Functional Compromise Reflected by Sarcopenia, Frailty, and Nutritional Depletion Predicts Adverse Postoperative Outcome After Colorectal Cancer Surgery

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Objective: To determine the association of sarcopenia with postoperative morbidity and mortality after colorectal surgery.

Background: Functional compromise in elderly colorectal surgical patients is considered as a significant factor of impaired postoperative recovery. Therefore, the predictive value of preoperative functional compromise assessment was investigated. Sarcopenia is a hallmark of functional compromise.

Methods: A total of 310 consecutive patients who underwent oncologic colorectal surgery were included in a prospective digital database. Sarcopenia was assessed using the L3 muscle index utilizing Osirix on preoperative computed tomography. Groningen Frailty Indicator and Short Nutritional Assessment Questionnaire scores were used to assess frailty and nutritional compromise. Predictors for anastomotic leakage, sepsis, and mortality were analyzed by logistic regression analysis.

Results: Age was an independent predictor of mortality [$P = 0.04$; odds ratio, 1.17; 95% confidence interval (CI), 1.01–1.37]. Thirty-day/in-hospital mortality rate in sarcopenic patients was 8.8% versus 0.7% in nonsarcopenic patients ($P = 0.001$; odds ratio, 15.5; 95% CI, 2.00–120). Sarcopenia was not predictive for anastomotic leakage or sepsis. Combination of high Short Nutritional Assessment Questionnaire score, high Groningen Frailty Indicator score, and sarcopenia strongly predicted sepsis ($P = 0.001$; odds ratio, 25.1; 95% CI, 5.11–123), sensitivity, 46%; specificity, 97%; positive likelihood ratio, 13 (95% CI, 4.4–38); negative likelihood ratio, 0.57 (95% CI, 0.33–0.97).

Conclusions: Functional compromise in colorectal cancer surgery is associated with adverse postoperative outcome. Assessment of functional compromise by means of a nutritional questionnaire (Short Nutritional Assessment Questionnaire), a frailty questionnaire (Groningen Frailty Indicator), and sarcopenia measurement (L3 muscle index) can accurately predict postoperative sepsis.

Keywords: colorectal surgery, frailty, functional compromise, nutritional depletion, sarcopenia

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With an increasingly ageing population, the number of older patients with cancer is concomitantly rising. Currently, 50% of patients with colorectal cancer are 70 years or older.[1] Older patients are at increased risk for developing perioperative complications and suffer from higher mortality rates.[2] Postoperative recovery plays a crucial role in cancer treatment with respect to survival, morbidity, and quality of life.[3–5] Hence, preoperative assessment is important to identify patients at risk for developing postoperative complications. Widely accepted risk assessments are, however, considered to be subjective and imprecise and not focused on patients with cancer.[6]

It is hypothesized that functional compromise in the older surgical patient is a significant predictor of postoperative complications.[7,8] A widely investigated aspect of functional compromise is frailty. Frailty is a state of increased vulnerability toward stressors in older individuals, leading to an increased risk of developing adverse health outcomes.[9] However, the definition of frailty remains controversial and there is no consensus about the clinical use of frailty as a preoperative predictor for postoperative outcome in elderly patients.[7] Weight loss, low muscle strength, reduced physical activity, exhaustion, and decreased walking speed are elements of a physical definition of frailty,[6,8] whereas comorbidity, polypharmacy use, physical functioning, nutritional and cognitive status, depression, and social support are a more multidimensional tool to assess frailty.[10–12] In addition, sarcopenia is an important factor in functional compromise and depletion of skeletal muscle can occur in normal weight, overweight, and obese patients and therefore does not equal ordinary weight loss or cachexia.[13,14] Malnutrition is another key element of functional compromise that is associated with poor clinical outcome.[15] In elderly patients, preoperative malnutrition is common and worsens the condition of this already vulnerable population.[16]

In this study, we investigated whether functional compromise is associated with postoperative morbidity and mortality after colorectal surgery. The following parameters of functional compromise were evaluated: computed tomography (CT)-based measurement of muscle mass, Groningen Frailty Index (GFI),[17] and Short Nutritional Assessment Questionnaire (SNAQ).[18]

MATERIALS AND METHODS

Patients

All consecutive patients who underwent oncologic colorectal surgery in a single nonacademic center with a dedicated team of colorectal surgeons from January 2010 until May 2012 were enrolled in a prospective digital cohort and analyzed retrospectively. The only exclusion criterion was unavailability of a preoperative CT scan. Data in the database included characteristics of the primary tumor and oncologic staging, specifications of surgical treatment, chemotherapy, radiotherapy, and postoperative complications and included a

preoperative CT scan of the abdomen, which was performed routinely for tumor staging.

Complications

The following complications were analyzed prospectively in detail: anastomotic leakage (surgically and/or radiologically) and/or intra-abdominal abscess diagnosed by CT examination or treated by percutaneous drainage or surgery, sepsis and septic shock [defined as ≥2 of the following criteria positive: (1) temperature >38°C or <36°C; (2) heart rate >90 beats/min; (3) respiratory rate >20 breaths/min or $Paco_2$ <32 mm Hg; (4) white blood cell count >12 × 10^9/L, <4 × 10^9/L, or >10% immature (band) forms plus documented infection and hypotension despite adequate fluid resuscitation (in case of septic shock)[19]], and postoperative mortality (within 30 days postoperatively or within same period of hospital admission). The 30-day mortality for patients discharged within this period was verified by checking the municipal personal records database.

Preoperative CT-based Muscle Measurements

All patients underwent a CT scan of the abdomen as part of routine preoperative assessment, which was delivered on CD-ROM or DVD. Measurements were performed using Osirix version 3.3 (32-bit; http://www.osirix-viewer.com). The cross-sectional skeletal muscle surface (cm^2) assessment of sarcopenia was performed at the level of the third lumbar vertebra (L3) on 2 consecutive transversal coupes on which both vertebral spines were visible.[20] The "Grow Region (2D/3D Segmentation)" tool in the menu of the program facilitated to automatically select all skeletal muscle mass in 1 coupe. The distinction between different tissues is based on Hounsfield units (HU). A threshold range of −30 HU to +110 HU was used for skeletal muscle. Muscles measured were psoas, paraspinal, transverse abdominal, external oblique, internal oblique, and rectus abdominis muscles (Fig. 1). Hand adjustment of the selected areas was performed if necessary, and the muscle area was calculated automatically.[20] The averages of the 2 measurements were used for calculations. Two investigators independently measured all L3 muscle area surface parameters (J.v.V. and J.T.). A third investigator (K.R.) performed a random control measurement on 10% of the CT scans. All investigators did not have specific skills in radiology.

FIGURE 1. CT scan at the third lumbar vertebral level. The following skeletal muscles are outlined in red: psoas, paraspinal, transverse abdominal, external oblique, internal oblique, and rectus abdominis muscles. This female sarcopenic patient had an L3 muscle index of 34.3 cm^2/m^2.

Sarcopenia

The L3 muscle area surfaces were normalized for patient height to calculate the L3 muscle index and expressed in cm^2/m^2. The cutoff values used for sarcopenia were 52.4 cm^2/m^2 for men and 38.5 cm^2/m^2 for women, based on the method of Prado et al.[14]

Groningen Frailty Indicator

The GFI has been developed as a simple screening instrument for frailty.[17] It screens on physical, cognitive, social, and emotional items (Appendix 1). The maximum score is 15 points. Patients scoring 5 or more points were considered frail.[17] A trained nurse routinely obtained GFI scores at preoperative consultation or hospital admission in patients 70 years or older.

Short Nutritional Assessment Questionnaire

The SNAQ is a valid and reproducible tool to detect malnourished hospitalized patients without the need to calculate percentage weight loss or body mass index.[18] The maximum score is 5 points (Appendix 2). Patients with a score of 3 points or more on the SNAQ were classified as malnourished (requiring nutritional support and supervision by a dietician).[18] A trained nurse routinely obtained SNAQ scores at preoperative consultation or hospital admission.

Statistical Analysis

Frequencies are presented as absolute numbers and percentages. Continuous data are presented as mean (standard error of the mean). Normality was tested using the Kolmogorov-Smirnov test. Differences between groups were analyzed using the Pearson χ^2 test for dichotomous parameters. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by logistic regression analysis. For the calculation of significant predictors of mortality and complications, univariate analyses with clinically relevant parameters were performed. Significant predictors ($P < 0.05$) or predictors showing a trend toward significance ($0.05 \leq P < 0.20$) based on univariate analysis were entered into multivariate logistic regression analysis. Interactions between sarcopenia, GFI scores, and SNAQ scores were tested. Functional compromise was defined as sarcopenia, high GFI score, and high SNAQ score. Diagnostic accuracy of functional compromise assessment to predict postoperative complications was evaluated by calculating sensitivity, specificity, positive likelihood ratio (LR+), and negative likelihood ratio (LR−) using crosstabs. The interobserver agreement (J.v.V., J.T., and K.R.) of the L3 muscle index assessment of sarcopenia was analyzed by the Pearson correlation and Cohen κ coefficients. Two-tailed P values less than 0.05 were considered significant. All statistical analyses were performed using SPSS (version 20.0; SPSS Inc, Chicago, IL).

RESULTS

Patients

A total of 340 patients were included in the prospective database. In 30 patients, no staging CT scan was available, for which the main reason was emergency surgery. Therefore, 310 patients undergoing both elective and acute colorectal resections were included in the analyses of the current study. The patient characteristics are listed in Table 1. Of these 310 patients, 148 (47.7%) were identified as sarcopenic as defined by muscle index at L3 level; 90 of 155 (58.1%) were males and 58 of 155 (37.4%) females. Mean L3 muscle indexes for males and females were 51.5 (0.65) cm^2/m^2 and

TABLE 1. Patient Characteristics

	No. Patients (%)	Mean (SEM)
Sex		
Male	155 (50.0)	
Female	155 (50.0)	
Age, yr		69 (0.6)
>70	159 (51.3)	
BMI, kg/m^2		
>25	182 (58.7)	
Length of hospital stay, d		11 (0.6)
ASA class		
I	17 (5.5)	
II	219 (70.6)	
III	62 (20.0)	
IV	12 (3.9)	
Laparoscopy	33 (10.6)	
Primary anastomosis	249 (80.3)	
Tumor location		
Colon	205 (66.1)	
Rectum	105 (33.9)	
Complications		
Anastomotic leakage and/or abscess	37 (14.9)	
Sepsis	14 (4.5)	
Death	14 (4.5)	
Cause-related death	8 (2.6)	

ASA indicates American Society of Anesthesiologists; BMI, body mass index.

TABLE 2. Causes of Mortality

	Cause	Postoperative Day of Mortality
Sarcopenic patients (n = 13)		
1	Pneumonia, sepsis, cardiorespiratory failure	47
2	Sepsis of surgical site origin	5
3	Sepsis of surgical site origin	2
4	Sepsis of surgical site origin	2
5	Cardiorespiratory failure after anastomotic leakage	25
6	Pneumonia	30
7	Sepsis of surgical site origin	7
8	Pneumonia	3
9	Cardiorespiratory failure	8
10	Pneumonia	7
11	Unknown cause, probably pneumonia	35
12	Intraoperative presacral bleeding	0
13	Gastric hemorrhage	10
Nonsarcopenic patients (n = 1)		
14	Anastomotic leakage	25

40.7 (0.53) cm^2/m^2, respectively. Of patients 70 years or older, 41 (24.6%) were frail as defined by a GFI score of 5 or more. SNAQ scores were 3 points or higher in 36 patients (11%).

Interobserver Agreement of CT-based Muscle Measurement by Osirix

Two independent investigators measured the L3 muscle areas of all patients, showing a strong and significant correlation ($R^2 = 0.98$; $P < 0.0001$). Bland-Altman analysis produced 95% limits of agreement, −5.9% to 8.7%. The κ of sarcopenia assessment by CT image analysis using Osirix was 0.87 (95% CI, 0.82–0.93). The random control measurement on 10% of the CT scans by a third investigator yielded excellent correlation ($R^2 = 0.98$; $P < 0.0001$) and a κ value of 0.74 (95% CI, 0.46–1.00).

Mortality

Fourteen patients (4.5%) died within 30 days or during hospital admission. Causes of mortality are listed in Table 2. In univariate analyses, sarcopenia ($P = 0.009$), male sex ($P = 0.02$), age ($P = 0.002$), epidural analgesia ($P = 0.14$), medical history of abdominal surgery ($P = 0.02$), ASA (American Society of Anesthesiologists) classification ($P = 0.02$), and stage 3 to 4 disease ($P = 0.14$) were significant predictors of postoperative mortality or showed a trend toward significance. Multivariate logistic regression revealed male sex (OR, 49.29; 95% CI, 2.48–978.4; $P = 0.01$), sarcopenia (OR, 43.30; 95% CI, 2.74–685.2; $P = 0.007$), age (OR, 1.17; 95% CI, 1.01–1.37; $P = 0.04$), and medical history of abdominal surgery (OR, 31.16; 95% CI, 3.09–313.9; $P = 0.004$) being independent predictors of mortality. Logistic regression results are summarized in Table 3.

To evaluate the effect of functional compromise on mortality in more detail, interactions between SNAQ score 3 or more, GFI score 5 or more, and sarcopenia were studied. None of the interactions increased the predictive value of sarcopenia.

Anastomotic Leakage

The incidence of anastomotic leakage and/or intra-abdominal abscess was 37 (14.9%) in patients with a primary anastomosis. Mortality within this group was 9.3%. Significant predictors or predictors showing a trend toward anastomotic leakage and/or intra-abdominal abscess were sarcopenia ($P = 0.13$), SNAQ score 3 or more ($P = 0.08$), medical history of abdominal surgery ($P = 0.06$), surgery of the rectum ($P = 0.02$), open surgery ($P = 0.10$), stapled anastomosis ($P = 0.06$), stage 3 to 4 disease ($P = 0.04$), and need for blood transfusion ($P < 0.001$). In multivariate analysis, stage 3 to 4 disease (OR, 3.68; 95% CI, 1.18–11.4; $P = 0.02$) and need for blood transfusion (OR, 7.81; 95% CI, 2.81–21.8; $P = 0001$) were independent predictors of anastomotic leakage and/or intra-abdominal abscess. Logistic regression results are summarized in Table 4.

To evaluate the effect of functional compromise on anastomotic leakage in more detail, interactions between SNAQ score 3 or more, GFI score 5 or more, and sarcopenia were studied. None of the interactions were significantly predictive of anastomotic leakage.

Sepsis

Fourteen patients (4.5%) developed sepsis. Mortality within this group was 36%. Univariate analysis demonstrated that GFI score 5 or more ($P = 0.03$), SNAQ score 3 or more ($P = 0.003$), age ($P = 0.03$), epidural analgesia ($P = 0.14$), and medical history of abdominal surgery ($P = 0.17$) were significant predictors of sepsis or showed a trend toward significance. In multivariate logistic regression analysis, SNAQ score 3 or more was independently predictive of postoperative sepsis (OR, 4.37; 95% CI, 1.07–17.9; $P = 0.04$). Logistic regression results are summarized in Table 5.

To evaluate the effect of functional compromise on sepsis in more detail, interactions between SNAQ score 3 or more, GFI score 5 or more, and sarcopenia were studied. The interaction between SNAQ score 3 or more and GFI score 5 or more compared with SNAQ score 3 or more alone increased the capability of predicting postoperative sepsis (OR, 13.1; 95% CI, 3.02–57.2; $P = 0.001$). The interactions between SNAQ score 3 or more, GFI score 5 or more, and sarcopenia further increased the risk of sepsis (OR, 25.1; 95% CI, 5.11–123; $P = 0.001$).

TABLE 3. Logistic Regression Analysis for Risk Factors of Mortality

		Univariate Analysis		Multivariate Analysis	
	Mortality Rate	**OR**	***P***	**OR**	***P***
Sarcopenia					
No	1/162	1		1	
Yes	13/148	15.50 (2.00–120.0)	0.009	43.30 (2.74–685.2)	0.007
GFI score ≥5					
No	8/114	1			
Yes	3/39	0.68 (0.09–5.45)	0.72		
SNAQ score ≥3					
No	8/185	1			
Yes	4/112	0.82 (0.24–2.79)	0.75		
Sex					
Female	2/155	1		1	
Male	12/155	6.42 (1.41–29.18)	0.02	49.29 (2.48–978.4)	0.01
Age		1.12 (1.04–1.20)	0.002	1.17 (1.01–1.37)	0.04
Epidural					
No	8/117	1			
Yes	6/193	0.44 (0.15–1.29)	0.14		
Previous abdominal surgery					
No	5/208	1		1	
Yes	9/102	3.93 (1.28–12.05)	0.02	31.16 (3.09–313.9)	0.004
ASA class					
I	0/17	1	0.02		
II	5/219	∞ (0.00–∞)	1.00		
III	8/62	∞ (0.00–∞)	1.00		
IV	1/12	∞ (0.00–∞)	1.00		
Disease stage					
1–2	3/107	1			
3–4	9/122	2.76 (0.73–10.48)	0.14		
BMI >25 kg/m^2					
No	8/128	1			
Yes	6/182	0.51 (0.17–1.51)	0.23		
Smoking					
No	4/170	1			
Yes	8/140	2.12 (0.62–7.21)	0.23		
Diabetes					
No	11/252	1			
Yes	3/58	1.20 (0.32–4.43)	0.79		

Definition of mortality: 30-day mortality and/or in-hospital mortality. Values in parentheses are 95% CIs.
ASA indicates American Society of Anesthesiologists; BMI, body mass index.

Diagnostic Accuracy of SNAQ/GFI/Sarcopenia Score to Predict Sepsis

As a strong association of functional compromise (the combination of high SNAQ score, high GFI score, and sarcopenia) with sepsis was shown by the previous data, the clinical applicability of this functional compromise assessment needed further exploration. Therefore, the diagnostic accuracy of (preoperative) functional compromise assessment to predict postoperative sepsis was investigated. A positive functional compromise test was defined as SNAQ score 3 or more, GFI score 5 or more, and sarcopenia (L3 muscle index <52.4 cm^2/m^2 for men, and <38.5 cm^2/m^2 for women). This resulted in sensitivity of 46%; specificity 97%, LR+ 13 (95% CI, 4.4–38) and LR− 0.57 (95% CI, 0.33–0.97). Subgroup analysis of patients undergoing rectal surgery revealed a higher diagnostic accuracy: sensitivity, 67%; specificity, 98%; LR+, 29 (95% CI, 3.61–239); and LR−, 0.34 (95% CI, 0.07–1.69).

DISCUSSION

The association of functional compromise and unfavorable postoperative outcome in colorectal surgery has been described before.[8,10] Robinson and coworkers[10] investigated frailty, an important aspect of functional compromise, using a scoring system based on 7 items of different domains and showed that frailty increased health care costs and 30-day readmission rates. However, postoperative complications were not specified.[10] Another study involving elderly patients undergoing colorectal surgery demonstrated a 4-fold increased risk for major postoperative complications when frailty was present.[8] The frailty assessment used was based on the criteria of Fried *et al*,[21] that is, 3 or more items of the following: unintentional weight loss (10 lb in past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity. The current study underlines and extends the abovementioned findings for several reasons. First, this is thus far the largest cohort addressing the influence of functional compromise including frailty on postoperative outcome in colorectal surgery. Second, the proposed functional compromise assessment is easy to perform as staging CT scans are routinely performed and SNAQ and GFI questionnaires can be completed in only few minutes. In most Dutch hospitals, nutritional assessment and GFI assessments are part of standard care at hospital admission. Third, this study highlights metabolic and functional compromise to be associated with postoperative mortality in colorectal surgery.

As in this study, elderly patients showed higher rates of short-term postoperative mortality and sepsis, pointing at the role of

TABLE 4. Logistic Regression Analysis for Risk Factors of Anastomotic Leakage

		Univariate Analysis		Multivariate Analysis	
	Anastomotic Leakage Rate	**OR**	***P***	**OR**	***P***
Sarcopenia					
No	24/133	1			
Yes	13/116	0.57 (0.28–1.19)	0.13		
GFI score ≥5					
No	12/92	1			
Yes	5/30	1.33 (0.42–4.15)	0.62		
SNAQ score ≥3					
No	21/147	1			
Yes	14/91	2.33 (0.90–6.00)	0.08		
Sex					
Female	16/126	1			
Male	21/123	1.42 (0.70–2.86)	0.33		
Age		0.99 (0.96–1.02)	0.57		
Previous abdominal surgery					
No	20/168	1			
Yes	17/81	1.97 (0.97–4.00)	0.06		
Disease stage					
1–2	6/97	1		1	
3–4	17/109	2.80 (1.06–7.43)	0.04	3.68 (1.18–11.4)	0.02
Tumor location					
Colon	22/188	1			
Rectum	15/61	2.46 (1.18–5.12)	0.02		
Type of surgery					
Laparoscopy	1/29	1			
Laparotomy	36/220	5.48 (0.72–41.56)	0.10		
Anastomosis					
Manual	15/137	1			
Stapled	21/106	2.01 (0.98–4.12)	0.06		
Blood transfusion					
No	19/207	1		1	
Yes	18/42	7.42 (3.43–16.06)	<0.001	7.81 (2.81–21.8)	<0.001
Smoking					
No	17/133	1			
Yes	20/116	1.47 (0.70–3.08)	0.30		
Diabetes					
No	31/203	1			
Yes	6/46	0.83 (0.33–2.13)	0.70		

Anastomotic leakage and/or intra-abdominal abscess in 249 patients with primary anastomosis. Values in parentheses are 95% CIs.

sepsis causing postoperative death in these patients. Moreover, 9 of 13 mortality cases in sarcopenic patients were caused by sepsis or pneumonia. In the context of major abdominal surgery, it could be assumed that sepsis may be the consequence of inadequate gut barrier function, especially in the cancer-bearing host. Loss of intestinal barrier function is indeed correlated with sepsis.[22–25] In addition, it has been demonstrated that gut barrier dysfunction and endotoxemia develop concurrently with cachexia in a mouse model of colorectal neoplasia.[26] In the current study, low muscle mass strongly correlated with mortality; however, the link with sepsis could not be made statistically. It could be hypothesized that sarcopenia reflects a state of prolonged catabolism impairing host immune function and leading to an inadequate response to inflammatory stimuli. A strong association with sepsis was found when muscle mass assessment was combined with SNAQ and GFI scores, indicating that muscle wasting as a reflection of the more comprehensive syndrome of functional compromise predicts postoperative morbidity. Although an elevated inflammatory response has been observed in sarcopenic patients with colorectal cancer,[27] future studies should address the unraveled link between frailty, gut barrier function, and development of sepsis.

A correlation between elevated serum markers of preoperative systemic inflammatory response and postoperative infectious complications and mortality has been established extensively.[28,29] Specifically, the Glasgow Prognostic Score comprising C-reactive protein and albumin levels is an easily obtainable and accurate scoring system to predict postoperative morbidity and mortality in patients undergoing colorectal surgery.[30] The current study presents another point of view of potentially the same phenomenon, namely, physical impairment of the cancer-bearing host reflected as functional compromise and systemic inflammation. Cause and effect remain to be determined, and in future studies, both SNAQ/GFI/sarcopenia score and Glasgow Prognostic Score should be acquired, as combination of both scores may increase predictive accuracy.

Remarkably, anastomotic leakage and/or intra-abdominal abscess could not be predicted by sarcopenia or SNAQ or GFI scores, nor by their interactions. The predictive factors found in this study were stage 3 to 4 cancer, that is, advanced disease and need for blood transfusion. This observation was in line with the results of the large prospective study of Boccola and colleagues.[31] The effect underlying the association between stage 3 to 4 disease and anastomotic leakage

TABLE 5. Logistic Regression Analysis for Risk Factors of Sepsis

		Univariate Analysis		Multivariate Analysis	
	Sepsis Rate	**OR**	***P***	**OR**	***P***
Sarcopenia					
No	6/162	1			
Yes	8/148	1.49 (0.50–4.39)	0.47		
GFI score ≥5					
No	5/114	1			
Yes	6/39	3.96 (1.14–13.83)	0.03		
SNAQ score ≥3					
No	6/185	1		1	
Yes	6/112	6.17 (1.84–20.64)	0.003	4.37 (1.07–17.9)	0.04
Sex					
Female	8/155	1			
Male	6/155	0.74 (0.25–2.19)	0.59		
Age		1.07 (1.01–1.14)	0.03		
Epidural					
No	8/117	1			
Yes	6/193	0.44 (0.15–1.29)	0.14		
Previous abdominal surgery					
No	7/208	1			
Yes	7/102	2.12 (0.72–6.20)	0.17		
Disease stage					
1–2	4/107	1			
3–4	4/122	0.87 (0.21–3.58)	0.85		
ASA class					
I	0/17	1	0.95		
II	10/219	∞ (0.00–∞)	1.00		
III	4/62	∞ (0.00–∞)	1.00		
IV	0/12	1.00 (0.00–∞)	1.00		
Smoking					
No	7/170	1			
Yes	7/140	1.21 (0.40–3.70)	0.74		
Diabetes					
No	11/252	1			
Yes	3/58	1.62 (0.50–5.29)	0.42		

Values in parentheses are 95% CIs.
ASA indicates American Society of Anesthesiologists.

has not been investigated in our study; however, a nutritional cause seems unlikely, as a high SNAQ score was not independently predictive in multivariate analysis. An increased inflammatory state could be hypothesized in advanced cancer stage, but markers for inflammation were not included in our analyses.

Identifying surgical patients at risk for developing complications remains challenging. Therefore, an important clinical implication can be drawn from this study. The easy-to-perform functional compromise assessment presented here (SNAQ, GFI, and sarcopenia) may be used to detect high-risk patients and to adapt treatment regimens accordingly, that is, primary diverting ileostomy or colostomy. The preoperative period can be considered to improve functional parameters by nutritional support and physical exercise.[32] Exercise may increase physical functioning and overall quality of life in patients with cancer.[33,34] The best anabolic response is obtained when exercise is combined with nutritional support, such as essential amino acid ingestion.[35,36] Physical exercise must be performed 2 to 3 days a week to increase muscle strength[37]; therefore, this should be supervised. Furthermore, many patients undergo neoadjuvant treatment that generates a time frame for prehabilitation strategies. Finally, as the SNAQ/GFI/sarcopenia score specifically predicts sepsis, intensive monitoring can be opted for patients at risk. Future studies may elucidate whether these high-risk patients could benefit from selective decontamination of the digestive tract.[38]

The L3 muscle index measure is a widely available, objective, and precise measurement for perioperative assessment of lean body mass. In the current study, a very good interobserver variability was demonstrated by 2 investigators who had not received any specific radiological training. As mentioned before, an important remark should be made regarding the cutoff values of the L3 index to diagnose sarcopenia. As these values are based on obese patients with cancer, they might not be applicable to all populations. Sarcopenia incidence by the definition in this study was 48%, which is a rather high number in patients with colorectal cancer who have not been reported to suffer from severe muscle wasting, potentially indicating an underestimated proportion of functional loss in this group. It is therefore highly desirable to define cutoff values based on healthy subjects and different cancer type populations. Nonetheless, the cutoff values described by Prado et al are based on mortality prediction, which was supported in the current study. Another limitation is the retrospective nature of the study. However, all patients in the study cohort were included in a prospective database (Dutch Surgical Colorectal Audit) and only patients without an available staging CT scan were excluded. As a consequence, the probability of selection bias was negligible. Because of the retrospective nature of the study, dual-energy x-ray absorptiometry scans and other tests for sarcopenia were not available. However, CT-based muscle area measurement is a well-documented and readily obtainable alternative to detect sarcopenia.[14] The findings

of this study should nonetheless be confirmed in a second, prospective cohort including other tests for sarcopenia.

CONCLUSIONS

This study shows that functional compromise in colorectal cancer surgery is associated with adverse postoperative outcome. Moreover, assessment of functional compromise by means of a nutritional questionnaire (SNAQ), a frailty questionnaire (GFI), and CT-based sarcopenia measurement (L3 muscle index), that is, the SNAQ/GFI/sarcopenia score, can accurately predict postoperative sepsis.

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APPENDIX 1
Items of Groningen Frailty Indicator Score[17]

Mobility

Is the patient able to carry out these tasks single-handed without any help? (The use of help resources, such as walking stick, walking frame, wheelchair, is considered independent.)

1. Shopping
2. Walking around outside (around the house or to the neighbors)
3. Dressing and undressing
4. Going to the toilet

Physical Fitness

5. What mark does the patient give himself/herself for physical fitness? (scale 0-10)

Vision

6. Does the patient experience problems in daily life due to poor vision?

Hearing

7. Does the patient experience problems in daily life due to being hard of hearing?

Nourishment

8. During the last 6 months has the patient lost a lot of weight unwillingly? (3 kg in 1 month or 6 kg in 2 months)

Morbidity

9. Does the patient take 4 or more different types of medicine?

Cognition (Perception)

10. Does the patient have any complaints about his/her memory or is the patient known to have a dementia syndrome?

Psychosocial

11. Does the patient sometimes experience emptiness around him/her?
12. Does the patient sometimes miss people around him/her?
13. Does the patient sometimes feel abandoned?
14. Has the patient recently felt downhearted or sad?
15. Has the patient recently felt nervous or anxious?

Sum

Scoring:

Questions 1–4: Independent = 0; dependent = 1
Question 5: 0–6 = 1; 7–10 = 0
Questions 6–9: No = 0; yes = 1
Question 10: No and sometimes = 0; yes = 1
Questions 11–15: No = 0; sometimes and yes = 1

APPENDIX 2
Items of Short Nutritional Assessment Questionnaire Score[18]

Item Score	
Did you lose weight unintentionally?	
More than 6 kg in the last 6 months	3
More than 3 kg in the last month	2
Did you experience a decreased appetite over the last month?	1
Did you use supplemental drinks or tube feeding over the last month?	1