



INFLUENCE OF MUSCLE MASS AREA AND VISCERAL OBESITY ON 30-DAY MORTALITY AFTER COLORECTAL SURGERY WITH PRIMARY ANASTOMOSIS

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ABSTRACT

Background: Muscle mass and visceral fat may be assessed at the level of the third lumbar vertebra (L3) in computed tomography (CT). Both variables have been related with adverse surgical outcomes. **Objective:** The objective of the study was to study the association of skeletal muscle index (SMI) and visceral fat area (VFA) with 30-day mortality in colorectal surgery. **Methods:** This is a retrospective cohort study conducted at a tertiary referral hospital in Mexico City. Patients who underwent colorectal surgery with primary anastomosis from January 2007 to December 2018 were included in the study. Their pre-operative CT scans were analyzed with the NIH ImageJ software at the level of the third lumbar vertebra to determine their SMI (L3-SMI) and the VFA. Logistic regression analysis (adjusted by surgery anatomical location) was used to determine the association between these variables and surgical 30-day mortality. **Results:** A total of 548 patients were included; 30-day mortality was 4.18% (23 patients). On univariable analysis, L3-SMI, low SMI, anastomosis leak, pre-operative albumin, estimated blood loss, age, steroid use, Charlson comorbidity index score >2, and type of surgery were associated with 30-day mortality. On multivariable analysis, low SMI remained an independent risk factor with an odds ratio of 4.74, 95% confidence interval 1.22-18.36 ($p = 0.02$). **Conclusion:** Low SMI was found to be an independent risk factor for 30-day mortality in patients submitted to colorectal surgery with a primary anastomosis, whether for benign or malignant diagnosis. VFA was not associated with 30-day mortality. (REV INVEST CLIN. 2021;73(6):379-87)

Key words: Sarcopenia. Skeletal muscle. Visceral fat. Colorectal surgery.

BACKGROUND

Body composition analysis by computed tomography (CT) has been studied in different medical outcomes.

Adipose and muscle tissue distribution are strongly correlated to the patients' metabolic and performance status, respectively; both features could influence surgical outcomes. The visceral fat area (VFA) and

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skeletal muscle area (SMA) may be assessed by the quantification of each tissue in a transversal CT image at the third lumbar vertebra (L3) with excellent inter and intraobserver agreement. Both variables have been identified as prognostic factors for oncologic and surgical outcomes among colorectal cancer surgery patients. The use of image analysis to determine fat and muscle distribution is an advantage because CT is widely available among this population^{1,2}.

Visceral obesity has been associated with longer operative times and hospital stays, as well as with increased morbidity^{3,4}. Low skeletal muscle mass is also known to have a negative effect on post-operative outcomes⁵, mainly among patients with cancer, increasing their morbidity and mortality. Most data regarding SMA and adipose tissue analysis focus on the oncological population, but there is a lack of information regarding patients with benign entities. The importance of identifying the implications of SMA and VFA in surgical outcomes relies on the implementation of interventions that target SMA and VFA to improve these outcomes.

Sarcopenia is defined by the Sarcopenia Working Group as a syndrome characterized by the loss of skeletal muscle mass and strength⁶. Since we only analyzed muscle area and not function, we decided not to use the term sarcopenia; instead, the term SMA or skeletal muscle index (SMI) will be used accordingly. SMI is obtained by dividing the patients' SMA by their height.

The objective was to study the association of VFA and SMI with 30-day mortality in patients undergoing any colorectal surgery including primary anastomosis. A secondary aim was to analyze the association between these variables and anastomosis leak (AL).

METHODS

Study Population

This study is a retrospective analysis of all patients who underwent colorectal surgery with primary anastomosis from January 2007 to December 2018 at a tertiary referral hospital in Mexico City. We excluded

54 patients who had incomplete medical charts since the variables needed for the study could not be obtained from the electronic or physical files or because no pre-operative CT was available. Finally, only 548 patients were included in the study. All surgeries were performed by the two chief surgeons of our colorectal surgery department.

Data Collection

For each patient, the following variables were collected: (1) patient characteristics, including age, sex, preoperative albumin, diagnosis (cancer or benign), steroid use, current smoker, comorbidities calculated with Charlson comorbidity index (CCI) score, weight, height, body mass index (BMI), VFA, and SMA; (2) operative details, including the type of surgery (right hemicolectomy, left hemicolectomy, surgeries with rectal anastomosis, and others) blood loss, type of case (urgent or elective surgery), number of anastomoses, type of anastomosis (manual or stapled), approach (open or laparoscopic), conversion, protective stoma, and operative time; and (3) post-operative outcomes: AL, length of stay, 30-day readmission, and 30-day mortality. This study was approved by our institution's Research Ethics Committee with the reference number GAS 3184 19 20 1.

Body Composition Analysis

Pre-operative CTs were assessed with NIH ImageJ software, version 1.48⁷. VFA and SMA were assessed at the level of L3. VFA was computed with a Hounsfield unit (HU) threshold between -30 and -190 HU, whereas SMA with a threshold between -29 and +150 HU. The L3-SMI was calculated by dividing SMA/height (cm²). Visceral obesity was defined as a VFA >100 cm², and low SMI was diagnosed if patients had an SMI <52.4 cm²/m² and <38.5 cm²/m² in men and women, respectively⁸. Agreement between raters to classify patients as having or not having low SMI was assessed with Cohen's kappa. We also computed the intraclass correlation coefficient of the estimated SMA⁹.

Statistical Analysis

Statistical analysis was performed using Stata 14 (StataCorp, Texas, USA). Continuous variables were

Table 1. Frequency of low SMI and visceral obesity by BMI (cm/m²) category

Characteristics	BMI <18.5 (n = 31)	BMI 18.5-24.9 (n = 246)	BMI 25-29.9 (n = 205)	BMI >30 (n = 66)
Low SMI ^a , n (%)	20 (64)	153 (62)	99 (48)	14 (21)
Visceral obesity ^b , n(%)	2 (6)	88 (36)	147 (72)	58 (88)

^aDefined as an SMI at the level of L3 of < 52.4 cm²/m² in men and < 38.5 cm²/m² in women.

^bDefined as visceral fat area >100 cm².

BMI: body mass index; SMI: skeletal muscle index.

presented as means \pm standard deviations and categorical variables as frequencies (n) and percentages. Variables were compared using the Chi-squared test or Fisher's exact test, and Student's t-test as appropriate. To study the association between body composition variables and the outcomes of interest (i.e., 30-day mortality and AL), we used logistic regression. Those variables with $p < 0.05$ were included in a multivariable analysis. We used the Box-Tidwell model to test the linearity of continuous variables and goodness-of-fit was assessed by the Hosmer-Lemeshow test.

RESULTS

General Characteristics of Patients

The study population consisted of 548 patients with a mean age of 57.4 \pm 17.4 years; 262 (47.7%) were male. The prevalence of low SMI was 52% (286 patients), and it was higher among men (60% vs. 45%, $p < 0.001$). The prevalence of visceral obesity was 53.7% (295 patients) and was also more common in men (69% vs. 40%, $p < 0.001$).

According to the BMI, among the overweight and obese patients, low SMI was found in 99 (48%) and 14 (21%), respectively; visceral obesity was found in 88 (36%) patients with normal BMI (Table 1). The prevalence of visceral obesity in conjunction with low SMI (i.e., low SMI and high VFA) was 28%; when obesity was defined by the BMI (i.e., >30) instead of VFA, the prevalence was 2.5%. The mean BMI was 25.2 \pm 5.1 kg/m².

The most common surgery was right hemicolectomy in 174 patients (32.5%). Two hundred and eighteen

(40%) cases were laparoscopic, and the conversion rate was 35%. Two hundred and seventy-six patients (50%) had colorectal cancer. The rest of the variables is described in Table 2.

Patients with low SMI were older (60.4 \pm 18.2 vs. 54.2 \pm 16.0 years; $p < 0.001$), had a lower BMI (23.9 \pm 3.8 vs. 26.8 \pm 5.8 kg/m²; $p < 0.001$), and had a higher 30-day mortality (6.6% vs. 1.5%; $p = 0.003$) than patients with a normal SMI. There were no differences in length of stay, 30-day readmission, or frequency of AL. Compared to non-obese patients, those with visceral obesity were more commonly men (62% vs. 32%; $p < 0.001$) and were older (60.2 \pm 15.3 vs. 54.1 \pm 19.1 years; $p < 0.001$). Table 3 compares patients according to their body composition. The 30-day mortality was similar in patients with and without visceral obesity in conjunction with low SMI (6.5% vs. 3.3%; $p = 0.09$). Cohen's kappa coefficient for the assessment of low SMI was 0.76 ($p < 0.001$), and the intraclass correlation coefficient for SMA was 0.96 ($p < 0.001$).

Features Associated with Mortality and AL

Thirty-day mortality was 4%. On univariable analysis (Table 4), factors associated with mortality were low SMI (odds ratio [OR] 4.59, 95% confidence interval [CI] 1.54-13.67; $p = 0.006$), the L3-SMI (OR 0.92, 95% CI 0.87-0.97; $p = 0.003$), AL (OR 8.62, 95% CI 3.57-20.82; $p < 0.001$), pre-operative albumin (OR 0.34, 95% CI, 0.20-0.56; $p < 0.001$), estimated blood loss (OR 1.00, 95% CI 1.00-1.001; $p = 0.02$), age (OR 1.06, 95% CI 1.03-1.09; $p < 0.001$), CCI score >2 (OR 10.30, 95% CI 3.75-28.26; $p < 0.001$), steroid use (OR 5.33, 95% CI 1.83-15.48; $p = 0.002$), and other type of surgery (i.e., total colectomy,

Table 2. General population characteristics (n = 548)

Patient characteristics	Total
Male, n (%)	262 (48)
Age (years), mean + SD	57.4 + 17.4
Low SMI ^a , n (%)	286 (52)
Visceral obesity ^b , n (%)	295 (54)
BMI (kg/m ²), mean + SD	25.3+5.1
Cancer diagnosis, n (%)	276 (50)
Pre-operative albumin (g/dL), mean + SD	3.8+0.7
Current smoker, n (%)	230 (42)
Steroid use, n (%)	31 (6)
Operative details	
Type of surgery, n (%)	
Right hemicolectomy	174 (32)
Sigmalectomy	128 (23)
Stoma closure	75 (14)
Total colectomy	25 (4)
Left hemicolectomy	37 (7)
Low anterior resection	42 (8)
Proctocolectomy + J pouch	26 (5)
Others ^c	116 (21)
Estimated blood loss (mL), mean + SD	374.5+371.5
Emergency surgery, n (%)	92 (17)
Surgical time (minutes), mean + SD	247.0+94.7
Manual anastomosis, n (%)	59 (11)
Laparoscopic surgery, n (%)	218 (40)
Conversion, n (%)	71 (35)
Loop ileostomy, n (%)	157 (29)
Post-operative outcomes	
30-day readmission, n (%)	38 (7)
30-day mortality, n (%)	23 (4)
AL, n (%)	53 (9.7)
Clavien-Dindo, n (%)	
I	76 (14.10)
II	67 (12.43)
IIIA	21 (3.90)
IIIB	33 (6.12)
IVA	42 (7.79)
IVB	25 (4.64)
V	23 (4)

BMI: body mass index; SMI: skeletal muscle index;

SD: standard deviation; AL: anastomosis leak.

^aDefined as an SMI at the level of L3 of <52.4 cm²/m² in men and <38.5 cm²/m² in women.^bDefined as visceral fat area >100 cm².^cStoma closure and segmental resection.

proctocolectomy, sigmoidectomy, and low anterior resection) (OR 2.78, 95% CI 0.95-8.07; p = 0.06). On multivariable analysis (Table 4), low SMI remained an independent risk factor for 30-day mortality as well as AL, age, steroid use, CCI >2, pre-operative serum albumin levels, estimated blood loss, and other types of surgery. The same variables were associated with 30-day mortality when including L3-SMI instead of low SMI in the multivariable analysis.

AL developed in 53 (9.7%) patients; blood loss, CCI >2, and other types of surgery were variables associated with AL in univariable and multivariable analyses (Table 5).

A sub-analysis of geriatric and oncological patients can be found in Supplementary Tables 1 and 2.

DISCUSSION

Body composition assessment through radiological evaluation has become an important pre-operative tool to identify patients with increased risk of poorer surgical outcomes. In this study, we investigated the association between SMA, assessed with the SMI, and VFA with 30-day mortality among colorectal surgery patients.

In this work, we found low SMI to be independently associated with 30-day mortality but not with AL. On the other hand, neither visceral obesity nor visceral obesity in conjunction with low SMI was associated with any of these outcomes. To the best of our knowledge, this is the first study comparing the influence of both visceral obesity and SMI on post-operative outcomes of patients undergoing colorectal surgery for oncologic and benign disorders in a Mexican population.

The prevalence of low SMI in our population was 52%, and 54% of patients had visceral obesity. Despite the high prevalence of low SMI in oncological patients, no difference in low SMI prevalence was found between oncological and non-oncological patients in our study. This underlines the importance of assessing muscle mass and function in all surgical patients, and not only in elderly or oncological patients.

Table 3. General characteristics by body composition

Variable	Normal SMI (n = 262)	Low SMI ^a (n = 286)	p-value	No visceral obesity (n = 253)	Visceral obesity ^b (n = 295)	p-value
Pre-operative characteristics						
Male, n (%)	105 (40)	157 (55)	<0.001	80 (32)	182 (62)	<0.001
Age (years), mean + SD	54.2 + 16.0	60.4 + 18.2	<0.001	54.1 + 19.1	60.2 + 15.3	<0.001
Charlson comorbidity index >2, n (%)	119 (45)	156 (54)	0.03	120 (47)	155 (52)	0.2
Cancer diagnosis, n (%)	134 (51)	142 (50)	0.7	132 (52)	144 (49)	0.2
BMI (kg/m ²), mean + SD	26.8 + 5.8	23.9 + 3.8	<0.001	22.8 + 3.8	27.4 + 5.1	<0.001
Albumin (g/dL), mean + SD	3.8 + 0.8	3.8 + 0.7	0.4	3.7 + 0.8	3.9 + 0.7	0.07
Surgical characteristics						
Surgical time (min), mean + SD	252.9 + 91.2	241.6 + 97.5	0.2	242.9 + 94.1	250.5 + 95.2	0.4
Manual anastomosis, n (%)	29 (11)	30 (10)	0.8	34 (13)	25 (8)	0.06
Laparoscopic, n (%)	119 (45)	99 (35)	0.009	92 (36)	126 (43)	0.1
Blood loss (mL), mean + SD	389.1.9 + 402.6	361.2 + 340.6	0.4	347.4 + 359.2	397.8 + 380.7	0.1
Conversion, n (%)	38 (34)	33 (36)	0.8	24 (28)	47 (41)	0.05
Loop ileostomy, n (%)	81 (31)	76 (26)	0.2	75 (29)	82 (28)	0.6
Post-operative outcomes						
AL, n (%)	24 (9)	29 (10)	0.7	20 (8)	33 (11)	0.2
Length of stay (days), mean + SD	14.3 + 23.7	14.7 + 24.8	0.8	13.9 + 23.1	15.0 + 25.3	0.6
30-day readmission, n (%)	18 (7)	20 (7)	0.9	19 (8)	19 (6)	0.6
30-day mortality, n (%)	4 (1.5)	19 (6.6)	0.003	10 (4)	13 (4)	0.8

^aDefined as an SMI at the level of L3 of <52.4 cm²/m² in men and <38.5 cm²/m² in women.

^bDefined as visceral fat area >100 cm².

BMI: body mass index; SD: standard deviation; SMI: skeletal muscle index. AL: anastomosis leak.

We found low SMI to be an independent predictor of 30-day mortality after colorectal surgery, as it has been previously described in patients with colorectal cancer¹⁰⁻¹³. Low SMI may imply a prolonged state of catabolism, impaired host immune function, and inadequate response to an inflammatory state¹⁴.

An association could not be found between AL and VFA or SMI, as described in other retrospective studies^{10,15-17}. Even a prospective cohort study of 80 patients who underwent elective surgery for colon cancer found no relationship between SMI and any post-operative morbidity¹⁸.

In opposition to this, other authors^{10,19-23} have found low SMI to be a predictor of overall complications and length of stay. Herrod et al.²¹ evaluated psoas density as a surrogate for SMI and found that patients with smaller psoas muscles had an OR of 14.37 for AL and 6.33 for overall complications, though mortality was not affected. The morphologic change of the psoas has also been described as an independent risk factor for overall complications and AL in surgical colorectal cancer patients²⁴. In addition, sarcopenic obesity in patients with gastrointestinal solid tumors has also been associated with⁸, longer length of stay, and higher readmission rates²⁴. In our population,

Table 4. Variables associated with 30-day mortality on univariable and multivariable analysis

Variable	Univariable		Multivariable ^a		Multivariable ^b	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Low SMI ^c	4.59 (1.54-13.67)	0.006	4.74 (1.22-18.36)	0.02	—	—
L3-SMI, cm ² /m ²	0.92 (0.87-0.97)	0.003	—	—	0.93 (0.87-0.99)	0.03
Visceral obesity ^d	1.12 (0.48-2.60)	0.8	—	—	—	—
VFA, cm ²	1.00 (0.99-1.00)	0.3	—	—	—	—
Low L3-SMI and visceral obesity	2.05 (0.88-4.79)	0.09	—	—	—	—
AL	8.62 (3.57-20.82)	<0.001	5.08 (1.53 - 16.85)	0.008	5.66 (1.70-18.83)	0.005
Albumin, g/dL	0.34 (0.20-0.56)	0.001	0.33 (0.16-0.68)	0.002	0.36 (0.17-0.73)	0.005
Blood loss, mL	1.00 (1.00-1.001)	0.02	1.00 (0.99-1.00)	0.3	1.00 (0.99-1.00)	0.5
Male sex	1.20 (0.52-2.76)	0.7	—	—	—	—
Age, years	1.06 (1.03-1.09)	<0.001	1.06 (1.01-1.09)	0.007	1.06 (1.02-1.10)	0.003
Steroid use	5.33 (1.83-15.48)	0.002	4.87 (1.09-21.64)	0.04	4.61 (1.09-19.51)	0.04
CCI >2	10.30 (3.75-28.26)	<0.001	4.64 (1.37-15.66)	0.01	4.32 (1.30-14.33)	0.02
BMI, kg/m ²	0.98 (0.90-1.08)	0.8				
Presence >1 anastomosis	1.62 (0.36-7.28)	0.5				
Loop ileostomy	1.09 (0.44-2.71)	0.8				
Type of surgery						
Right hemicolectomy	Reference	0.9	Reference	0.6	Reference	0.7
Left hemicolectomy	0.94 (0.11-8.28)		1.65 (0.14-19.49)		1.53 (0.11-19.71)	
Surgeries with rectal anastomosis ^e	0.97 (0.27-3.41)	0.9	1.71 (0.38-7.74)	0.4	2.21 (0.49-9.80)	0.3
Others	2.78 (0.95-8.07)	0.06	8.89 (2.04-38.78)	0.004	9.59 (2.20-41.73)	0.003

^aConsidering low SMI,^bconsidering L3-SMI.^cDefined as a SMI at the level of L3 of <52.4 cm²/m² in men and <38.5 cm²/m² in women.^dDefined as VFA >100 cm².^eTotal colectomy, proctocolectomy, sigmoidectomy, and low anterior resection.

BMI: body mass index; CI: confidence interval; OR: odds ratio; SMI: skeletal muscle index. VFA: visceral fat area; AL: anastomosis leak;

CCI: Charlson comorbidity index.

Table 5. Variables associated with AL on univariable and multivariable analysis

Variable	Univariable		Multivariable	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Low SMI ^a	1.11 (0.63-1.97)	0.7		
L3-SMI, cm ² /m ²	1.00 (0.97-1.03)	0.7		
Visceral obesity ^b	1.47 (0.82-2.62)	0.2		
VFA, cm ²	1.00 (0.99-1.00)	0.1		
Low L3-SMI and visceral obesity	1.37 (0.75-2.50)	0.3		
Albumin, g/dL	0.76 (0.53-1.10)	0.1		
Blood loss, mL	1.00 (1.00-1.001)	0.006	1.00 (1.00-1.001)	0.007
Male sex	1.36 (0.77-2.40)	0.3		
Age, years	1.01 (0.99-1.02)	0.2		
Steroid use	1.41 (0.47-4.21)	0.5		
CCI >2	1.89 (1.05-3.40)	0.03	2.07 (1.13-3.81)	0.02
BMI, kg/m ²	1.03 (0.97-1.08)	0.2		
Loop ileostomy	1.32 (0.72-2.40)	0.4		
Type of surgery				
Right hemicolectomy	Reference		Reference	
Left hemicolectomy	2.86 (0.90-9.10)	0.07	3.36 (1.03-10.89)	0.04
Surgeries with rectal anastomosis ^c	1.79 (0.77-4.18)	0.2	1.96 (0.83-4.65)	0.1
Others	3.12 (1.39-6.97)	0.005	3.26 (1.44-7.37)	0.004

^aDefined as a SMI at the level of L3 of <52.4 cm²/m² in men and <38.5 cm²/m² in women.

^bDefined as VFA > 100 cm². ^cTotal colectomy, proctocolectomy, sigmoidectomy, and low anterior resection.

BMI: body mass index; CI: confidence interval; OR: odds ratio; SMI: skeletal muscle index. VFA: visceral fat area; AL: anastomosis leak; CCI: Charlson comorbidity index.

visceral obesity in conjunction with low SMI was not related to any adverse outcomes.

Other predictive factors for 30-day mortality besides skeletal muscle in multivariate analysis were AL, pre-operative albumin levels, age, CCI >2, "other" types of

surgery, and steroid use. AL is a very threatening complication in colorectal surgery, whose association with 30-day has been previously described²⁵.

Concerning pre-operative albumin, patients with lower albumin may have a poorer nutritional status that

relates to negative outcomes²⁶. Patients with greater estimated blood loss may have had more difficult operative courses, linked to longer operative times and more blood transfusions. All these elements may be related to adverse post-operative outcomes and, thus, more mortality. Moreover, blood loss has been related to a depleting effect in the immune system^{27,28}. Steroid use may be associated with mortality because of impaired tissue healing and immune response²⁹. Mortality is also expected to be more prevalent among older people, with more comorbidities as our study suggested. The increased 30-day mortality among patients who had other types of surgery (including stoma closure and segmental colonic resection) cannot be explained, as it is expected that surgeries with rectal anastomosis are more challenging²⁵. However, since these surgeries were also related to AL, a high 30-day mortality is expected.

Visceral obesity has been related to adverse outcomes in colorectal surgery³⁰⁻³³, including a higher incidence of systemic complications presumably caused by longer operative times, a higher frequency of metabolic, cardiovascular comorbidities³⁴, and more operative blood loss³⁵. At least two meta-analyses by Yang et al.³⁶ and Cakir et al.⁴ found that post-operative complications in laparoscopic procedures were more frequent in patients with visceral obesity. However, we could not corroborate these data. Visceral obesity was not associated with mortality or AL. Other authors have also found no increased morbidity among patients with visceral obesity³⁷⁻³⁹, and the reason behind this discrepancy may be that visceral obesity mainly seems to affect laparoscopic approaches, and only 40% of the cases in our cohort were laparoscopic. A meta-analysis on the association between visceral obesity and AL could not draw appropriate conclusions due to the heterogeneity between studies, but a tendency against an association between AL and visceral obesity was established⁴⁰.

Our study has several limitations, the most important one being its retrospective nature. Although an association between low SMI and mortality was found, prospective studies are needed to confirm the association and explore whether preconditioning and muscle mass improvement may reduce mortality. Another limitation is that our study only evaluates

SMI. Muscle function was not considered in this analysis, so its interaction with surgical outcomes could not be described. Finally, the number of outcomes in our study was limited, and therefore, the results of the multivariable analysis should be interpreted with caution.

In conclusion, SMI, but not visceral obesity, was independently associated with 30-day mortality. Neither low SMI nor visceral obesity was associated with AL. The role of preconditioning in elective surgeries to improve outcomes needs to be further explored.

Supplementary Data

Supplementary data are available at Revista de Investigación Clínica online (www.clinicalandtranslational-investigation.com). These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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