TNM stage was found to be inconsistent and threshold dependent in the present study (see *Tables* 4a and 4b). These results may suggest that surveillance of muscularity should occur

**Table 7a** The relationship between clinicopathological characteristics, BMI, CT-derived adipose measurements, CT sarcopenia score (CT-SS Caan/Xiao), systemic inflammation, and overall survival in patients undergoing potentially curative surgery for CRC ($n$ = 1002)

| | HR (univariate) | $P$-value[a] | HR (multivariate) | $P$-value[a] |
|---|---|---|---|---|
| Age | 1.46 (1.19–1.77) | <0.001 | - | 0.293 |
| Sex | 1.21 (0.89–1.64) | 0.232 | - | - |
| ASA | 1.68 (1.37–2.05) | <0.001 | 1.43 (1.14–1.81) | <0.001 |
| MUST | 2.07 (1.72–2.48) | <0.001 | 1.80 (1.49–2.17) | <0.001 |
| Tumour site | 0.75 (0.55–1.04) | 0.080 | - | 0.521 |
| TNM stage | 1.65 (1.33–2.04) | <0.001 | 1.52 (1.21–1.91) | <0.001 |
| BMI | 0.71 (0.60–8.34) | <0.001 | - | 0.362 |
| High SFI | 0.77 (0.54–1.10) | 0.148 | - | - |
| High VFA | 0.85 (0.61–1.19) | 0.346 | - | - |
| CT sarcopenia score (0/1/2) | 1.39 (1.17–1.64) | <0.001 | - | 0.077 |
| mGPS | 1.55 (1.30–1.84) | <0.001 | 1.22 (1.01–1.48) | 0.040 |
| NLR | 1.46 (1.21–1.77) | <0.001 | - | 0.052 |

[a]*P*-value is from univariate and multivariate Cox regression analysis.

**Table 7b** The relationship between clinicopathological characteristics, CT-derived adipose measurements, CT sarcopenia score (CT-SS Caan/Xiao), systemic inflammation, and overall survival in patients undergoing potentially curative surgery for CRC, excluding BMI ($n$ = 1002)

| | HR (univariate) | $P$-value[a] | HR (multivariate) | $P$-value[a] |
|---|---|---|---|---|
| Age | 1.46 (1.19–1.77) | <0.001 | - | 0.376 |
| Sex | 1.21 (0.89–1.64) | 0.232 | - | - |
| ASA | 1.68 (1.37–2.05) | <0.001 | 1.53 (1.24–1.88) | <0.001 |
| MUST | 2.07 (1.72–2.48) | <0.001 | 1.77 (1.46–2.14) | <0.001 |
| Tumour site | 0.75 (0.55–1.04) | 0.080 | - | 0.442 |
| TNM stage | 1.65 (1.33–2.04) | <0.001 | 1.54 (1.22–1.93) | <0.001 |
| High SFI | 0.77 (0.54–1.10) | 0.148 | - | - |
| High VFA | 0.85 (0.61–1.19) | 0.346 | - | - |
| CT sarcopenia score (0/1/2) | 1.39 (1.17–1.64) | <0.001 | - | 0.077 |
| mGPS | 1.55 (1.30–1.84) | <0.001 | 1.22 (1.01–1.48) | 0.040 |
| NLR | 1.46 (1.21–1.77) | <0.001 | - | 0.052 |

[a]*P*-value is from univariate and multivariate Cox regression analysis.

across the different stages of the patient trajectory and even at the earlier TNM stages. As such, the present observations are in keeping with those of a recent review by our group, of 160 studies of CT-derived SMI and SMD that found poor muscle status was endemic in patients with cancer, suggesting that tumour stage was not a major determinant of sarcopenia.[6] Furthermore, in the review we also hypothesized that the prognostic value of sarcopenia may reflect its measure of the nutritional and functional reserve of the cancer patient and that it is imperative that such body composition measurements be used in conjunction with potential confounding factors such as systemic inflammation.[6] Hacker and co-workers reported similar observations in a recent longitudinal study of patients with advanced gastric and oesophagogastric junctional cancer.[34] Therefore, taken together, the studies support this hypothesis and that sarcopenia measurements (such as the CT-SS) should be used in conjunction with measures of systemic inflammation.

In the present cohort, a low skeletal muscle mass and density were found to be prevalent across disease stages, on a background of CT-derived obesity, in patients with colorectal cancer. These observations are consistent with recent work by Martin and co-workers who reported that a low skeletal muscle mass and density were endemic in an obese population, across a range histological subtypes and disease stages.[35] However, it was of interest that neither of the CT-derived measures of adiposity such as SFI and VFA had prognostic value. Furthermore, neither the presence of a high SFI or high VFA could further stratify survival in patients who had CT-derived sarcopenic (CT-SS $\geq$ 1, $P$ = 0.209 and $P$ = 0.674, respectively). Therefore, the present results are consistent with the work of Caan and co-workers.[28]

There are a number of limitations to the present study. Firstly, this is a single centre study and may be subject to bias. However, the present observations were made using routine clinical available measures and should be readily validated. Lastly, CT analysis of SMD has been shown to be dependent on methodology, such contrast enhancement.[36] However, in the present study only patients who underwent CT-imaging with intravenous contrast were included in the analysis.

In conclusion, CT-derived muscle measurements, SMI and SMD, when used in combination have additional prognostic value in patients with colorectal cancer. The objective CT-SS was significantly associated with older age, co-morbidity, nutritional risk, systemic inflammation and poorer survival, irrespective of thresholds used.

## Funding

This study was funded by the Academic Unit of Surgery, University of Glasgow.

## Conflict of interest

None declared.

## References

1. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;**48**:16–31.
2. Granger CL, McDonald CF, Parry SM, Oliveira CC, Denehy L. Functional capacity, physical activity and muscle strength assessment of individuals with non-small cell lung cancer: a systematic review of instruments and their measurement properties. *BMC Cancer*. 2013;**13**:135. https://doi.org/10.1186/1471-2407-13-135
3. Dolan RD, Daly LE, Simmons CP, Ryan AM, Sim WM, Fallon M, et al. The Relationship between ECOG-PS, mGPS, BMI/WL Grade and Body Composition and Physical Function in Patients with Advanced Cancer. *Cancer*. 2020;**12**:1187. https://doi.org/10.3390/cancers12051187
4. Martin L, Birdsell L, Macdonald N, Reiman T, Clandinin MT, McCargar LJ, et al. Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. *J Clin Oncol Off J Am Soc Clin Oncol*. 2013;**31**:1539–1547.
5. Prado CM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. *Lancet Oncol*. 2008;**9**:629–635.
6. McGovern J, Dolan RD, Horgan PG, Laird BJ, McMillan DC. Computed tomography-defined low skeletal muscle index and density in cancer patients: observations from a systematic review. *J Cachexia Sarcopenia Muscle*. n/a. **12**:1408–1417.
7. Albano D, Messina C, Vitale J, Sconfienza LM. Imaging of sarcopenia: old evidence and new insights. *Eur Radiol*. 2020;**30**:2199–2208.
8. Kim D, Sun JS, Lee YH, Lee JH, Hong J, Lee JM. Comparative assessment of skeletal muscle mass using computerized tomography and bioelectrical impedance analysis in critically ill patients. *Clin Nutr (Edinburgh, Scotland)*. 2019;**38**:2747–2755.
9. Bredella MA, Ghomi RH, Thomas BJ, Torriani M, Brick DJ, Gerweck AV, et al. Comparison of DXA and CT in the assessment of body composition in premenopausal women with obesity and anorexia nervosa. *Obesity (Silver Spring)*. 2010;**18**:2227–2233.
10. Amini B, Boyle SP, Boutin RD, Lenchik L. Approaches to Assessment of Muscle Mass and Myosteatosis on Computed Tomography: A Systematic Review. *J Gerontol A Biol Sci Med Sci*. 2019;**74**:1671–1678.
11. Aubrey J, Esfandiari N, Baracos VE, Buteau FA, Frenette J, Putman CT, et al. Measurement of skeletal muscle radiation attenuation and basis of its biological variation. *Acta Physiol (Oxf)*. 2014;**210**:489–497.
12. Abbass T, Dolan RD, McMillan DC. Computed tomography-derived body composition analysis in patients with advanced cancer: clinical utility and future research. *Curr Opin Support Palliat Care*. 2020;**14**:309–315.
13. Correa-de-Araujo R, Addison O, Miljkovic I, Goodpaster BH, Bergman BC, Clark RV, et al. Myosteatosis in the Context of Skeletal Muscle Function Deficit: An Interdisciplinary Workshop at the National Institute on Aging. *Front Physiol*. 2020;**11**:963. https://doi.org/10.3389/fphys.2020.00963
14. Zamboni M, Gattazzo S, Rossi AP. Myosteatosis: a relevant, yet poorly explored element of sarcopenia. *Eur Geriatr Med*. 2019;**10**:5–6.
15. West MA, van Dijk DPJ, Gleadowe F, Reeves T, Primrose JN, Abu Hilal M, et al. Myosteatosis is associated with poor physical fitness in patients undergoing hepatopancreatobiliary surgery. *J Cachexia Sarcopenia Muscle*. 2019;**10**:860–871.
16. Lee CM, Kang J. Prognostic impact of myosteatosis in patients with colorectal cancer: a systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle*. 2020;**11**:1270–1282.
17. Vergara-Fernandez O, Trejo-Avila M, Salgado-Nesme N. Sarcopenia in patients with colorectal cancer: A comprehensive review. *World J Clin Cases*. 2020;**8**:1188–1202.
18. Trejo-Avila M, Bozada-Gutiérrez K, Valenzuela-Salazar C, Herrera-Esquivel J, Moreno-Portillo M. Sarcopenia predicts worse postoperative outcomes and decreased survival rates in patients with colorectal cancer: a systematic review and meta-analysis. *Int J Colorectal Dis*. 2021;**36**:1077–1096.
19. Meza-Valderrama D, Marco E, Dávalos-Yerovi V, Muns MD, Tejero-Sánchez M, Duarte E, et al. Sarcopenia, Malnutrition, and Cachexia: Adapting Definitions and Terminology of Nutritional Disorders in Older People with Cancer. *Nutrients*. 2021;**13**:761. https://doi.org/10.3390/nu13030761
20. Abbass T, Dolan RD, Laird BJ, McMillan DC. The Relationship between Imaging-Based Body Composition Analysis and the Systemic Inflammatory Response in Patients with Cancer: A Systematic Review. *Cancer*. 2019;**11**:1304. https://doi.org/10.3390/cancers11091304
21. Almasaudi AS, McSorley ST, Dolan RD, Edwards CA, McMillan DC. The relation between Malnutrition Universal Screening Tool (MUST), computed tomography–derived body composition, systemic inflammation, and clinical outcomes in patients undergoing surgery for colorectal cancer. *Am J Clin Nutr*. 2019;**110**:1327–1334.
22. Dripps RD, Lamont A, Eckenhoff JE. The Role of Anesthesia in Surgical Mortality. *JAMA*. 1961;**178**:261–266.
23. Sobin LH, Fleming ID. TNM Classification of Malignant Tumors, fifth edition (1997). Union Internationale Contre le Cancer and the American Joint Committee on Cancer. *Cancer*. 1997;**80**:1803–1804.
24. McSorley ST, Black DH, Horgan PG, McMillan DC. The relationship between tumour stage, systemic inflammation, body composition and survival in patients with colorectal cancer. *Clin Nutr*. 2018;**37**:1279–1285.
25. Feliciano EMC, Kroenke CH, Meyerhardt JA, Prado CM, Bradshaw PT, Kwan ML, et al. Association of Systemic Inflammation and Sarcopenia With Survival in Nonmetastatic Colorectal Cancer: Results From the C SCANS Study. *JAMA Oncol*. 2017;**3**:e172319. https://doi.org/10.1001/jamaoncol.2017.2319
26. Ebadi M, Martin L, Ghosh S, Field CJ, Lehner R, Baracos VE, et al. Subcutaneous adiposity is an independent predictor of mortality in cancer patients. *Br J Cancer*. 2017;**117**:148–155.
27. Doyle SL, Bennett AM, Donohoe CL, Mongan AM, Howard JM, Lithander FE, et al. Establishing computed tomography-defined visceral fat area thresholds for use in obesity-related cancer research. *Nutr Res (New York, NY)*. 2013;**33**:171–179.
28. Caan BJ, Meyerhardt JA, Kroenke CH, Alexeeff S, Xiao J, Weltzien E, et al. Explaining the Obesity Paradox: The Association between Body Composition and Colorectal Cancer Survival (C-SCANS Study). *Cancer Epidemiol Biomarkers Prev*. 2017;**26**:1008–1015.
29. Xiao J, Caan BJ, Weltzien E, Cespedes Feliciano EM, Kroenke CH, Meyerhardt JA, et al. Associations of pre-existing co-morbidities with skeletal muscle mass and radiodensity in patients with non-metastatic colorectal cancer. *J Cachexia Sarcopenia Muscle*. 2018;**9**:654–663.
30. McMillan DC. Systemic inflammation, nutritional status and survival in patients with

cancer. *Curr Opin Clin Nutr Metab Care*. 2009;**12**:223–226.
31. Shachar SS, Williams GR, Muss HB, Nishijima TF. Prognostic value of sarcopenia in adults with solid tumours: A meta-analysis and systematic review. *Eur J Cancer*. 2016;**57**:58–67.
32. Aleixo GFP, Shachar SS, Nyrop KA, Muss HB, Malpica L, Williams GR. Myosteatosis and prognosis in cancer: Systematic review and meta-analysis. *Crit Rev Oncol Hematol*. 2020;**145**:102839. https://doi.org/10.1016/j.critrevonc.2019.102839
33. Engelke K, Museyko O, Wang L, Laredo J-D. Quantitative analysis of skeletal muscle by computed tomography imaging-State of the art. *J Orthop Translat*. 2018;**15**:91–103.
34. Hacker UT, Hasenclever D, Baber R, Linder N, Busse H, Obermannova R, et al. Modified Glasgow prognostic score (mGPS) is correlated with sarcopenia and dominates the prognostic role of baseline body composition parameters in advanced gastric and esophagogastric junction cancer patients undergoing first-line treatment from the phase III EXPAND trial. *Ann Oncol*. 2022;**33**:685–692.
35. Martin L, Gioulbasanis I, Senesse P, Baracos VE. Cancer-Associated Malnutrition and CT-Defined Sarcopenia and Myosteatosis Are Endemic in Overweight and Obese Patients. *JPEN J Parenter Enteral Nutr*. 2020;**44**:227–238.
36. van Vugt JLA, Coebergh van den Braak RRJ, Schippers HJW, Veen KM, Levolger S, de Bruin RWF, et al. Contrast-enhancement influences skeletal muscle density, but not skeletal muscle mass, measurements on computed tomography. *Clin Nutr*. 2018;**37**:1707–1714.