Prehabilitation in major abdominal surgery

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DOI:
10.33612/diss.224332213

Publication date:
2022

CHAPTER 6

The association between preoperative body composition and aerobic fitness in patients scheduled for colorectal surgery

Colorectal Disease. 2021;00:1–9.

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ABSTRACT

Background: Although cardiopulmonary exercise testing (CPET) is considered the gold standard, a preoperative abdominal CT scan might also provide information concerning preoperative aerobic fitness for risk assessment. This study aimed to investigate the association between preoperative CT-scan-derived body composition variables and preoperative CPET variables of aerobic fitness in colorectal surgery.

Methods: In this retrospective cohort study, CT images at level L3 were analysed for skeletal muscle mass, skeletal muscle radiation attenuation, visceral adipose tissue (VAT) mass and subcutaneous adipose tissue mass. Regression analyses were performed to investigate the relation between CT-scan- derived body composition variables, CPET-derived aerobic fitness and other preoperative patient-related variables. Logistic regression analysis was performed to predict a preoperative anaerobic threshold (AT) ≤ 11.1 ml/kg/min as cut-off for having a high risk for postoperative complications.

Results: Data from 78 patients (45 men; mean [SD] age 74.5 [6.4 years]) were analysed. A correlation coefficient of 0.55 was observed between absolute AT and skeletal muscle mass index. Absolute AT ($R2$ of 51.1%) was lower in patients with a lower skeletal muscle mass index, together with higher age, lower body mass and higher American Society of Anaesthesiologists (ASA) score. Higher ASA score (odds ratio 5.64; $P = 0.033$) and higher VAT mass (odds ratio 1.02; $P = 0.036$) were associated with an increased risk of an AT ≤ 11.1 ml/kg/min.

Conclusion: Body composition variables from the preoperative CT scan were moderately associated with preoperative CPET-derived aerobic fitness. Higher ASA score and higher VAT mass were associated with an increased risk of an AT ≤ 11.1 ml/kg/min.

INTRODUCTION

Colorectal cancer is the third most common type of cancer.[1] After resection for colon or rectal carcinoma, 15% and 20% of the patients respectively have a complicated course within 30 days after surgery, which might lead to a prolonged hospital stay of >14 days or even mortality.[2] Reducing complications will result in considerable cost savings.[3] Preoperative risk assessment might identify patients at high risk of postoperative complications; these patients may benefit from preoperative preventive interventions (prehabilitation).[4,5]

Cardiopulmonary exercise testing (CPET) is increasingly utilised for risk assessment before major surgery to evaluate the risk of adverse perioperative events.[5] CPET is an objective and precise method of evaluating a patient's preoperative aerobic fitness. In general, patients with a lower oxygen uptake at the anaerobic threshold (AT) and/or a lower oxygen uptake at peak exercise (VO_{2peak}) have an increased risk of postoperative complications.[6–9] Despite its usefulness in perioperative medicine, CPET it is not always available in clinical practice, is relatively expensive and time-consuming, and requires well-trained personnel for an adequate interpretation of its results.

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For preoperative risk assessment, measurements of body composition using the routinely performed abdominal computed tomography (CT) scan is increasingly gaining ground. Sarcopenia,[10] a low skeletal muscle radiation attenuation (SM-RA),[11,12] and a high visceral adipose tissue (VAT) mass[13,14] have all been reported to be associated with poor clinical outcome following abdominal surgery. Furthermore, Boo and others[15] demonstrated that skeletal muscle mass is closely associated with aerobic fitness (the AT and VO_{2peak}) in community-dwelling elderly men, while a recent study of West and others[16] in patients undergoing hepatopancreatobiliary surgery reported that SM-RA and not skeletal muscle mass (assessed by a preoperative CT-scan) were associated with aerobic fitness (assessed with preoperative CPET).

Although CPET is the gold standard to assess aerobic fitness, it would be of interest for time and cost savings to investigate whether the routinely performed preoperative abdominal CT-scan can (assist to pre)select unfit patients. Therefore, the aim of this study was to preoperatively investigate the association between body composition variables derived from the abdominal CT-scan and CPET variables of aerobic fitness in patients scheduled for colorectal surgery.

METHODS

The present retrospective study was reported according to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guideline.

Participants

Data from all patients ≥60 years with colorectal cancer or dysplasia planned for elective colorectal resection at the hospital Medisch Spectrum Twente, with a veterans-specific activity questionnaire (VSAQ) score ≤7 metabolic equivalents of task (METs) and who underwent a preoperative abdominal CT-scan and preoperative CPET between February 2013 and May 2017 were included. The VSAQ is a brief self-administered questionnaire to estimate aerobic fitness, in which a score ≤7 METs was used to preselect those patients with a low perceived aerobic fitness.[17] These formed the study data and were retrospectively analysed after this period. Ethical approval for the study protocol (registration number P13-18) was provided by the Medical Ethics Committee Twente (Dr. J.F.F. Lekkerkerker, clinical pharmacologist, chairman) in September 2013, and written informed consent was obtained from each participant. Patients were excluded if the time between CPET and CT was >60 days, or when acute surgery of the tumour was necessary.

Computed tomography scan

A single slice of each patient's routinely performed preoperative abdominal CT-scan was selected at the level of the third lumbar vertebra (L3) on which both transverse processes were visible. CT-scans were all screened for their quality. Patients with a CT-scan of poor quality (e.g., large radiation artefacts, low-dose) were excluded from analysis. Scans were analysed using sliceOmatic 5 (TomoVision, Magog, Canada) software for Microsoft Windows®. The cross-sectional areas (cm^2) of skeletal muscle tissue, VAT, and subcutaneous adipose tissue (SAT) were coloured automatically, and manually corrected if necessary, by two trained and blinded researchers (LvW and checked by DvD, both blinded for CPET analyses). Skeletal muscle tissue, VAT, and SAT areas were normalised for the patient's body height to calculate the L3 index in cm^2/m^2. The SM-RA was assessed by calculating the average Hounsfield Units (HU) value of skeletal muscle mass. Low SM-RA is associated with increased inter- and intramyocellular fat (myosteatosis).[18]

Cardiopulmonary exercise testing

As part of the study protocol an incremental CPET was performed by patients preoperatively under controlled conditions at the lung function department, using a calibrated electronically braked cycle ergometer in upright position (Ergoline, Ergoselect 100, Bitz, Germany). The following standardised pre-test instructions were given to the patients: 1) consume the last (light) meal at least two hours before exercise testing, 2) adhere to usual use of medication, and 3) wear comfortable sporting clothes and shoes. CPET comprised a two-minute resting phase to assess baseline cardiopulmonary values, followed by three minutes of unloaded cycling (warm-up), where after the work rate was progressively increased with constant increments of 5, 10, or 15 W/min, depending on the patient's subjective physical fitness level and aimed at reaching a maximal effort within eight to twelve minutes. Throughout CPET, patients had to maintain a pedalling frequency between 60 and 80 revolutions/min. The protocol continued until the patient's pedalling frequency fell definitely <60 revolutions/min, despite strong verbal encouragement. After test termination, the patient completed a five minute-recovery phase of unloaded cycling (cool-down).

During CPET, patients breathed through a facemask (Hans Rudolph, Kansas City, MO, USA) connected to a Triple V volume transducer to calculate breath-by-breath minute ventilation (VE), oxygen uptake (VO_2), carbon dioxide production (VCO_2), and the respiratory exchange ratio (RER) averaged at ten-second intervals (Oxycon Pro, Jaeger, Hoechberg, Germany). Flow-volume (three-litre syringe) and gas calibration (ambient air and a gas mixture of 16% oxygen and 5% carbon dioxide) were performed manually before each test. Heart rate (HR), twelve-lead electrocardiography, blood pressure, and pulse oximetry were continuously monitored.

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CPET data were interpreted by a trained and experienced clinical exercise physiologist (BB, blinded for CT-scan analyses). The highest HR achieved during the CPET was defined as HR_{peak}. Data from other outcome variables were averaged over 30 seconds of exercise. VO_{2peak} values were considered valid when at least one of the following criteria was met: a heart rate at peak exercise >95% of predicted (predicted peak heart rate [beats min^{-1}] = 208 – 0.7 × age [years]) or a respiratory exchange ratio at peak exercise >1.10. The AT was defined as the point at which the ventilatory equivalent for oxygen and the partial end-tidal oxygen tension reached a minimum and thereafter began to rise in a consistent manner, coinciding with an unchanged ventilatory equivalent for carbon dioxide and partial end-tidal carbon dioxide tension.[19] In case this ventilatory equivalents method provided uncertain results, the V-slope method was used to estimate the AT (the point at which the linear slope of the relation between the VCO_2 and VO_2 changed).[20] Finally, the oxygen uptake efficiency slope (OUES), which provides a valid objective effort-independent measure of aerobic fitness in elderly patients scheduled for major colorectal surgery was calculated.[21] Absolute VO_{2peak}, AT, and OUES values were normalised for body mass as well.[21]

Patient characteristics and outcome measures

Baseline patient characteristics included sex, age, body height, body mass, body mass index (BMI), smoking status, use of beta-blocker, METs score on the veterans-specific activity questionnaire, clinical signs of metastasis, American Society of Anaesthesiologists (ASA) score (I-IV), and Charlson comorbidity index (divided in three groups: 0, 1, and 2+). Body composition and aerobic fitness outcomes were reported separately for men and women, as it is known that values significantly differ between sexes.

Statistical analysis

Data were analysed with the Statistical Package for the Social Sciences for Windows (version 23.0; IBM, SPSS Inc., Chicago, IL, USA). Continuous data were presented as mean and standard deviation (SD), or as median and interquartile range (IQR), where appropriate. Categorical data were summarised by frequency and percentage. Pearson or Spearman correlation coefficients were calculated to examine univariable associations between continuous variables, depending upon the distribution of the variables. To investigate the univariable association between a continuous variable (e.g., AT) and a categorical variable, the one-way ANOVA, the independent samples t-test, or the Mann Whitney U test, as appropriate, was used. Univariable associations with a $P<0.10$ were included in the multivariable analysis. For predicting continuous outcomes, linear regression analyses (method: enter) were performed to investigate the association between continuous CPET variables (dependent variable, e.g., AT) and preoperative independent variables.

A multivariable logistic regression analysis was performed to predict whether a patient had a relative AT ≤11.1 mL/kg/min. Preoperative variables were tested for their association with a relative AT ≤11.1 mL/kg/min ($P<0.10$), using the t-test, Mann Whitney U test, Fisher's exact test, or Chi^2 test, as appropriate. A logistic regression model was performed to select which of the remaining variables were significant in a forward stepwise procedure (*P* in 0.10, *P* out 0.15). In case of multicollinearity between variables, the variable that produced the best model fit (based on the -2 log likelihood) was included in the model. With the final selected significant variables, a new logistic regression model was made (method: enter) to utilise the maximum number of observations. Receiver operator curve (ROC) analysis was used to assess the independent ability of predictive variables to discriminate between patients with and without a relative AT ≤11.1 mL/kg/min; this AT cut-off was based on the work by West and others [8] in patients undergoing major colorectal surgery. The optimal cut-off point from the ROC analysis was based on our preference to have primarily a high sensitivity (with a reasonable specificity), as we aim to detect almost all high-risk patients that might benefit from a preoperative intervention (e.g., prehabilitation). A $P<0.05$ was considered statistically significant.

RESULTS

Patients

Between February 2013 and May 2017, a total of 371 potential patients ≥60 years with a colorectal tumour were assessed for eligibility. Of these patients, 189 (50.9%) had a VSAQ score ≤7 METs, of which 91 patients (48.1%) underwent a preoperative CPET. Of these 91 patients, 13 patients were excluded: in two patients (2.2%) skeletal muscle radiation attenuation could not be measured using their CT-scan; in nine patients (9.9%) raw preoperative CPET data was not available; and in two patients (2.2%) the AT and VO_{2peak} could not be determined due to a poor effort at the CPET (invalid test). Patient characteristics of the remaining 78 patients (45 males and 33 females, mean age 74.5 ± 6.4 SD years, range 61.5 to 90.3 years) are presented in Table 1.

Table 1. Patient characteristics

Parameter	**Total (*n* = 78)**
Age (years)	74.5 ± 6.4
Sex (males)	45 (57.7)
Body height (cm)	169.9 ± 9.3
Males	175.1 ± 7.1
Females	163.0 ± 7.2
Body mass (kg)	84.5 ± 14.3
Males	89.0 ± 13.7
Females	78.5 ± 12.9
Body mass index (kg/m^2)	29.2 ± 3.8
Males	29.0 ± 3.8
Females	29.5 ± 3.9
Smoking [a]	11 (15.7)
VSAQ score (METs) [b]	5 ± 1
Charlson comorbidity index	
0	23 (29.5)
1	27 (34.6)
≥ 2	28 (35.9)
ASA score	
I and II	61 (78.2)
III and IV	17 (21.8)

Table 1. Continued

Parameter	**Total (*n* = 78)**
Tumour localisation	
Ascending colon	29 (37.2)
Transverse colon	7 (9.0)
Descending colon	5 (6.4)
Sigmoid	23 (29.5)
Rectum [c]	11 (14.1)
Other [d]	3 (3.8)
Clinical metastasis category	
cM0	67 (85.9)
cM1	5 (6.4)
Not applicable [e]	6 (7.7)

Values are presented as mean ± SD or as n (%).
Abbreviations: ASA=American Society of Anaesthesiologists; MET=metabolic equivalent of task; VSAQ=veterans-specific activity questionnaire.
[a]: 8 missing values.
[b]: 13 missing values.
[c]: 4 patients with a rectal tumour received neoadjuvant chemoradiation, 1 patient received neoadjuvant radiotherapy.
[d]: 2 patients had a tumour in both the ascending and transverse colon, 1 patient had metachronous colorectal liver metastasis.
[e]: includes dysplasia (*n*=5) and metachronous colorectal liver metastasis (*n*=1).

All 78 patients performed the CPET without any complications or adverse events during or after the test. The AT was undeterminable in two (2.6%) patients, while they attained a valid VO_{2peak}. Normalised for body mass, mean ± SD values of VO_{2peak} and AT were 15.6 ± 3.7 mL/kg/min and 10.6 ± 1.9 mL/kg/min, respectively. Mean ± SD time between the CT-scan and CPET was 15.2 ± 15.3 days. CPET results are shown in Table 2.

Mean ± SD skeletal muscle mass index was 50.9 ± 10.6 cm^2/m^2 in males (range 31.1 to 91.5) and 36.6 ± 8.1 cm^2/m^2 in women (range 20.4 to 66.7). CT-scan measurements are depicted in Table 2.

Table 2. Preoperative body composition parameters derived from the abdominal CT-scan and preoperative CPET parameters.

Parameter	Total (n = 78)	Males (n = 45)	Females (n = 33)	P-value[f]
CT-scan parameters				
Skeletal muscle mass index (cm^2/m^2)	44.9 ± 11.9	50.9 ± 10.6	36.6 ± 8.1	<0.001
SM-RA (HU)	29.1 ± 7.6	30.3 ± 7.8	27.5 ± 7.2	0.110
VAT mass (cm^2/m^2)	77.8 ± 38.2	86.3 ± 37.9	66.2 ± 36.1	0.021
SAT mass (cm^2/m^2)	80.0 ± 30.4	65.2 ± 26.5	100.1 ± 22.9	<0.001
CPET parameters				
HR_{peak} (beats/min) [a]	129 ± 19	128 ± 19	130 ± 19	0.751
Without beta blocker [b]	135 ± 17	137 ± 15	133 ± 20	0.429
With beta blocker [b]	120 ± 18	119 ± 19	122 ± 18	0.728
RER_{peak}	1.14 ± 0.11	1.16 ± 0.10	1.12 ± 0.11	0.059
WR_{peak} (W)	98 ± 32	110 ± 32	83 ± 25	<0.001
WR_{peak} (W/kg)	1.2 ± 0.3	1.2 ± 0.3	1.1 ± 0.3	0.030
VO_{2peak} (mL/min)	1312 ± 351	1413 ± 348	1173 ± 309	0.002
VO_{2peak} (mL/kg/min)	15.6 ± 3.7	16.0 ± 3.8	15.1 ± 3.5	0.262
AT (mL/min) [c]	889 ± 181	937 ± 175	824 ± 171	0.006
AT (mL/kg/min) [c]	10.6 ± 1.9	10.6 ± 1.9	10.5 ± 1.7	0.823
O_2-pulse$_{peak}$ (mL/beat) [a]	10.3 ± 2.6	11.2 ± 2.7	9.0 ± 2.0	<0.001
O_2-pulse$_{peak}$ (mL/kg/beat × 100) [a, d]	12.3 ± 2.3	12.8 ± 2.6	11.7 ± 1.9	0.056
VE/VCO_2-slope [e]	33.2 ± 6.6	33.8 ± 7.8	32.4 ± 4.6	0.375
VE_{peak} (L/min)	56.6 ± 17.0	62.5 ± 16.7	48.7 ± 14.1	<0.001
VE_{peak} (L/kg/min)	0.7 ± 0.2	0.7 ± 0.2	0.6 ± 0.2	0.094
OUES	1576 ± 444	1695 ± 428	1413 ± 418	0.005
OUES/kg	18.7 ± 4.5	19.2 ± 4.7	18.0 ± 4.2	0.248

Values are presented as mean ± SD.
Abbreviations: AT=anaerobic threshold; CPET=cardiopulmonary exercise testing; CT=computed tomography; HR_{peak}=heart rate at peak exercise; HU=Hounsfield Units; O_2-pulse$_{peak}$=oxygen pulse at peak exercise; OUES=oxygen uptake efficiency slope; RER_{peak}=respiratory exchange ratio at peak exercise; SAT=subcutaneous adipose tissue; SD=standard deviation; SM-RA=skeletal muscle radiation attenuation; VAT=visceral adipose tissue; VE_{peak}=minute ventilation at peak exercise; VE/VCO_2-slope=minute ventilation to carbon dioxide production relationship; VO_{2peak}=oxygen uptake at peak exercise; WR_{peak}=work rate at peak exercise.
[a]: heart rate was invalid in 8 patients (10.3%, 6 males and 2 females), so in this case n=70.
[b]: a beta-blocker was used by 26 patients (17 males and 9 females), 43 patients did not use a beta blocker, and in 1 patient beta blocker use was unknown.
[c]: the AT was not determinable in two patients (2.6%, 1 male and 1 female), so in this case n=76.
[d]: O_2-pulse values normalised for body mass are multiplied by 100 to increase readability.
[e]: the VE/VCO_2-slope was calculated using data up to the respiratory compensation point.
[f]: independent samples t-tests.

Association between preoperative body composition parameters derived from the abdominal computed tomography-scan and preoperative cardiopulmonary exercise testing parameters

In the univariable analysis (Table 3), a Pearson correlation coefficient of 0.55 (P<0.001) was found between the absolute AT and skeletal muscle mass index. Between the relative AT and skeletal muscle mass index, a correlation coefficient of 0.16 (P=0.156) was observed. A Pearson correlation coefficient of 0.28 (P=0.014) was found between the relative AT and SM-RA.

Variables with a P<0.10 in the univariable analysis (age, body mass, body height, ASA, sex, skeletal muscle mass index, and VAT mass) were included in a multivariable linear regression analysis to predict the absolute AT. BMI was also associated with absolute AT (P<0.10) but was not included in the multivariable analysis because of multicollinearity between BMI, body mass, and body height. In the final multivariable model (R^2 51.1%), a lower age, a higher body mass, a lower ASA score, and a higher skeletal muscle mass index were associated with a higher absolute AT (Table 4). In a formula, absolute AT (mL/min) = 848.6 – (4.99 × age in years) + (4.18 × body mass in kg) – (124.4 × ASA score) + (4.65 × skeletal muscle mass index in cm^2/m^2). For an ASA score 1 or 2, a 1 must be used, whereas for an ASA score 3 or 4 a 2 should be used in the equation.

Moreover, variables with a P<0.10 in the univariable analysis (BMI, ASA, VSAQ score, SM-RA, and VAT mass) were included in the multivariable linear regression analysis to predict the relative AT. Body mass was also associated with relative AT (P<0.10) but was not included in the multivariable analysis because of multicollinearity between body mass and BMI. In the final multivariable model (R^2 28.6%), a higher BMI, a higher ASA score, and a lower SM-RA were associated with a lower relative AT (Table 4). In a formula, relative AT (mL/kg/min) = 15.1 – (0.13 × BMI in kg/m^2) – (1.80 × ASA score) + (0.05 × SM-RA). For an ASA score 1 or 2, a 1 must be used, whereas for an ASA score 3 or 4 a 2 should be used in the formula. The multivariable linear regression analyses to predict the absolute and relative VO_{2peak} can be found in Table 4.

Prediction of a preoperative relative anaerobic threshold ≤11.1 mL/kg/min

A multivariable logistic regression analysis was performed to investigate if a preoperative relative AT ≤11.1 mL/kg/min can be predicted from body composition variables derived from the abdominal CT-scan and other patient characteristics. In the univariable analysis, age, body mass, BMI, VAT mass, ASA score, VSAQ score, and Charlson score were associated with a relative AT ≤11.1 mL/kg/min (with a P<0.10) and were included in a forward stepwise multivariable analysis. A higher ASA score (odds ratio [OR] 6.95, 95% confidence interval (CI) 0.81 to 59.3, P=0.076) and a higher VAT mass (OR 1.01, 95% CI 1.00 to 1.03, *P*=0.090) were associated with an increased risk of a relative AT ≤11.1 mL/kg/min. Another logistic regression model was made (method: enter) with ASA and VAT mass, to include all patients (as, though ≤7 METs, the exact VSAQ score of thirteen patients were missing). In this final model, a higher ASA score (OR 5.64, 95% CI 1.15 to 27.7, *P*=0.033) and a higher VAT mass (OR 1.02, 95% CI 1.00 to 1.03, *P*=0.036) were associated with an increased risk of a relative AT ≤11.1 mL/kg/min. Patients with ASA score of 3 or 4 were almost six times more likely to have a relative AT ≤11.1 mL/kg/min.

Table 3. Correlation coefficients between preoperative body composition parameters derived from the abdominal CT-scan and preoperative CPET parameters.

Parameter	Skeletal muscle mass index (cm^2/m^2)	SM-RA (HU)	VAT mass (cm^2/m^2)	SAT mass (cm^2/m^2)
AT (mL/min) [a]	0.55 (*P*<0.001)	0.08 (*P*=0.472)	0.22 (*P*=0.063)	0.03 (*P*=0.783)
AT (mL/kg/min) [a]	0.16 (*P*=0.156)	0.28 (*P*=0.014)	-0.24 (*P*=0.040)	-0.16 (*P*=0.177)
VO_{2peak} (mL/min)	0.51 (*P*<0.001)	0.10 (*P*=0.369)	0.18 (*P*=0.122)	-0.09 (*P*=0.427)
VO_{2peak} (mL/kg/min)	0.22 (*P*=0.058)	0.26 (*P*=0.020)	-0.17 (*P*=0.130)	-0.24 (*P*=0.034)
VE/VCO_2-slope [b]	-0.12 (*P*=0.281)	-0.17 (*P*=0.127)	-0.02 (*P*=0.889)	-0.10 (*P*=0.390)
OUES	0.40 (*P*<0.001)	<-0.01 (*P*=0.991)	0.23 (*P*=0.045)	<-0.01 (*P*=0.979)
OUES/kg	0.13 (*P*=0.246)	0.15 (*P*=0.202)	-0.12 (*P*=0.287)	-0.18 (*P*=0.120)

Abbreviations: AT=anaerobic threshold; CPET=cardiopulmonary exercise testing; CT=computed tomography; HU=Hounsfield Units; OUES=oxygen uptake efficiency slope; SAT=subcutaneous adipose tissue; SM-RA=skeletal muscle radiation attenuation; VAT=visceral adipose tissue; VE/VCO_2-slope=minute ventilation to carbon dioxide production relationship; VO_{2peak}=oxygen uptake at peak exercise.

[a]: the AT was not determinable in two patients (2.6%, 1 male and 1 female), so in this case *n*=76.

[b]: the VE/VCO_2-slope was calculated using data up to the respiratory compensation point.

ROC analysis for predicting patients with a relative AT ≤11.1 mL/kg/min from ASA score and VAT mass gave an AUC of 0.71 (95% CI 0.60 to 0.83, *P*=0.002) (Figure 1). Patients with a relative AT ≤11.1 mL/kg/min can be predicted with the formula: 1/1+e(-(-0.74 + (0.02 × VAT mass) + (1.73 × ASA)). For an ASA score 1 or 2, a 0 must be used, whereas for an ASA score 3 or 4 a 1 should be used in the equation. When choosing a cut-off point of 0.55, sensitivity was 82.7%, and specificity was 46.2%, while the positive predictive value was 75.4% and the negative predictive value was 57.1%.

Table 4. Multivariable linear regression analysis to predict the preoperative absolute and relative AT and absolute and relative VO_{2peak}.

Predicted CPET variable	Parameter	B	95% CI	*P*-value
Absolute AT (mL/min)	Age (years)	-5.00	-9.80 to -0.19	0.042
	Body mass (kg)	4.18	1.69 to 6.66	0.001
	ASA score	-124	-199 to -49.8	0.001
	Skeletal muscle mass index (cm^2/m^2)	4.65	1.69 to 7.62	0.003
Relative AT (mL/kg/min)	Body mass index (kg/m^2)	-0.13	-0.23 to -0.03	0.014
	ASA score	-1.80	-2.70 to -0.90	<0.001
	SM-RA (HU)	0.05	-0.004 to 0.10	0.071
Absolute VO_{2peak} [a] (mL/min)	Age (years)	-12.0	-21.3 to -2.63	0.013
	Body height (cm)	12.5	5.34 to 19.7	0.001
	ASA score	-270	-413 to -128	<0.001
	Skeletal muscle mass index (cm^2/m^2)	8.22	2.69 to 13.8	0.004
Relative VO_{2peak} [b] (mL/kg/min)	Age (years)	-0.14	-0.24 to -0.04	0.008
	Body mass index (kg/m^2)	-0.42	-0.59 to -0.25	<0.001
	ASA score	-2.40	-4.11 to -0.69	0.007
	Charlson comorbidity index	-1.12	-1.98 to -0.26	0.012
	Skeletal muscle mass index (cm^2/m^2)	0.09	0.03 to 0.15	0.003

Abbreviations: ASA=American Society of Anaesthesiologists; AT=anaerobic threshold; CI=confidence interval; HU=Hounsfield Units; SM-RA=skeletal muscle radiation attenuation; VO_{2peak}=oxygen uptake at peak exercise.

[a]: In a formula, absolute VO_{2peak} (mL/min) = 34.9 – (12.0 × age in years) + (12.5 × body height in cm) – (270 × ASA score) + (8.22 × skeletal muscle mass index in cm^2/m^2). For an ASA score 1 or 2, a 1 must be used, whereas for an ASA score 3 or 4 a 2 should be used in the equation.

[b]: In a formula, relative VO_{2peak} (mL/kg/min) = 38.4 – (0.14 × age in years) – (0.42 × BMI in kg/m^2) – (2.40 × ASA score) – (1.12 × Charlson score) + (0.09 × skeletal muscle mass index in cm^2/m^2). For an ASA score 1 or 2, a 1 must be used, whereas for an ASA score 3 or 4 a 2 should be used in the equation. For a Charlson score 0, a 0 should be used, for a Charlson score 1, a 1 must be used, and for a Charlson score 2+, a 2 should be used in the equation.

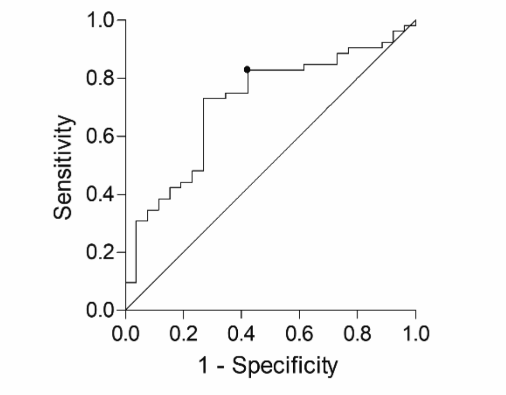

Figure 1. ROC analysis for predicting patients with a relative AT ≤11.1 mL/kg/min from ASA score and visceral adipose tissue (AUC 0.71; 95% CI 0.60 to 0.83; *P*=0.002).

Abbreviations: ASA=American Society of Anaesthesiologists; AT=anaerobic threshold; AUC=area under the curve; CI=confidence interval; ROC=receiver operator characteristic.

DISCUSSION

This study aimed to investigate the association between body composition variables derived from the preoperative abdominal CT-scan and preoperative CPET variables of aerobic fitness in patients scheduled for colorectal surgery, to evaluate whether the preoperative CT-scan can (assist to pre)select unfit patients. Results demonstrated that body composition variables were significantly associated with preoperative aerobic fitness, expressed as the absolute and relative AT, absolute and relative VO_{2peak}, and OUES. In the multivariable regression model to predict the preoperative absolute AT, it was found that the absolute AT (R^2 51.1%) was lower in patients with a lower skeletal muscle mass index, together with a higher age, a lower body mass, and a higher ASA score. Variation in relative AT values (R^2 28.6%) could be less well explained by body composition variables and other patient-related variables.

Body composition variables such as skeletal muscle mass correlate better with absolute measures of aerobic fitness (AT, VO_{2peak}, and OUES) than with relative variables (here normalised for body mass) of aerobic fitness. This can be explained by the fact that skeletal muscle mass represents an absolute measure of the body's skeletal muscle mass, and a higher absolute skeletal muscle mass generally results in greater exercise-induced peripheral oxygen extraction and utilization by the exercising muscles, which is an important determinant for absolute aerobic fitness. Aerobic fitness refers to the maximal capacity of the pulmonary and cardiovascular system to take in and transport oxygen to the exercising muscles, and of those exercising muscles to extract and utilise oxygen from the blood for aerobic respiration.[22] Thus, aerobic fitness not merely depends on skeletal muscle mass and SM-RA, which might explain the weak-to-moderate correlation coefficients found in the current study. Findings of the current study are consistent with the literature in which aerobic fitness was significantly reduced in patients with low skeletal muscle mass index.[23–25] However, limited research is available that describes the association between aerobic fitness objectively measured with CPET and body composition variables derived from the abdominal CT-scan. In a recent study, West and others[16] assessed the association of CT-scan derived body composition with selected CPET variables in patients scheduled for hepato-pancreato-biliary surgery. They found that patients with lower SM-RA values had a statistically significantly lower relative AT (r 0.44, *P*<0.001) and relative VO_{2peak} (r 0.57, *P*<0.001). The current study also found that SM-RA was significantly correlated with relative AT and relative VO_{2peak} in the univariate analysis (Table 3); however, SM-RA values were not statistically significantly associated with relative AT and relative VO_{2peak} in the multivariable model (Table 4). Concerning skeletal muscle mass index, West and others[16] reported a weak association (r 0.24, P=0.010) with relative VO_{2peak}. Consistent with the current study results, no significant correlation coefficient was found between skeletal muscle mass index and relative AT.

A previous study has shown that patients undergoing major elective colorectal surgery with an AT ≤11.1 mL/kg/min have an increased risk for postoperative complications (OR 7.56, 95% CI 4.44 to 12.86, P<0.001).[8] Therefore, this study investigated whether a patient with a relative AT ≤11.1 mL/kg/min could be predicted from body composition variables derived from the preoperative abdominal CT-scan combined with other patient characteristics. A higher ASA score and a higher VAT mass were associated with an increased risk of a relative AT ≤11.1 mL/kg/min. However, with an AUC of 0.71, the combination of ASA score and VAT mass had only a moderate ability to discriminate between patients with and without a relative AT ≤11.1 mL/kg/min. Nevertheless, this finding suggests that preoperatively assessing body composition from the routinely performed preoperative CT-scan, combined with other patient-related variables, might be useful to enable a preselection of potentially unfit patients, without the need for using additional questionnaires or tests. These potentially unfit (high-risk) patients should subsequently perform a preoperative CPET to determine the need for a preoperative preventive intervention (e.g., multimodal prehabilitation to improve preoperative aerobic capacity and muscle mass). This preselection might reduce the number of preoperative CPET procedures, thereby saving time and resources.

Preoperative risk assessment is important, as it is the less physically fit patient that will benefit the most from prehabilitation.[26,27] Despite mounting evidence that prehabilitation has the potential to improve preoperative physical fitness and postoperative outcomes[28,29], there remains work to be done in order to develop a cost-effectiveness tool that gives clinicians and policy makers insight in the value of preoperative risk assessment followed by preventive interventions in the right patients. As our results suggest, body composition variables derived from the routinely performed abdominal CT-scan, together with other patient characteristics, provides at best limited information on a patient's aerobic fitness. Therefore, the relatively complex and expensive CPET cannot be fully replaced by the preoperative abdominal CT scan. The extent to which other, less sophisticated, tests like the steep ramp test, timed up-and-go test, six-minute walk test, and short physical performance battery could refer to preoperative aerobic fitness remains to be evaluated.

The explorative nature of the study, the limited number of patients, and the absence of a prospective sample size calculation are limitations of the present study. Additionally, the fact that only patients with a VSAQ score ≤7 METs were referred for CPET might have biased the results, as having all patients perform a CPET prior to colorectal surgery probably would lead to greater accuracy in determining the association between preoperative CT scan-derived body composition variables and preoperative aerobic fitness. These aspects affect statistical analysis and generalizability. Moreover, the studied population is limited to patients undergoing colorectal surgery, who do not necessarily represent the general (surgical) population.

CONCLUSION

Body composition variables derived from the preoperative CT-scan are moderately associated with aerobic fitness as determined from the preoperative CPET. A higher ASA score and a higher VAT mass were associated with an increased risk of a relative AT ≤11.1 mL/kg/min as a cut-off to classify patients scheduled for colorectal surgery as having an increased risk for postoperative morbidity. It seems the CT-scan cannot replace the CPET for preoperative risk assessment on aerobic fitness; however, it may contribute to the (pre)selection of unfit patients.

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