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Visceral fat area, not body mass index, predicts postoperative 30-day morbidity in patients undergoing colon resection for cancer

Benjamin A. Kuritzkes[1], **Emmanouil P. Pappou**[2], **Ravi P. Kiran**[1,3], **Onur Baser**[3], **Liqiong Fan**[3], **Xiaotao Guo**[4], **Binsheng Zhao**[4], and **Stuart Bentley-Hibbert**[5]

[1]Division of Colorectal Surgery, New York Presbyterian/Columbia University Medical Center, Herbert Irving Pavilion, 8th Fl., 161 Fort Washington Avenue, New York, NY 10032, USA

[2]Division of Colorectal Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA

[3]Center for Innovation and Outcomes Research, New York Presbyterian/Columbia University Medical Center, New York, NY, USA

[4]Computational Image Analysis Laboratory, Department of Radiology, New York Presbyterian/Columbia University Medical Center, New York, NY, USA

[5]Division of Abdominal Radiology, New York Presbyterian/Columbia University Medical Center, New York, NY, USA

Abstract

Purpose—Colectomy for cancer in obese patients is technically challenging and may be associated with worse outcomes. Whether visceral obesity, as measured on computed tomography, is a better predictor of complication than body mass index (BMI) or determines long-term oncologic outcomes has not been well characterized. This study examines the association between derived anthropometrics and postoperative complication and long-term oncologic outcomes.

Methods—Retrospective review of patients undergoing elective colectomy for cancer at a single tertiary-care center from 2010 to 2016. Adipose tissue distribution measurements, including visceral fat area (VFA), were determined from preoperative imaging. The primary outcome was 30-day postoperative complication; secondary outcomes included overall and disease-free survival. Multivariable logistic regression was performed to determine association between obesity metrics and outcome.

Results—Two hundred and sixty-four patients underwent 266 primary resections of colon cancer. Twenty-eight patients (10.5%) developed major morbidity (Clavien-Dindo grade ≥ III).

✉Benjamin A. Kuritzkes, bak2146@cumc.columbia.edu.

Compliance with ethical standards

This study was approved by the Columbia University Medical Center Institutional Review Board with waiver of informed consent.

Conflict of interest This manuscript has been reviewed by all authors, who declare no conflict of interest.

Disclaimer None.

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VFA but not BMI was significantly associated with morbidity in multivariate analysis ($p = 0.004$, odds ratio 1.99, 95% confidence interval 1.25–3.19). No other imaging-derived anthropometric was associated with increased morbidity. In receiver operating characteristic analysis, VFA was predictive of major morbidity (area under curve 0.660). A cutoff value of VFA ≥ 191 cm^2 was associated with 50% sensitivity and 76% specificity for predicting major morbidity. Patients with VFA ≥ 191cm^2 had 19.4% risk of morbidity, whereas those with < 191 cm^2 had 7.2% risk (relative risk ratio 2.69, unadjusted $p = 0.004$). Neither VFA nor BMI was associated with overall or disease-free survival.

Conclusion—VFA but not BMI predicts morbidity following elective surgery for colon cancer.

Keywords

Colon cancer; Visceral obesity; Abdominal obesity; Visceral fat area; Clinical outcomes

Introduction

Colon cancer remains a leading cause of cancer-related morbidity and mortality in the USA [1,2]. Surgery is the mainstay of treatment for localized disease; however, postoperative complications potentially delay institution of adjuvant therapy and may adversely influence oncologic outcomes [3–5].

Obesity, as defined by body mass index (BMI) ≥ 30 kg/m^2, has been reported by some to be associated with increased risk of postoperative morbidity and mortality [6–8], including in patients undergoing colorectal surgery [9, 10]. Obesity has also been linked to longer operating times and risk of conversion from laparoscopic to open technique [11]. However, other series have failed to demonstrate an association between increasing BMI and postoperative morbidity or mortality [12–15]. This so-called obesity paradox, first postulated in the cardiology literature [16, 17], has prompted a search for superior anthropometric predictors of outcome, including such metrics of abdominal obesity as waist circumference (WC) [18] and waist-to-hip ratio (WHR) [19].

Recently, there has been considerable interest in the use of computed tomography (CT) to quantify abdominal adipose tissue [20, 21]. Measurement of the cross-sectional distribution of abdominal fat has led to the development of several novel anthropometric variables, including visceral fat area (VFA), subcutaneous fat area (SFA), total fat area (TFA), and the ratio of visceral-to-total fat areas (VTR). Whether such CT-derived anthropometrics are better predictors of postoperative morbidity than BMI remains unclear.

Studies examining the potential association between “visceral obesity,” as defined by high VFA, and outcomes after colorectal surgery report discordant results. Some authors have found that high VFA is predictive of increased postoperative morbidity [22–25], whereas others have found no such relationship [26–28].

Direct comparison among these studies is challenging, in large part, because they apply markedly different methods for analyzing these novel variables. Nearly all of these studies treated visceral obesity as a dichotomous variable, defined by a given cutoff value of VFA.

However, there is currently no consensus cutoff value to define “visceral obesity”; authors cited here selected values ranging from 90 cm^2 [27] to 192 cm^2 [22]. Moreover, many of these threshold values are based on the association between VFA and metabolic syndrome [29–31] and thus may not be relevant to predicting outcomes in surgical populations. Application of these cutoff values may inadvertently introduce interpretation bias into previously reported findings. To avoid such bias, it may be prudent to consider VFA and related variables as continuous, rather than categorical, variables.

Given the discordant reports in the existing literature, the clinical utility of visceral obesity in preoperative evaluation and risk stratification remains poorly characterized. This study aims to overcome the drawbacks of previous studies while evaluating the association between CT-derived anthropometries of abdominal fat distribution and 30-day morbidity and long-term oncologic outcomes in patients undergoing elective surgery for colon cancer.

Materials and methods

This study was approved by the Columbia University Medical Center Institutional Review Board with waiver of informed consent. Patients who underwent primary elective surgery for colon adenocarcinoma at Columbia University Medical Center between January 2010 and July 2016 were identified from a prospectively collected database. All procedures were performed by fellowship-trained colorectal attending surgeons. Patients were excluded if they underwent emergency surgery or surgery for recurrent disease, if their malignancy was located in the rectum, if they had a histopathologic diagnosis other than adenocarcinoma, if they received neoadjuvant chemotherapy, or if they did not have an accessible CT scan of the abdomen and pelvis within 2 months prior to surgery. Clinical and pathologic data were obtained from review of the medical record. Variables retrieved included baseline patient and disease characteristics, comorbidity, and intra-operative, postoperative, and pathologic outcomes. Thirty-day postoperative complications evaluated included need for reoperation, readmission, and mortality. Long-term outcomes including disease recurrence and survival were also evaluated. Preoperative CT scans for all patients were analyzed to obtain CT-derived anthropometric variables. VFA, SFA, TFA, and VTR were quantified from axial images at the L4/L5 intervertebral space using a proprietary computer algorithm, as previously described (Fig. 1) [32]. Pixels having Hounsfield units of between – 190 and – 30 were considered to correspond to adipose tissue, per common practice [33, 34]. Body and visceral compartment contours were examined and adjusted for anatomic correctness by a single reviewer (BAK), under the supervision of an attending radiologist (SBH).

The primary endpoint was 30-day major morbidity, defined as Clavien-Dindo classification grade ≥ III. The Clavien-Dindo classification scheme is a validated scoring system for quality assessment in surgery; briefly, complications grade ≥ III include those requiring surgical, endoscopic, or radiologic intervention (grade III); threat to life requiring ICU-level care (grade IV); and/or death (grade V) [35]. Secondary endpoints included overall survival and disease-free survival (DFS). Overall survival (OS) was defined as time from the date of surgery to death from any cause; DFS was defined as time from the date of surgery until endoscopic, radiologic, or histologic evidence of disease recurrence as documented by an attending medical oncologist. Univariable and multivariable Cox proportional hazards

models were designed to determinen whether body fat distribution variables were associated with OS and DFS.

To avoid interpretation bias, CT-derived anthropometric variables were evaluated as continuous variables, rather than collapsing them into dichotomous variables (i.e., viscerally obese vs. viscerally non-obese). Continuous variables are presented as median with interquartile range (IQR), and were evaluated with Mann-Whitney *U* test or ANOVA; ordinal variables were evaluated with Spearman's rank correlation coefficient or Kendall's tau-b correlation coefficient; and categorical variables were evaluated with Pearson's chi-squared test, or Fisher's exact test, as appropriate. Two-tailed p values <0.05 were considered to be statistically significant. Multiple logistic regression models were constructed to identify whether body fat distribution variables were predictive of 30-day major morbidity. Cox proportional hazards models were constructed to determine the relationship between exposure variables and OS and DFS. Other potential explanatory covariates adjusted for include age; gender; medical comorbidities, including hypertension, diabetes mellitus, coronary artery disease, congestive heart failure, and COPD; American Society of Anesthesiologists (ASA) physical fitness grade ≥ III; American Joint Committee on Cancer (AJCC) staging; and extent of colonic resection. Stepwise selection was used to select covariates that were significant at the p <0.01 level. Survival functions were estimated using the Kaplan-Meier method, and compared with the Mantel-Cox log-rank test. Univariable receiver operating characteristic (ROC) analysis, including derivation of areas under the ROC curve (AUC), was performed to assess prediction of postoperative morbidity by exposure variables. Novel threshold values were identified to maximize Youden's *J* statistic [36, 37]. The linearity in the logit assumption and proportional hazards assumption were assessed and met. Statistical analyses were performed using SPSS® version 23.0 (IBM, Armonk, NY, USA) or SAS® version 9.4 (SAS Institute, Cary, NC, USA).

Results

Of 338 patients who underwent primary elective colon resection for colon cancer during the study period, 74 patients were excluded. Fifty-one patients did not have an accessible CT scan performed within 2 months prior to surgery, 15 patients had a diagnosis of malignancy other than colon adenocarcinoma, and 8 patients underwent emergency colectomy. Two patients each underwent two elective colectomies for metachronous primary colon cancers. Thus, 264 patients, who underwent a total of 266 elective colon resections, were included in the final analysis (Fig. 2).

Patient demographic characteristics and medical comorbidities are given in Table 1. The median age of the patients was 67.5 years (IQR, 56–77 years), and 126 patients (47.3%) were female. Median preoperative BMI was 26.9 kg/m^2 (IQR, 23.8–30.5 kg/m^2); 74 patients (27.8%) were obese as defined by BMI ≥ 30 kg/m^2. ASA class grade was ≥ III in 145 patients (54.5%). Primary lesions were predominantly right sided (n = 146, 54.9%), and 189 (71%) operations were performed laparoscopically. Median estimated blood loss (EBL) was 77.5 mL (IQR, 35–150 mL), and median operative time 183 min (IQR, 161–255 min). The distribution of cancers by AJCC staging was as follows: stage I, n = 57 (21.4%); stage II, n = 101 (38.0%); stage III, n = 89 (33.5%); and stage IV, n = 19 (7.1 %).

CT-derived anthropometric results

Median VFA was 122.7 cm^2 (IQR, 73.4–196.52 cm^2), median SFA 251.5 cm^2 (IQR, 181.4–377.1 cm^2), median TFA 402.0 cm^2 (IQR, 273.1–518.7 cm^2, and median VTR 0.34 (IQR, 0.24–0.43). BMI was significantly correlated with VFA, SFA, and TFA (p <0.001, for each independent variable). Increasing ASA physical status grade was also significantly associated with VFA ($p = 0.02$), but not SFA or TFA ($p = 0.79$, and $p = 0.35$, respectively). Estimations of collinearity between patient characteristics and CT-derived anthropometric variables are given in Table 2.

Short-term outcomes

Twenty-eight patients (10.5%) developed 30-day major morbidity, defined as Clavien-Dindo classification grade ≥ III. Complications included sepsis requiring ICU-level care ($n = 10$), respiratory insufficiency requiring unplanned reintubation ($n = 6$), myocardial infarction ($n = 3$), and acute renal failure requiring urgent initiation of renal replacement therapy (n = 3). Three patients died in the 30 days after surgery, and nine needed unplanned reoperation, including three emergency laparotomies performed for concern for anastomotic leak. On regression analysis, increasing VFA but not BMI was associated with increased risk of 30-day major morbidity ($p = 0.002$ vs. $p = 0.17$, respectively). After adjusting for covariates and stepwise selection, VFA remained associated with increased risk of 30-day major morbidity in multivariable analysis ($p = 0.004$, OR 1.998, 95% CI 1.249–3.195). No other body fat distribution variable was associated with increased risk of 30-day major morbidity (Table 3).

ROC analysis was performed to determine the accuracy of VFA in predicting 30-day major morbidity. Area under the ROC curve (AUC) was 0.660. A cutoff value of VFA ≥ 191 cm^2, selected for maximizing Youden's J statistic, was associated with 50% sensitivity and 76% specificity for 30-day morbidity (Fig. 3). In an unadjusted analysis, patients with VFA ≥ 191 cm^2 had a 19.4% probability of developing 30-day major morbidity, compared with 7.2% probability in patients with VFA < 191 cm^2 (relative risk ratio, 2.69, $p = 0.004$). By comparison, obesity status as defined by BMI ≥ 30 kg/m2 was not associated with major morbidity ($p = 0.73$) (Fig. 4). The incidence of major comorbidities for the total cohort, and for patients with VFA ≥ 191 cm^2 and VFA < 191 cm^2, is given in Table 4.

Long-term outcomes

Of the 264 patients, 31 patients (11.7%) died during the study period. Median duration of follow-up was 20.1 months (IQR, 9.4–45.6 months). In univariable analysis, increasing patient age, history of CHF, ASA ≥ 3, increasing AJCC stage, and 30-day major morbidity were each associated with decreased OS; however, no body fat distribution variable was significantly associated with decreased OS (Fig. 5).

Of the 245 patients with stages I–III disease at time of surgery, 27 patients (11.0%) developed disease recurrence. Median duration of surveillance was 15.2 months (IQR, 5.9–29.8 months), and median time to recurrence was 13.4 months (IQR, 5.8–27.6 months). No body fat distribution variable was significantly associated with decreased DFS in univariable analysis (Fig. 6).

Discussion and conclusion

The ability to identify patients at increased risk for complication after surgery facilitates peri-operative decision making and may improve outcomes. In contrast to such factors as comorbidity, ASA class, and functional status, obesity may influence outcomes by virtue of its impact on operative difficulty in addition to physiological systemic effects [9, 10]. Although BMI remains the most widely used metric in defining obesity, its association with adverse postoperative outcome is not clear. The results presented here suggest that neither increasing BMI nor BMI ≥ 30 kg/m^2 was significantly associated with risk of major morbidity.

The concept of visceral obesity marks an important advancement in the understanding of metabolism and physiology and holds promise for improved prediction of perioperative and cardiovascular risk. Various measurements, including WC, WHR, and most recently VFA and other CT-derived anthropometrics, have been proposed to quantify visceral obesity. To date, efforts to determine the association between VFA and postoperative outcomes in patients undergoing colorectal surgery have reported conflicting results. These studies have the primary drawback of evaluating VFA as a dichotomous variable, which assumes a predetermined cutoff value of VFA to define visceral obesity, when in fact, no consensus cutoff value exists. Further, although many of the adopted cutoff values are sensitive and specific for the diagnosis of metabolic syndrome, a known risk factor for future cardiovascular events, their accuracy in predicting short- or long-term outcomes after surgery is not well established. To counter these drawbacks, VFA and other CT-derived measurements of abdominal fat distribution were analyzed in the present study as continuous, rather than dichotomous, variables. Only after establishing the association of VFA with postoperative morbidity in multivariate analysis was an appropriate cutoff value defined, and the distribution of outcomes detected. Consequently, the results presented here may be more robust than those published elsewhere.

This study suggests that increasing VFA but not BMI is positively associated with risk of 30-day major morbidity following elective colectomy for colon cancer. These findings are novel, and stand in contrast to much of the published literature regarding the potential association between VFA and postoperative morbidity [26–28]. Unlike in previous studies, the cutoff value presented here for defining visceral obesity (VFA ≥ 191 cm^2) is based on the treatment of VFA as a continuous variable and is specific for the prediction of postcolectomy complication. In unadjusted analysis, patients with VFA ≥ 191 cm^2 were significantly more likely to suffer major morbidity than patients with VFA < 191 cm^2 (relative risk ratio 2.69, $p = 0.004$). The physiologic mechanism responsible for the association between VFA and postoperative morbidity remains unclear. VFA was not significantly associated with either EBL or procedure time, suggesting that increasing visceral adipose tissue did not contribute to intraoperative technical difficulty. Conceivably, VFA could be a marker of comorbidity, rather than an independent predictor of postoperative risk—indeed increasing VFA was associated to hypertension, type 2 diabetes mellitus and cardiovascular disease (Table 2)—however, the effect of such confounders should have been limited by multivariable analysis.

Neither VFA nor any other CT-derived anthropometric variable was associated with OS or DFS. This result was somewhat unexpected, as visceral obesity is highly correlated with metabolic syndrome, hepatic steatosis [20, 30], coronary artery disease, and increased long-term risk of acute coronary syndrome and mortality [31]. Visceral obesity has also been implicated in colonic inflammation, carcinogenesis, and tumor invasion [39–41]. Nevertheless, our finding is consistent with similar studies, which reported no association between VFA and long-term oncologic outcomes in patients undergoing surgery for colorectal cancer [26, 38]. The relatively short median duration of follow-up of the present series, and the low incidence of mortality and recurrence, may have limited the statistical power of the survival analyses.

The strengths of this study over others are the use of a computerized algorithmic approach to measuring CT-derived anthropometrics, the relatively short accrual period, and strict inclusion and exclusion criteria, which limit the heterogeneity of the study population. Neither attending surgeon nor study year had significant interaction with outcome in univariable analysis ($p \geq 0.05$); thus, surgeon learning curve did not appear to influence results. Other series examined the interaction between VFA and longterm oncologic outcomes, which included patients with rectal cancer who received neoadjuvant therapy as well as treatment-naïve patients with colon cancer [26, 38]. Potential limitations of the present series however include the single center nature of the study population and short follow-up for oncological outcomes.

This study finds that VFA but not BMI is associated with risk of major morbidity following surgery for colon cancer and may have some utilities in preoperative risk stratification. Although the AUC of VFA in predicting major morbidity was modest (0.660), VFA is clearly a more accurate predictor of morbidity than BMI, and thus provides clinicians with superior information than is traditionally available. The results of this study are broadly relevant to ongoing efforts to predict the risk of major postoperative morbidity in patients undergoing elective colon resection. Whereas other studies have only examined the association between "visceral obesity" and morbidity, the present study conclusively demonstrates that increasing VFA is significantly associated with risk of morbidity.

As computerized algorithms for calculating VFA become commercially available, there may be utility in incorporating VFA into peri-operative risk models. Whether visceral obesity is a modifiable risk factor remains poorly understood. Future investigations, perhaps incorporating volumetric quantification of adipose tissue distribution or more diverse patient populations, may yet improve the sensitivity and specificity of this anthropometric in assessing patients' operative risk.

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What does this paper add to the literature?

This manuscript examines the relationship between computed tomography-derived measures of body fat distribution and morbidity and long-term oncologic outcomes after colectomy for cancer. This study seeks to overcome some of the drawbacks of prior studies of this subject. In our series, on multivariate analysis visceral fat area (VFA), but not BMI predicted morbidity following elective surgery for colon cancer. Neither VFA nor BMI was associated with overall or disease-free survival.

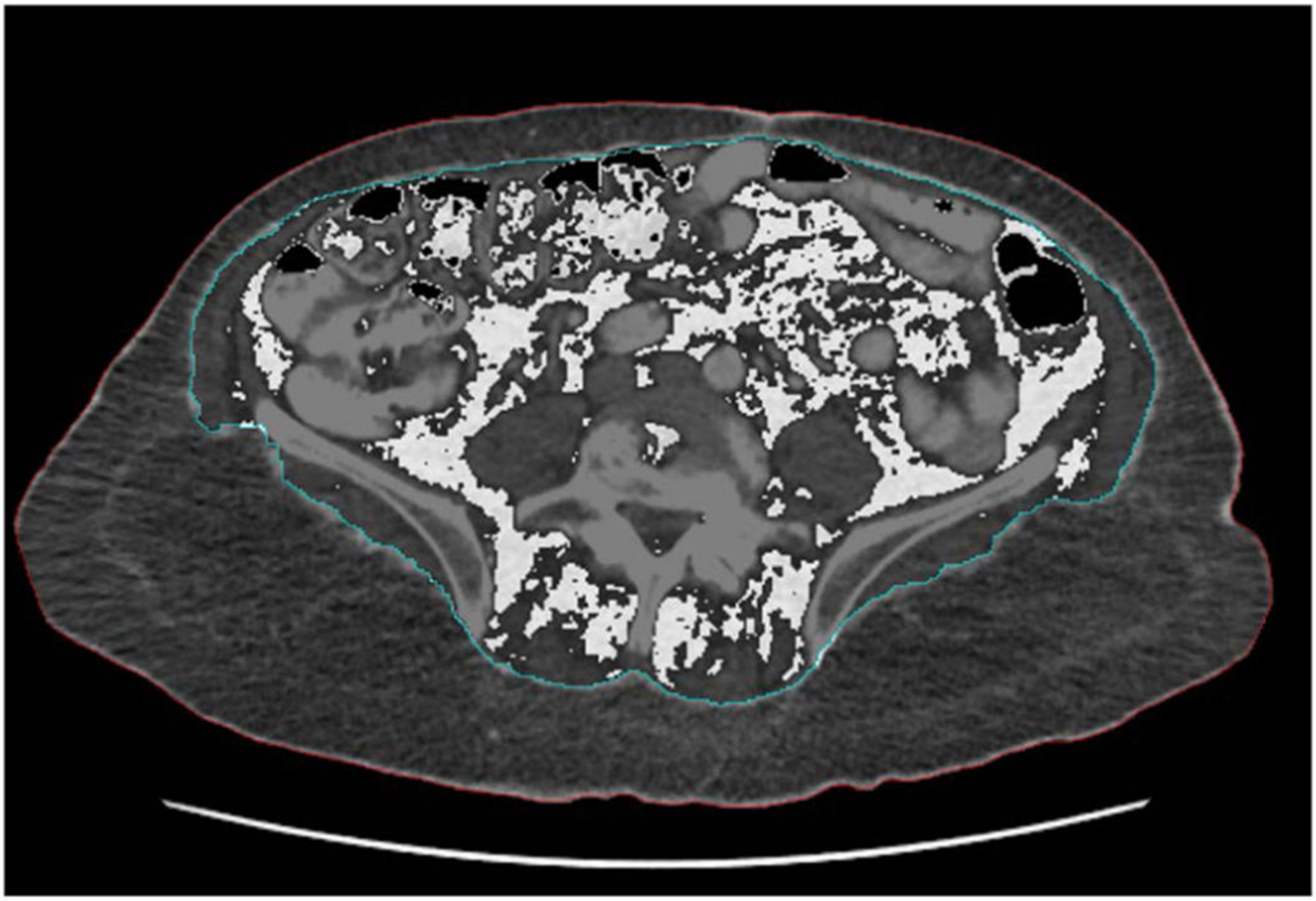

Fig. 1.
Representative axial image, taken at L4/L5 intervertebral level, demonstrating computer-derived body (red) and visceral compartment (blue) contours. Visceral fat area highlighted

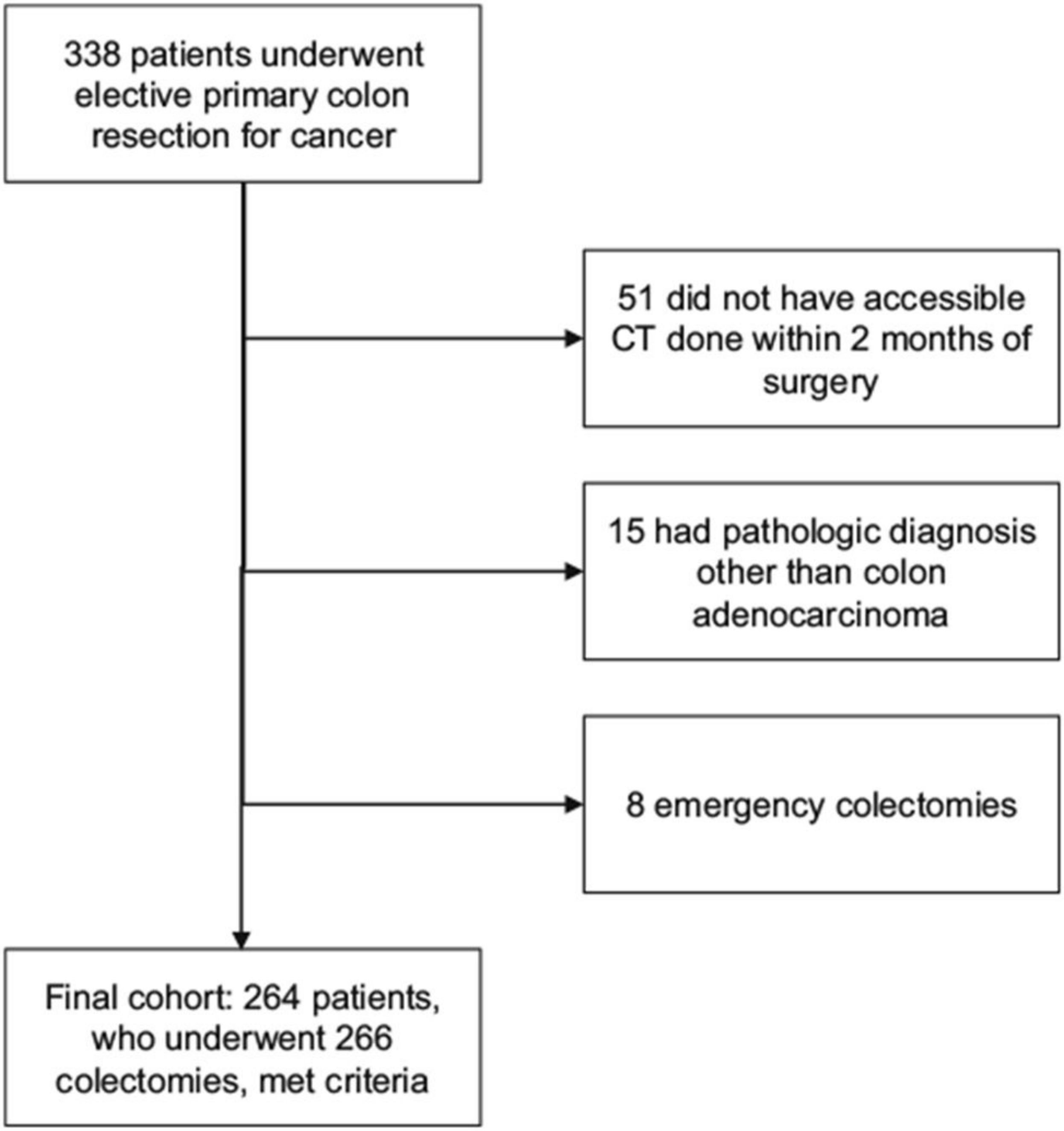

Fig. 2.
Flowchart of exclusion criteria to arrive at final cohort

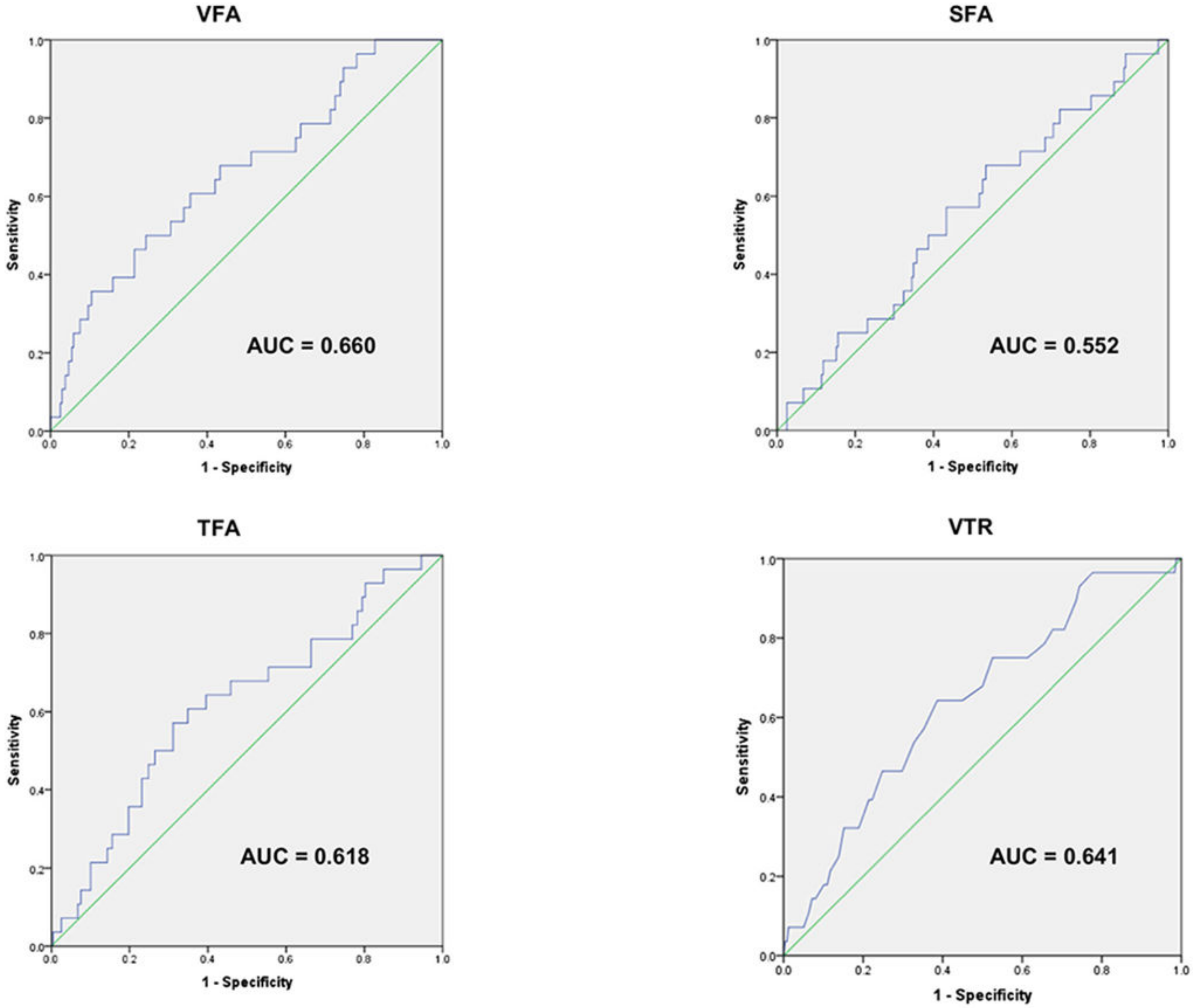

Fig. 3.

ROC curves demonstrating accuracy of exposure variables in predicting 30-day major morbidity. ROC receiver operating characteristic, AUC area under the ROC curve, VFA visceral fat area, SFA subcutaneous fat area, TFA total fat area, VTR visceral-to-total fat ratio

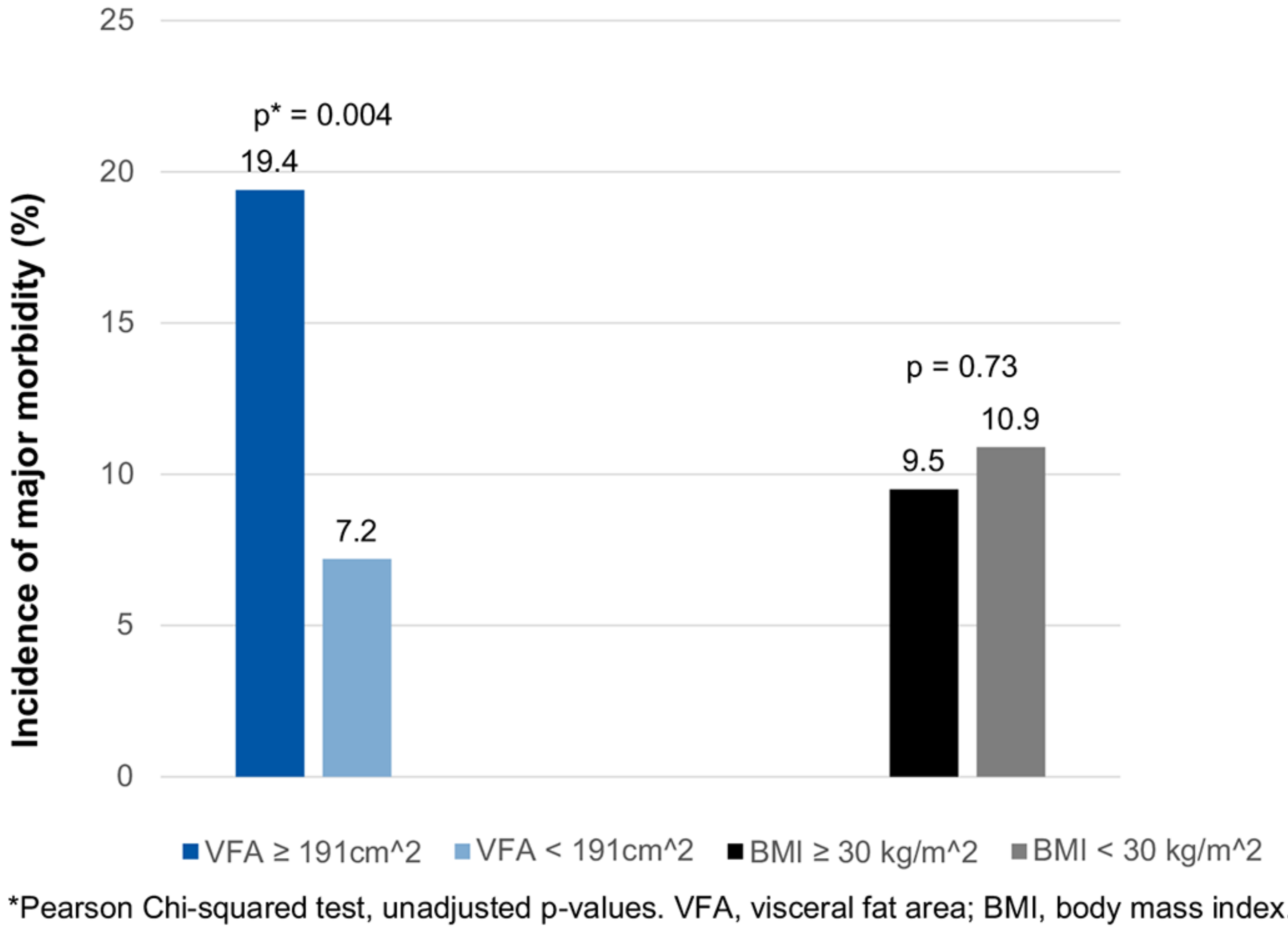

Fig. 4.

Comparison of VFA and BMI as predictors of morbidity, based on obesity cutoff values of VFA ≥ 191 cm^2 and BMI ≥ 30 kg/m^2. *Unadjusted *p* values, Pearson chi-squared test. VFA visceral fat area, BMI body mass index

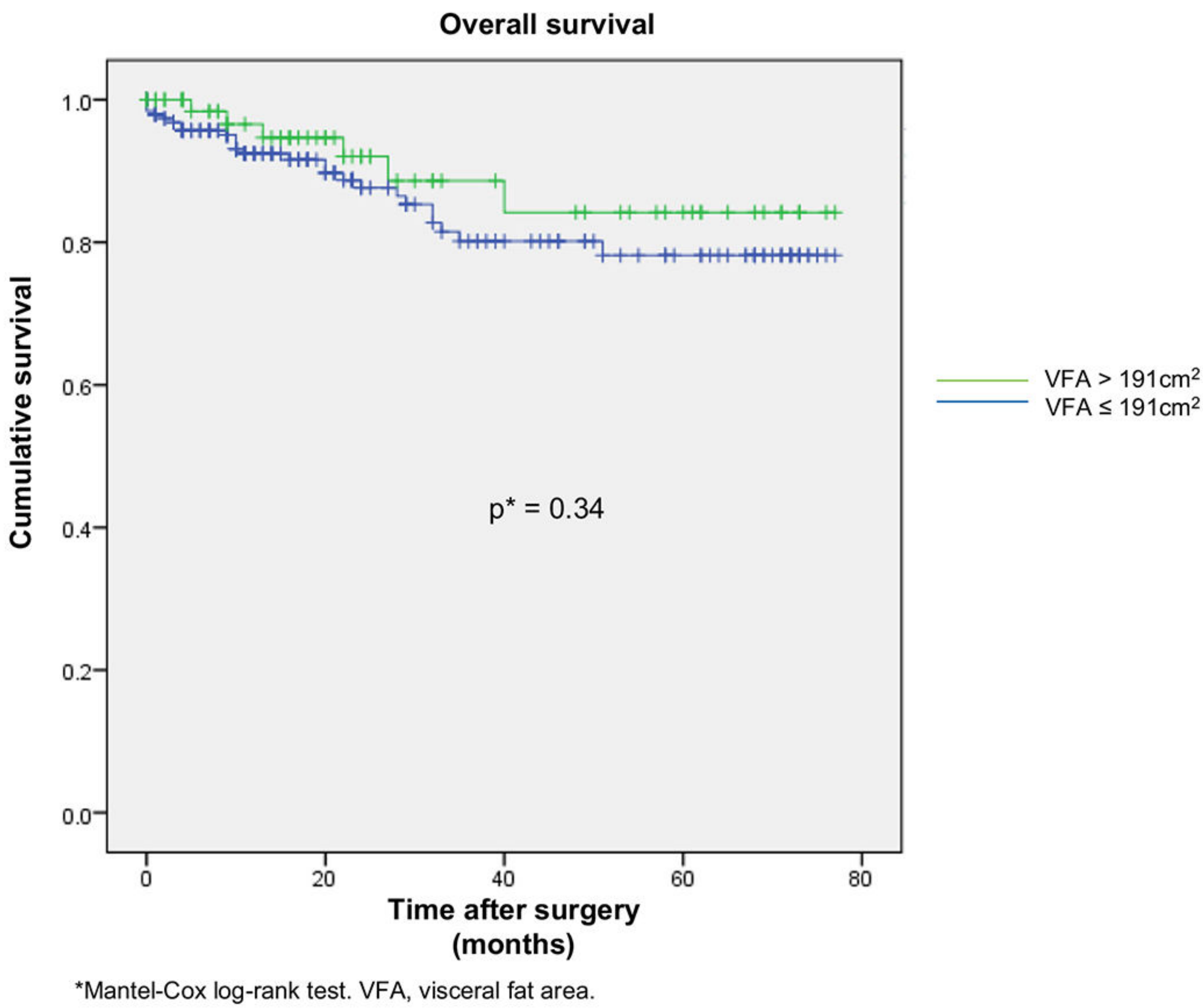

Fig. 5.

Kaplan-Meier estimates of overall survival after elective colectomy for cancer, stratified by VFA ≥ 191 cm^2. *P value, Mantel-Cox log-rank test. VFA visceral fat area

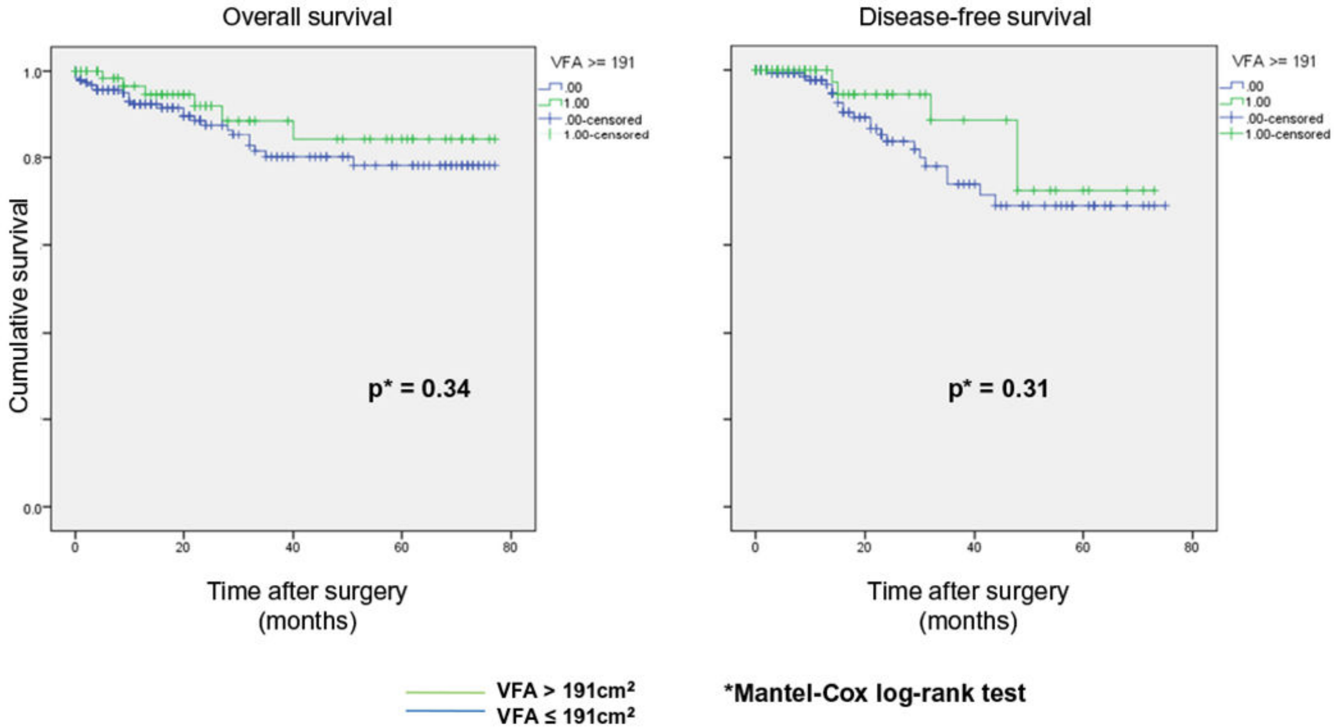

Fig. 6.

Kaplan-Meier estimates of disease-free survival after elective colectomy for cancer, stratified by VFA ≥ 191 cm^2. *P value, Mantel-Cox log-rank test. VFA visceral fat area

Table 1

Patient baseline characteristics

	Number of cases (total *n* = 266)
Median age (years)	67.5 (56–77) *
Female gender	126 (47.3)
Median body mass index (kg/m^2)	26.9 (23.8–30.5) *
Medical comorbidities	
Hypertension	177 (66.5)
Diabetes mellitus	79 (29.7)
Coronary artery disease/myocardial infarction	75 (28.2)
Congestive heart failure	32 (12.0)
Chronic obstructive pulmonary disease	21 (7.9)
ASA physical fitness grade ≥ III	145 (54.5)
AJCC staging	
I	57 (21.4)
II	101 (38.0)
III	89 (33.5)
IV	19(7.1)
Site of primary lesion	
Right	146 (54.9)
Transverse	8 (3.0)
Left	30 (11.3)
Sigmoid	82 (30.8)

Values presented are count (percentage) except

*median (interquartile range, IQR)

ASA American Society of Anesthesiologists, *AJCC* American Joint Committee on Cancer

Table 2

Degree of collinearity between patient baseline characteristics and CT-derived anthropometries

	VFA	SFA	TFA	VTR
Age[a]	*< 0.001*	*0.004*	0.76	*< 0.001*
Female gender[b]	*< 0.001*	*0.001*	0.81	*< 0.001*
Body mass index[a]	*< 0.001*	*< 0.001*	*< 0.001*	0.92
Medical comorbidities[b]				
Hypertension	*< 0.001*	0.08	*< 0.001*	*< 0.001*
Diabetes mellitus	*< 0.001*	0.06	*0.001*	*0.009*
Coronary artery disease/myocardial infarction	*0.001*	0.80	0.15	*< 0.001*
Congestive heart failure	*0.01*	0.86	0.14	*0.01*
Chronic obstructive pulmonary disease	0.75	0.09	0.37	*0.04*
ASA ≥ III[b]	*0.01*	0.55	0.30	*0.001*
AJCC staging[c]	0.23	0.97	0.54	0.42
Site of primary lesion[d]	0.25	0.08	0.05	0.68

Values presented are *p* values, those reaching statistical significance of $p < 0.05$ are in italics.

VFA visceral fat area, *SFA* subcutaneous fat area, *TFA* total fat area, *VTR* visceral-to-total fat ratio

[a]Pearson product-moment correlation

[b]Mann-Whitney *U* test with two independent samples

[c]Kendall's tau-b test

[d]One-way ANOVA

Table 3

Univariable and multivariable of 30-day major morbidity

	Major 30-day morbidity	No major 30-day morbidity	Univariable p[c]	Multivariable analysis	
				Odds ratio[b]	P
No. (%)	28 (10.5)	238 (89.5)			
Mean age[a] (years)	69.1 (9.2)	66.1 (14.7)	0.14		
Female gender	11 (39.3)	115 (48.3)	0.43		
ASA ≥ 3	21 (75)	124 (52.1)	0.03		
Hypertension	21 (75)	156 (65.5)	0.40		
Hyperlipidemia	17 (60.7)	103 (43.3)	0.11		
Diabetes mellitus	15 (53.6)	64 (26.9)	0.007		
Coronary artery disease/myocardial infarction	9 (32.1)	66 (27.7)	0.66		
Laparoscopy	14 (50)	175 (73.5)	0.03		
Site of lesion			0.43		
Right	13 (46.4)	133 (55.9)			
Transverse	0 (0)	8 (3.4)			
Left	5 (17.9)	25 (10.5)			
Sigmoid	10 (35.7)	72 (30.3)			
Body mass index[a]	28.8 (8.7)	27.2 (5.3)	0.36[d]	1.04 (0.97–1.11)	0.26
VFA[a]	188.4 (98.5)	135 (81.5)	0.002[d]	*2.00 (1.25–3.20)*	*0.004*
SFA[a]	284.2 (127.5)	263.4 (129.2)	0.42[d]	1.07 (0.78–1.48)	0.66
TFA[a]	472.6 (190.5)	398.4 (178.3)	0.04[d]	1.20 (0.94–1.51)	0.14
VTR[a]	0.398 (0.128)	0.335 (0.127)	0.01[d]	27.90 (0.96–810.08)	0.05

Values in parentheses are percentages unless otherwise indicated. All variables with $P < 0.01$ in univariable analysis were considered in multivariable stepwise logistic regression analysis.

Statistically significant results of multivariable analysis are presented in italics

ASA American Society of Anesthesiologists, *VFA* visceral fat area, *SFA* subcutaneous fat area, *TFA* total fat area, *VTR* visceral-to-total fat ratio

[a]Values in parentheses are standard deviations

[b]Values in parentheses are 95% CI

[c] Fisher's exact test

[d] Student's *t* test

Table 4

Incidence of 30-day major morbidity (Clavien-Dindo grade ≥ III) in overall cohort, and in obesity cohorts defined by VFA ≥ 191 cm^2 and BMI ≥ 30 kg/m^2

	Overall cohort	VFA ≥ 191 cm^2	VFA < 191 cm^2	*P* value[a]	BMI ≥ 30 kg/m^2	BMI < 30 kg/m^2	*P* value[a]
30-day major morbidity, n (%)	28 (10.5)	14 (19.4)	14 (7.2)	0.004	7 (9.5)	21 (10.9)	0.73
Reoperation	9 (3.4)	4 (5.6)	5 (2.6)	–	2 (2.7)	7 (3.6)	–
Cerebrovascular accident	1 (0.4)	0	1 (0.4)	–	0	1 (0.5)	–
Acute myocardial infarction	3 (1.1)	2 (2.8)	1 (0.5)	–	1 (1.4)	2 (1.0)	–
Respiratory failure requiring intubation	6 (2.3)	3 (4.2)	3 (1.5)	–	3 (4.1)	3 (1.6)	–
Acute renal failure requiring dialysis	3 (1.1)	2 (2.8)	1 (0.5)	–	2 (2.7)	1 (0.5)	–
Sepsis	10 (3.8)	5 (6.9)	5 (2.6)	0.01	3 (4.1)	7 (3.6)	–
Death	3 (1.1)	0	3 (1.5)	–	1 (1.4)	2 (1.0)	–

Some patients suffered multiple Clavien-Dindo grade ≥ III complications. Outcomes not meeting the minimum expected $n \geq 5$ have been excluded

[a] Pearson chi-squared test