The Overweight Paradox: Impact of Body Mass Index on Patients Undergoing VATS Lobectomy or Segmentectomy

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Abbreviations: BMI, Body Mass Index; VATS, Video-Assisted Thoracic Surgery; DFS, Disease Free Survival; OS, Overall Survival; WHO, World Health Organization; IRB, Institutional Review Board; FEV1, Forced Expiratory Volume in the 1st second; FVC, Forced Vital Capacity; DLCO/Va, diffusing capacity of the lungs for carbon monoxide/ alveolar volume; IQR, Interquartile Range; OR, Odds Ratio; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus

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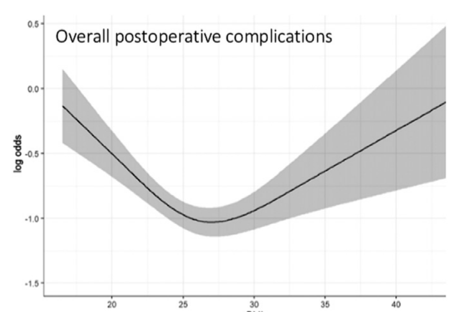
The aim of this study was to assess the impact of BMI on perioperative outcomes in patients undergoing VATS lobectomy or segmentectomy. Data from 5088 patients undergoing VATS lobectomy or segmentectomy, included in the VATS Group Italian Registry, were collected. BMI (kg/m^2) was categorized according to the WHO classes: underweight, normal, overweight, obese. The effects of BMI on outcomes (complications, 30-days mortality, DFS and OS) were evaluated with a linear regression model, and with a logistic regression model for binary endpoints. In overweight and obese patients, operative time increased with BMI value. Operating room time increased by 5.54 minutes (S.E. = 1.57) in overweight patients, and 33.12 minutes (S.E. = 10.26) in obese patients ($P < 0.001$). Compared to the other BMI classes, overweight patients were at the lowest risk of pulmonary, acute cardiac, surgical, major, and overall postoperative complications. In the overweight range, a BMI increase from 25 to 29.9 did not significantly affect the length of stay, nor the risk of any complications, except for renal complications (OR: 1.55; 95% CI: 1.07−2.24; $P = 0.03$), and it reduced the risk of prolonged air leak (OR: 0.8; 95% CI: 0.71−0.90; $P < 0.001$). 30-days mortality is higher in the underweight group compared to the others. We did not find any significant difference in DFS and OS. According to our results, obesity increases operating room time for VATS major lung resection. Overweight patients are at the lowest risk of pulmonary, acute cardiac, surgical, major, and overall postoperative complications following VATS resections.



BMI influence on postoperative complications: overweight patients are at the lowest risk.

Central Message

Obesity increases operating room time for VATS lung resections. Overweight patients are at the lowest risk of most postoperative complications. 30-days mortality is higher in the underweight group.

The risk of most postoperative complications progressively increases as the BMI deviates from the point at the lowest risk, towards both extremes of BMI values. Thirty days mortality is higher in the underweight group, with no differences in DFS and OS.

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Keywords: Obesity paradox, Overweight paradox, VATS, Body Mass Index (BMI), Thoracic surgery, Lung resection

Perspective Statement

When BMI was investigated as a predictor of postoperative outcomes in general and cardiac surgery, patients at the extremes of BMI have the highest postoperative risk, which is not increased in overweight and mildly obese. In our study, after VATS major lung resections, overweight patients are at the lowest risk of pulmonary, acute cardiac, surgical, major, and overall postoperative complications.

INTRODUCTION

Large-scale studies suggested that all-cause, metabolic, cancer and cardiovascular morbidity begin to rise when Body Mass Index (BMI) is ≥ 25, which is considered medically significant and worthy of therapeutic intervention by most physicians.[1−4] In contrast to this widely accepted view, several studies found an inverse correlation between BMI and mortality, especially in chronically ill patients and in patients undergoing certain procedures.[5,6] These observations gave rise to a medical hypothesis, known as "the obesity paradox," which holds that excess weight may be protective on mortality in some groups of people.[7] When BMI was investigated as a predictor of postoperative outcomes after various surgical procedures, evidence in support of the presence of an obesity paradox has been observed, suggesting that the perioperative risk associated with obesity might have been overestimated.[8,9] Specifically, several studies found that patients at the extremes of BMI (underweight and class III obesity) have the highest postoperative mortality risk, which is not increased in overweight and mildly obese population. In cardiac surgery, a field where this relationship has raised great interest among surgeons, overweight and obese patients do not seem to experience greater morbidity and mortality.[8,10,11] Similar findings were seen in general nonbariatric surgery,[9] after gastrectomy,[12] and pancreaticoduodenectomy.[13]

Regarding thoracic surgery, surgeons consider operating on obese patients as technically challenging, since excessive fatty tissue impairs access to the surgical site and to the mediastinal structures. Moreover, obese patients are perceived at an increased risk of postoperative complications, due to less efficient pulmonary mechanics and associated comorbidities. However, some studies in thoracic surgery support that postoperative outcomes are better for patients who are overweight,[14,15] and this may be justified by the theory that extra fat may play a physiological buffer role against the trauma of surgery.

Thanks to the widespread diffusion of video-assisted thoracoscopic surgery (VATS), surgeons became able to perform lung resections with minimal chest wall trauma, leading to decreased postoperative morbidity compared to open surgery. Given that VATS is particularly beneficial to frail patients at increased risk for open surgery, it is reasonable to hypothesize that the minimally invasive procedure may further minimize the differences in outcomes between BMI classes. However, no literature specifically exploring the association of BMI and outcomes after VATS pulmonary resections is available, even though there are some studies on robotic surgery[16,17] or including VATS cases.[18]

The aim of this study was to assess the impact of BMI on perioperative outcomes in patients undergoing VATS major lung resections (lobectomy or segmentectomy).

PATIENTS AND METHODS

This study has been approved by the AOU Maggiore della Carità di Novara Institutional Review Board (IRB approval number, CE 194/20, 08/06/2020). The IRB waived the need for informed written consent for publication. Data collected from the VATS Group Italian Registry, a national database established in 2014, were retrospectively reviewed. As of April 2020, 57 Italian institutions were contributing to the registry. All patients who underwent VATS major lung resection in all thoracic units that contributed to the registry between January 1st, 2014 and April 23, 2020 were considered. The body mass index was calculated according to the standardized definition of a person's weight in kilograms divided by the square of the person's height in meters (kg/m^2). Patients whose BMI data were missing were excluded from the study. Since BMI data were entered only in the second version of the database, implemented in July 2017, 5088 patients were included in the final analysis.

Patient data included the following entries: demographics, performance status, oncological history, lung function testing, comorbidities, preoperative diagnosis and staging, surgical technique, operating time (knife to skin), pathology report, postoperative outcomes. Comorbidities were classified as: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, COPD, diabetes mellitus with or without organ damage.

Short-term outcome data included days with chest drain, length of hospital stay, perioperative adverse events. Follow-up data were entered every 6 months.

Staging was performed according to the 8th edition of the American Joint Committee on Cancer staging system.[14] Complications were classified as (1) pulmonary (prolonged air leak, ARDS, residual pleural space, pneumonia, effusion, empyema, reintubation, mechanical ventilation, middle lobe torsion, atelectasis, sputum retention), (2) cardiac (atrial fibrillation, dysrhythmia), (3) acute cardiac (acute peripheral arterial thromboembolism, cardiac arrest, myocardial infarction, transient ischemic attack, stroke), (4) pulmonary embolism, (5) surgical (hemothorax, bronchopleural fistula, chylothorax, recurrent laryngeal nerve palsy or dysphonia, blood transfusions), (6) renal (acute renal failure, urinary tract infection, dialysis), (7) gastrointestinal (antibiotic-associated diarrhea, pancreatitis, intestinal infarction, acute abdomen, bowel obstruction), (8) critical care (prolonged mechanical ventilation, postoperative intensive-care unit), (8) overall postoperative complications. Thirty days mortality, disease free survival (DFS) and overall survival (OS) were also collected. Patients with primary lung cancer were included in the survival analysis. BMI (kg/m^2) was categorized according to WHO classes: underweight (≤18.5), normal (18.5−24.9), overweight (25−29.9), obese (≥30).

STATISTICAL ANALYSIS

Data were reported as median (I and III quartiles) for continuous variables and percentage (absolute values) for qualitative variables. The Wilcoxon-Kruskal-Wallis test was performed for continuous variables and the Pearson chi-square test (or Fisher's exact test where appropriate) for categorical variables.

The BMI effect on the binary endpoint was evaluated by considering a logistic regression model estimation. The continuous endpoints were modeled by considering a linear regression model. The restricted cubic splines were used to capture non-linear effects. For example, it could be probable that the BMI effect on the outcome of interest is not constant per unit increment; however, it may vary over certain ranges of BMI values.

The model effects, beta estimates for continuous outcome, or odds ratio for binary endpoints, were reported for each BMI class.

According to known risk factors and clinical judgment, the BMI effects were adjusted in multivariable models by considering comorbidities, gender, age, FEV1%, DLCO/Va, and smoking status.

The cumulative incidence functions from competing risks data and test equality across groups for mortality and relapse rates according to the Gray method, were produced.[19] In these analyses, patients with benign and metastatic disease were excluded.

All tests are 2-tailed with a significance level of 0.05. Statistical analyses were performed using the R 3.6 system[20] and the rms package.[21]

RESULTS

Demographics, clinical characteristics, and comorbidities

Overall, 5088 patients were included. The details regarding demographics, clinical characteristics, and comorbidities according to BMI are listed in Table 1.

Most patients were classified as normal weight (n = 2070) or overweight (n = 2011), followed by obese (n = 910). Only 97 patients were underweight. Median BMI was 17.8 (IQR 17.3−18.3) for underweight patients, 23 (IQR 21.5−24.1) in the normal weight group, 27 (IQR 26−28.1) in the overweight group, and 32.5 (IQR 31.1−35.3) for obese patients. The majority of obese patients fall into class I obesity (BMI 30−34.9, 661 patients), whereas obesity class II (BMI 35−39.9, 155 patients) and III (BMI≥ 40, 94 patients) were not well represented. Underweight patients were active smokers more frequently (47%) than any other BMI class. Among the obese, more patients had quit smoking (46%) and fewer were active smokers (27%) compared to other classes. Preoperative FEV1% and FVC% both decreased as BMI increased, while preoperative DLCO/Va does the opposite, as it increased with higher BMIs.

Oncological and surgical characteristics

Oncological and surgical details are shown in Table 2. Based on the 8th edition of the American Joint Committee on Cancer (AJCC) TNM system, 89% of cancers were finally classified as I or II stage. Overall, 88% of patients underwent pulmonary lobectomy.

Intraoperative and postoperative outcomes

The final model for complications and intraoperative outcomes was adjusted for gender, age, smoking status, FEV1%, DLCO/Va%, and comorbidities. The log odds of complications as a function of BMI, adjusted for the aforementioned variables, were calculated and curves are shown in Figures 1−3. Median operative time (Fig. 2b) and adjusted hospital length of stay (Fig. 4) as a function of BMI are shown.

Intraoperative outcomes

In overweight and obese patients, operative time was directly proportional to the BMI value. For overweight population, operating room time increased by 5.34 minutes (S.E. = 1.58), and by 32.14 minutes (S.E. = 10.28) for obese BMI values ($P <$ 0.001). However, BMI did not influence the risk of conversions to thoracotomy (P = 0.75), or the extent of lymphadenectomy (P = 0.24).

Postoperative outcomes

As listed in Table 3, the most common complications were pulmonary (n = 750, 15%), and hospital median length of stay was 6 (IQR 5−9) days.

Length of hospital stay decreased as BMI increased within the normal weight range (β −1.37; S.E. = 0.33; P < 0.001), showed little variation in overweight patients, and then increased again for BMIs higher than 30 (β 2.52; S.E. = 0.91; P < 0.001), as shown in Figure 4.

Regarding the association between BMI and postoperative complications, the following relationships were identified.

Within the normal weight range, increasing BMI from the lower to the upper limit (18.5−24.9) reduced the risk of pulmonary (OR: 0.47; 95% CI: 0.37−0.6; P < 0.001), surgical (OR: 0.53; 95% CI: 0.33−0.84; P = 0.02), overall complications (OR: 0.53; 95% CI: 0.43−0.65; P < 0.001), and it decreased the length of stay (β −1.37; S.E. = 0.33; P < 0.001),

Table 1. Clinical Characteristics of Patients Undergoing VATS Major Lung Resection, According to BMI

	Evaluable Patients	Underweight BMI ≤ 18.5 (n = 97)% (n), or median (interquartile range)	Normal Weight BMI 18.6–24.9 (n = 2070)% (n), or median (interquartile range)	Overweight BMI 25–29.9 (n = 2011)% (n), or median (interquartile range)	Obese BMI ≥ 30 (n = 910)% (n), or median (interquartile range)	Overall (n = 5088)% (n), or median (interquartile range)	*P* Value
BMI	5088	17.8 (17.3–18.3)	23 (21.5–24.1)	27 (26–28.1)	32.5 (31.1–35.3)	25.8 (23.4–28.6)	<0.001
Age	5088	65 (57–72)	69 (61–75)	70 (64–75)	69 (62–74)	69 (63–75)	<0.001
Gender, male	5088	25% (24)	52% (1078)	69% (1382)	62% (561)	60% (3045)	<0.001
Smoking status	5088						
Never		28% (27)	34% (707)	28% (568)	27% (247)	30.5% (1549)	<0.001
Former		25% (24)	33% (690)	41% (828)	46% (418)	38.5% (1960)	<0.001
Current		47% (46)	33% (673)	31% (615)	27% (245)	31% (1579)	<0.001
Preoperative FEV1 %	4980	96 (80–110)	95 (81–107)	91.2 (79–105)	92 (78–104)	93 (80–106)	<0.001
Preoperative FVC %	4980	102.5 (88–115.2)	100 (88–114)	96 (85–109.5)	95 (84–110)	98 (86–111)	<0.001
Preoperative DLCO/Va %	4980	70 (59–89.25)	81 (70–92)	84 (73–96)	86 (75–100)	83 (71–95)	<0.001
Comorbidities	5088						
Myocardial infarction		4% (4)	7% (135)	12% (243)	13% (115)	10% (497)	<0.001
Congestive heart failure		2% (2)	3% (50)	4% (73)	6% (51)	3% (176) <0.001	<0.001
Peripheral vascular disease		11% (11)	13% (266)	18% (360)	18% (168)	16% (815)	<0.001
Cerebrovascular disease		4% (4)	5% (109)	6% (131)	5% (47)	6% (293)	0.53
Dementia		1% (1)	1% (11)	1% (12)	0% (2)	1% (26)	0.51
COPD		28% (27)	21% (413)	23% (480)	26% (237)	23% (1157)	0.01
DM, End-organ damage		0% (0)	0% (5)	0% (7)	1% (9)	0% (21)	<0.001 —-
DM, Uncomplicated		4% (4)	8% (155)	15% (305)	21% (196)	13% (660)	<0.001

COPD, chronic obstructive pulmonary disease; DLCO/Va, diffusing capacity of the lung for carbon monoxide/alveolar volume; DM, diabetes mellitus; FEV1, Forced Expiratory Volume in the 1st second.

Table 2. Surgical and Oncological Characteristics of Patients Undergoing VATS Major Lung Resection, According to BMI

	Evaluable Patients	Underweight BMI ≤ 18.5 (n = 97)% (n), or median (interquartile range)	Normal Weight BMI 18.6−24.9 (n = 2070)% (n), or median (interquartile range)	Overweight BMI 25−29.9 (n = 2011)% (n), or median (interquartile range)	ObeseBMI ≥ 30 (n = 910)% (n), or median (interquartile range)	Overall (n = 5088)% (n), or median (interquartile range)	*P* Value
Histology	5088						
Adenocarcinoma		64% (62)	66% (1376)	65% (1315)	60% (548)	65% (3301)	**0.005**
Squamous		18% (17)	13% (267)	15% (294)	15% (141)	14% (719)	
Induction treatments	5088	1% (1)	3% (69)	3% (62)	4% (34)	3% (166)	0.491
Chemotherapy	166	1% (1)	3% (66)	3% (60)	4% (33)	3% (160)	0.975
Radiotherapy	166	0% (0)	0.5% (12)	0.3% (6)	0.3% (3)	0.4% (21)	0.476
TNM Stage, 8th	4537						0.75
I		74% (64)	71% (1251)	69% (1295)	71% (583)	70% (3193)	
II		14% (12)	18% (324)	19% (353)	18% (152)	19 (841)	
III		12% (10)	11% (185)	12% (221)	11% (87)	11% (503)	
Resection	5088						0.282
Upper lobectomy		49% (48)	50% (1028)	51% (1021)	51% (465)	50% (2562)	
Lower lobectomy		2% (2)	1% (20)	1% (19)	1% (11)	1% (52)	
Middle lobectomy		14% (14)	8% (161)	7% (140)	7% (63)	7% (378)	
Upper bilobectomy		1% (1)	1% (24)	1% (19)	2% (15)	1% (59)	
Lower bilobectomy		2% (2)	1% (20)	1% (19)	1% (11)	1% (52)	
Apical segmentectomy upper lobe		2% (2)	4% (78)	3% (65)	4% (34)	4% (179)	
Basal segmentectomy		0% (0)	2% (34)	1% (22)	1% (7)	1% (63)	
Apical segmentectomy lower lobe		3% (3)	3% (54)	4% (75)	3% (23)	3% (155)	
Lingulectomy		1% (1)	2% (32)	2% (36)	1% (10)	2% (79)	

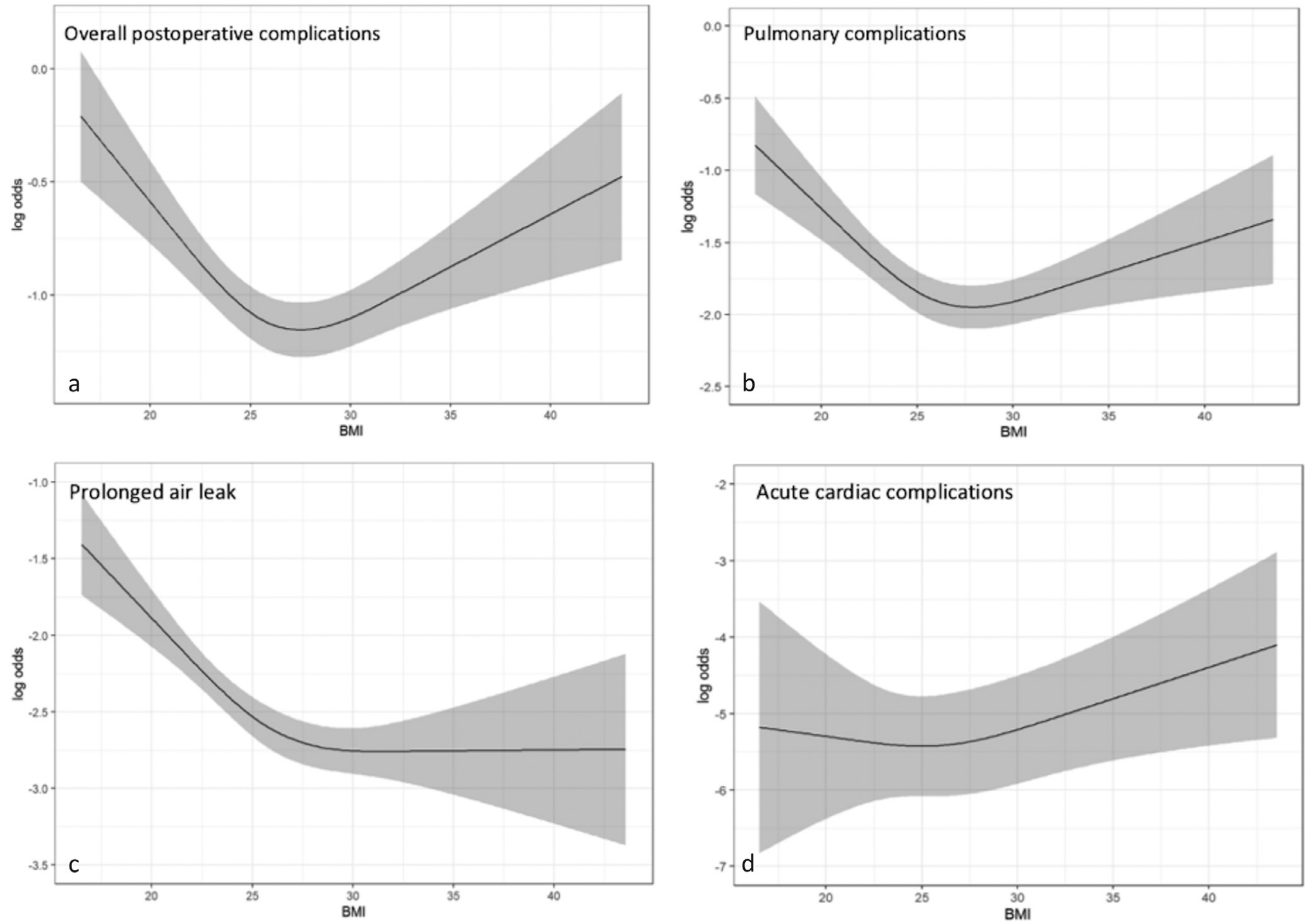

Figure 1. Postoperative complications curves as a function of BMI, adjusted for gender, age, smoking status, FEV1%, DLCO/Va%, and comorbidities. The grey bands represent 95% confidence interval. BMI influence on most postoperative complications follows a U-shaped curve, whose inflection point falls in the BMI range between 25 and 30, putting overweight patients at the lowest risk of (a) overall (BMI inflection point = 27.5), (b) pulmonary (BMI inflection point = 27.9), (d) acute cardiac (BMI inflection point = 25.8) complications and (c) prolonged air leak (BMI inflection point = 31.1).

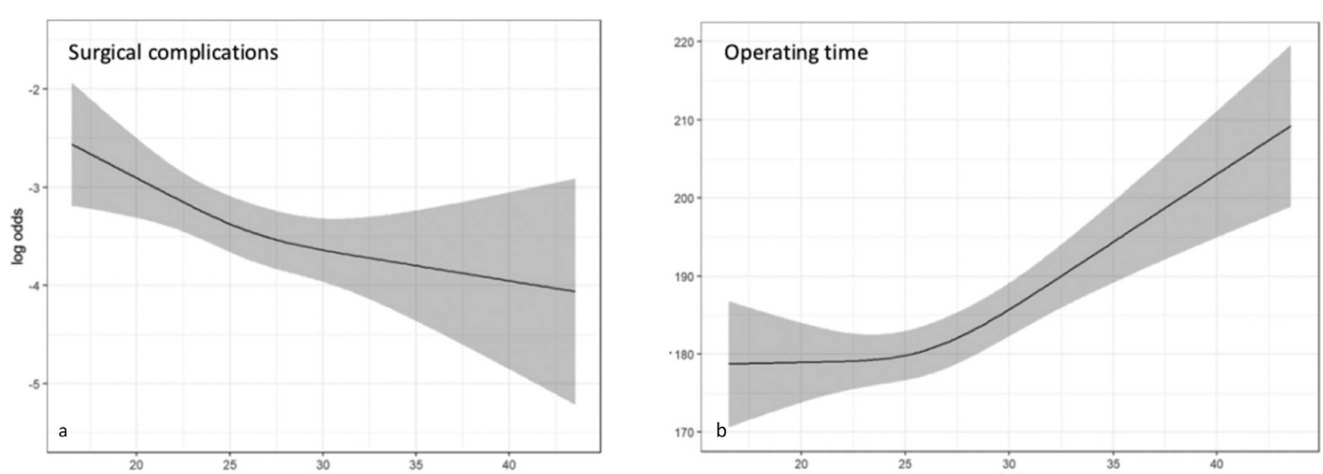

Figure 2. (a) Surgical complications curve as a function of BMI, adjusted for gender, age, smoking status, FEV1%, DLCO/Va%, and comorbidities. The curve is U-shaped with inflection point at BMI= 28.1. (b) Median operative time (minutes) curve as a function of BMI. The grey bands represent 95% confidence interval.

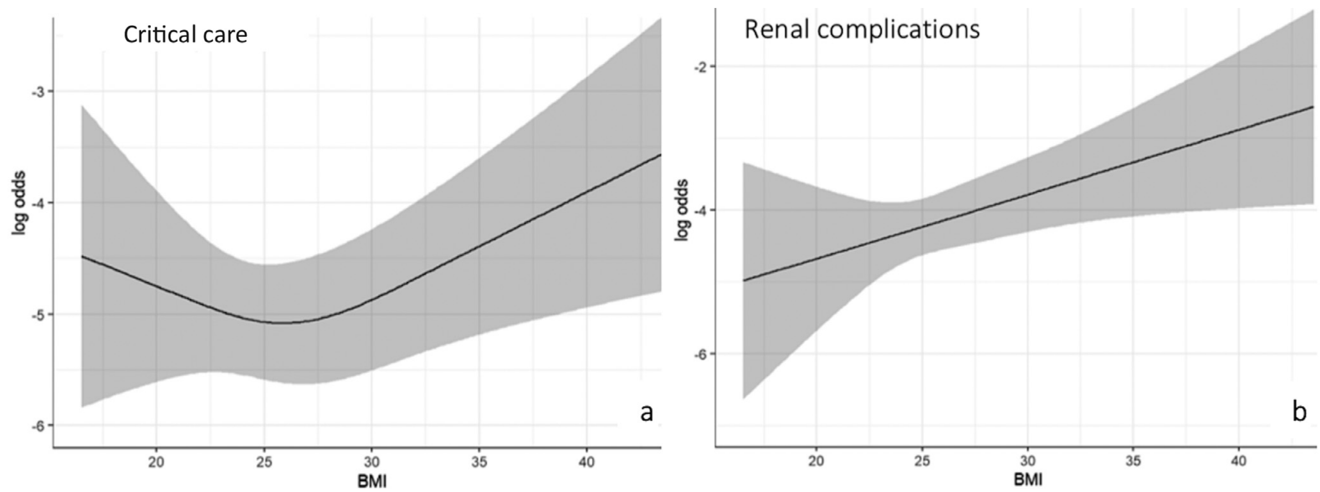

Figure 3. a) critical care and b) renal complications curves as a function of BMI, adjusted for gender, age, smoking status, FEV1%, DLCO/Va%, and comorbidities. The critical care complications curve is U-shaped, with inflection point at BMI = 24.1. The grey bands represent 95% confidence interval.

as well as the risk of prolonged air leak (OR: 0.35; 95% CI: 0.25−0.5; $P < 0.001$).

A BMI increase within the overweight range, from 25 to 29.9, did not increase the length of stay, nor the risk of any complications, except for renal complications (OR: 1.55; 95% CI: 1.07−2.24; $P = 0.03$). Interestingly, it reduced the risk of prolonged air leak (OR: 0.8; 95% CI: 0.71−0.90; $P < 0.001$).

When considering obese patients, as BMI increases from 30 to more than 40, the risk of pulmonary (OR: 2.38; 95% CI: 1.03−5.52; $P < 0.001$), renal (OR 6.08; 95% CI: 1.21−30.48; $P = 0.03$), critical care (OR 6.98; 95% CI: 1.85−26.3; $P = 0.02$), and overall complications (OR: 3.47; 95% CI: 1.67−7.19; $P < 0.001$) increased. A higher BMI was associated with a longer length of stay (β 2.52; S.E. = 0.91; $P < 0.001$).

The incidence of pulmonary embolism was not increased in patients with higher BMIs ($P = 0.5$).

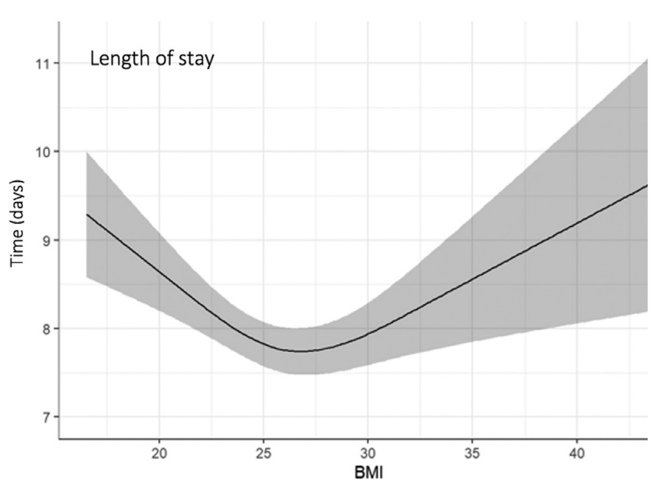

Figure 4. Adjusted length of hospital stay (days) curve as a function of BMI. The grey bands represent 95% confidence interval.

Mortality, relapse and survival

The 30-days survival curve was not reported, given the small number of events (Table 3).

Thirty days mortality is higher in the underweight group compared to the others (1% vs 0%, $P = 0.007$). Cumulative risk curves for mortality and relapse rates are shown in Figure 5. No significant difference in mortality and relapse outcomes was demonstrated among the BMI classes ($P = 0.12$ and $P = 0.64$, respectively).

Further analyses on subgroups of patients can be found in the Appendix.

DISCUSSION

We investigated the interactions of BMI and short-term outcomes after VATS lung resections, using a national database collecting VATS lobectomies and segmentectomies. According to our results, the risk of most postoperative complications progressively increases as the BMI deviates from the point at the lowest risk, toward both extremes of BMI values.

Intraoperative outcomes

Our results showed that operating room time increased for major lung resections in overweight, and even more in obese patients, as previously reported by St Julien et al.,[22] and in contrast with results reported for robotic lobectomy.[23] We also explored differences in number of lymph nodes removed, risk of conversion, and blood loss, but results fell within confidence bands.

Postoperative outcomes, mortality, relapse, and survival

Our analysis found that being overweight or mildly obese is not a perioperative risk factor for patients undergoing VATS lobectomy or segmentectomy, after adjusting for imbalances in the preoperative risk factors (gender, age, smoking status, FEV1%, DLCO/Va%, and comorbidities). In our database,

Table 3. Outcomes After VATS Major Lung Resection, According to BMI

	Evaluable Patients	Underweight BMI ≤ 18.5 (n = 97)% (n), or median (interquartile range)	Normal Weight BMI 18.6−24.9 (n = 2070)% (n), or median (interquartile range)	Overweight BMI 25−29.9 (n = 2011)% (n), or median (interquartile range)	Obese BMI ≥ 30 (n = 910)% (n), or median (interquartile range)	Overall (n = 5088)% (n), or median (interquartile range)	*P* Value
Complications	5088						
Overall		39% (38)	23% (464)	23% (471)	22% (204)	23% (1177)	**0.002**
Cardiac		9% (9)	5% (104)	7% (137)	5% (50)	6% (300)	0.123
Acute cardiac		1% (1)	0% (9)	1% (13)	1% (10)	1% (33)	0.239
Pulmonary embolism		0% (0)	0% (5)	0% (9)	0% (3)	0% (17)	0.717
Pulmonary		28% (27)	16% (324)	13% (269)	14% (130)	15% (750)	**<0.001**
Surgical		8% (8)	4% (72)	4% (74)	2% (18)	3% (172)	**0.005**
Renal		0% (0)	1% (10)	1% (30)	2% (16)	1% (56)	**0.032**
Gastrointestinal		0% (0)	0% (6)	0% (10)	1% (5)	0% (21)	0.588
Critical care		2% (2)	1% (10)	1% (12)	3% (23)	1% (47)	**<0.001**
Length of stay (days)	5088	7 (5−10)	6.5 (5-9)	6 (5-9)	6.5 (5-9)	6 (5-9)	0.348
30-days mortality	5088	1% (1)	0% (1)	0% (2)	0% (0)	0% (4)	**0.007**

FEV1% was significantly lower in patients with higher BMI values, while DLCO/Va% follows the opposite trend. This result seems concordant with those of a meta-analysis of clinical trials which found that FEV1 decreased with increasing BMI,[24] and with those of a meta-analysis published in 2018, which selected 44 studies and found that overweight/obese subjects had 2.2% lower percent-predicted FEV1.[25]

Since smokers, who are subject to higher morbidity and mortality rates, also tend to be leaner, inadequate adjustment for smoking would lead to underestimations of the risk ratios associated with excess weight. For these reasons, analyses of outcomes were adjusted also for these lung function variables and smoking status.

The risk of postoperative complications seemed to progressively increase as the BMI deviated from the point at the lowest risk. Indeed, BMI influence on most postoperative complications followed a U-shaped curve, whose inflection point falls in the BMI range between 25 and 30, putting overweight patients at the lowest risk of many complications (Figs. 1−3).

Similar trend lines were seen for most complications, except for renal, non-acute cardiac, and gastrointestinal complications.

Pulmonary complications were the most common in our study, and the risk decreased as BMI increased until the inflection point at BMI = 27.8, and then increased again for higher values.

Specifically, the risk of air leak is higher among underweight patients, decreases until BMI = 31, and stabilizes above this value, as similarly reported by Thomas et al.[26] and Attaar et al.[27] This finding was not surprising, as a low BMI may be a marker of poor nutritional status and wound healing, or pulmonary mechanics in overweight and obese patients may create intrathoracic conditions which favors sealing of parenchymal tears.

Indeed, comparable results on respiratory complications were shown by Montané et al.[23] after robotic-assisted pulmonary lobectomy, when obese patients faced a higher risk of postoperative pneumonia, and a lower risk of prolonged air leak compared to overweight and normal weight patients. In a study by Petrella et al.,[28] a 5-fold increase in respiratory complications after pneumonectomy was reported in obese patients, with no increased risk among underweight patients. According to Ferguson et al.,[29] underweight patients were at significantly increased risk of pulmonary complications and mortality (similarly to our results). The incidence of complications decreased with increasing BMI up to 25, and it stabilized above that value, with a suggestive uptick for higher BMIs for pulmonary complications which did not reach statistical significance. Acute cardiac complications did not consistently differ between nonobese BMI classes, while spline curves showed a higher risk of acute cardiac complications in obese patients. Other studies have demonstrated no difference between obese and nonobese patients.[23,29−32] Curves depicting overall complications and length of stay resembled the ones showing pulmonary complications. Since pulmonary are the most common

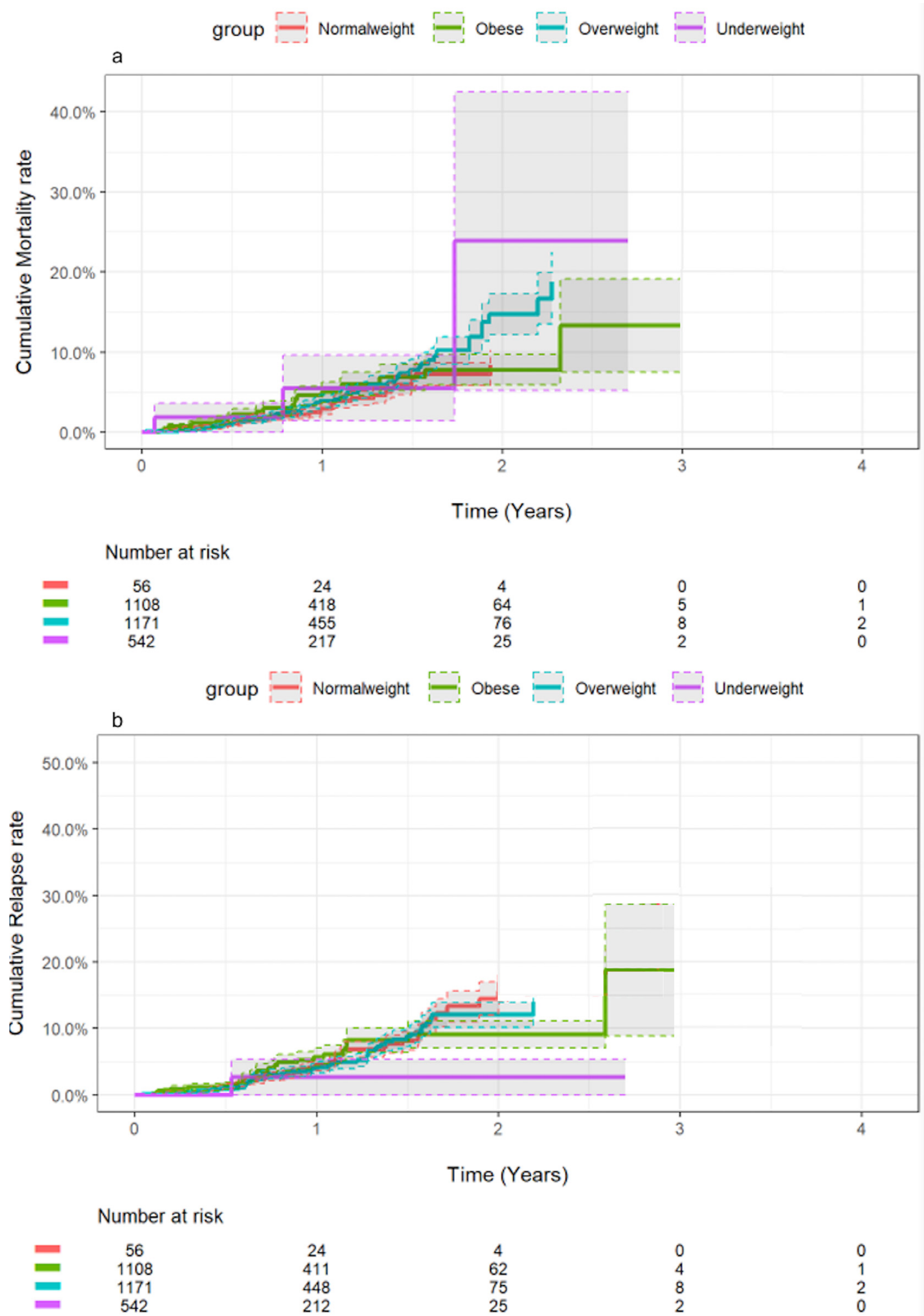

Figure 5. Cumulative risk curves for (a) mortality and (b) relapse rates according to the BMI classes. The grey bands represent 95% confidence interval. Number of patients at risk are reported below the curves.

complications, they are also the main factor influencing length of stay.

On the contrary, our findings on morbidity seemed partially in contrast with other studies on pulmonary resections, such as the ones carried out by Smith et al.[31] and Launer et al.,[30] who demonstrated no difference in perioperative mortality or morbidity between obese and nonobese patients. Tulinsky et al.[33] published a single institution series showing that obesity does not increase short-term complications after lobectomy, with slightly better outcomes in obese patients vs nonobese patients. Dhakal et al.[32] likewise explored the association between BMI and perioperative morbidity after 320 lung cancer resections, and found that overweight and obese patients do not differ significantly in rates of perioperative morbidities, 30-day mortality, and length of stay, compared to normal weight patients. However, these four studies did not consider BMI as a continuous variable, and dichotomized BMI values for comparisons (obese vs nonobese or overweight vs normal weight). This limits the analysis of outcomes at the extremes, especially if the curve is U-shaped as it seems to be according to our findings.

The observation of rising renal complications when BMI increases is not entirely intuitive, but may be mediated through components of the metabolic syndrome or facilitated by the presence of an unrecognized vasculopathy exacerbated by intraoperative hypotension.[34,35]

With regards to mortality, our analysis found that obesity did not increase 30-day mortality, as already suggested by other studies.[22,29−31,33] Thomas et al.[26] reported that operative mortality was lower among overweight and obese patients, showing an obesity paradox in mortality that we did not find in our analysis. A lesser level of cytokine response has been reported following VATS, which brings levels of inflammation down compared to open technique.[36] As a potential explanation to our findings we might speculate that, when considering only patients undergoing minimally invasive procedure, the advantage conferred by extra fat after more traumatizing approaches may be reduced.

Long-term outcomes

We did not find any significant difference in DFS and OS between the groups. The majority of studies investigated short-term outcomes, while some also reported survival.[6,12,13,37−39] Regarding long-term outcomes, most authors seem to agree that being underweight is an unfavorable factor.[37,39] A survival benefit for overweight and obese patients has been reported after gastrectomy,[12] pancreaticoduodenectomy,[13] percutaneous coronary intervention, coronary artery bypass grafting, and valve surgery,[6,8] while other studies did not demonstrate any influence of BMI after esophagectomy[38] and coronary artery bypass grafting.[40]

Limitations

We identified some limitations in this study. First, this work is limited by its retrospective nature. Although we controlled for confounding variables, it is likely that all factors influencing outcomes were not accounted for in the analysis.

Second, despite the large sample size, a limitation is the small number of underweight patients that could not be analyzed separately to obtain robust data.

Third, the database was not specifically designed to study the obesity paradox as a primary goal, thus important potential shortcomings of this study are mainly due to the absence of data on predisease BMI, recent weight loss, and nutritional status. Specifically, a possible bias may be due to illness-related weight loss, which may increase morbidity risk in the normal weight group, creating the appearance that overweight was protective. However, the majority of lung cancer cases included in this work are stage I and II, thus we think that the impact of cancer-related weight loss was marginal.

Moreover, BMI itself is defective, since it does not discriminate between fat and lean mass, and it may be imprecisely used as a proxy of body fat composition. Indeed, individuals with BMIs between 25 and 30 may fall into this category due to an above-average muscle mass, and this would be a reasonable explanation to these findings. Further investigations on this topic should include additional measures that may provide more accurate information on body composition, nutritional status and sarcopenia.

For instance, body composition could be measured using the Dual-Energy X-ray Absorptiometry (DEXA) which provides rapid and accurate estimates of three components that comprise body mass, lean soft tissue, bone mineral, and fat mass.[41,42] Alternatively, another reliable method seems the bioelectrical impedance analysis (BIA), which is also validated by the Food and Drug Administration,[43] based on the principle of resistance and reactance imposed by cells to the electric current emitted by a device. Several blood biochemicals, including albumin, prealbumin, hemoglobin, total cholesterol, and total protein, are useful biomarkers for adult malnutrition.[44] Although BMI has traditionally been the chosen method by which to measure bod size, alternative measures such as waist circumference, waist-to-hip ratio and waist-to-height ratio have been suggested to be superior to BMI.[45]

CONCLUSIONS

According to our results, obesity increases operating room time for VATS major lung resection.

Interestingly, overweight patients are at the lowest risk of pulmonary, acute cardiac, surgical, major, and overall postoperative complications following VATS lobectomy and segmentectomy (Fig. 6).

The risk of postoperative complications progressively increases as the BMI deviates from the point at the lowest risk, towards both extremes of BMI values. 30-days mortality is higher in the underweight group compared to the others, however, we did not find any significant difference in disease-free survival and overall survival.

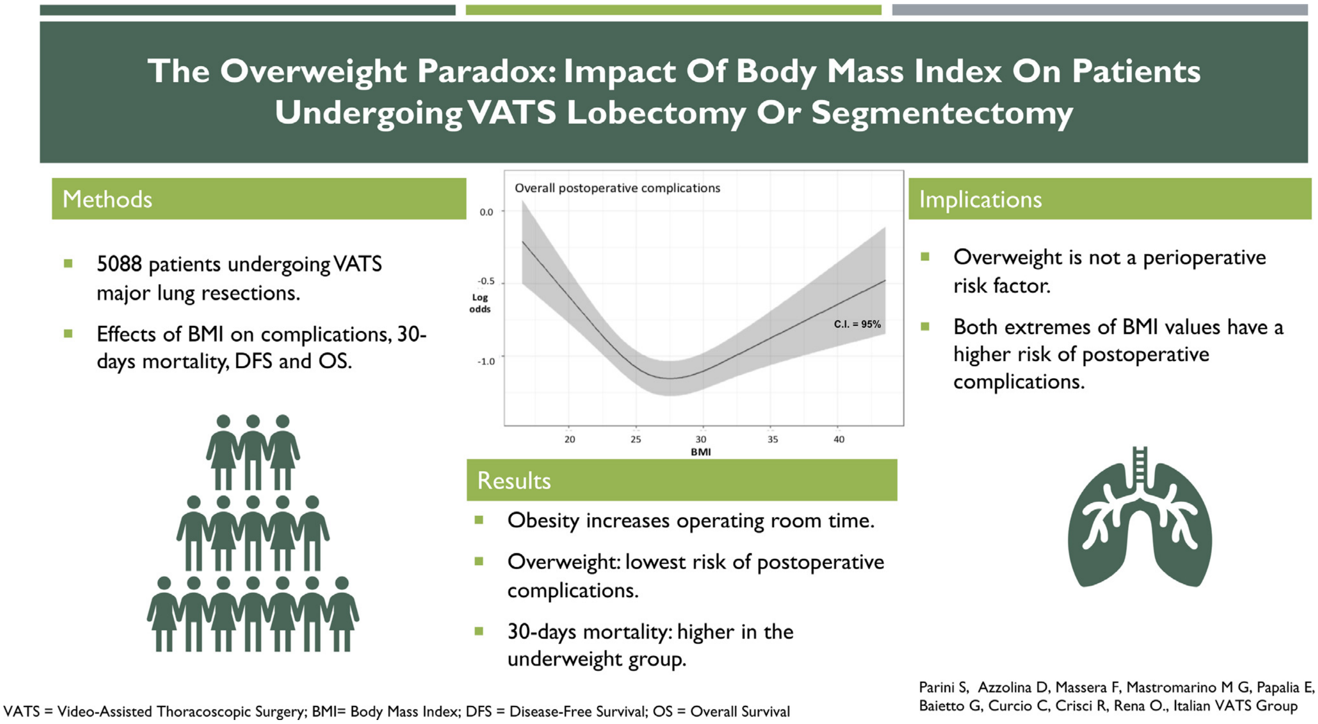

Figure 6. Graphical abstract depicting the methods, results, and implications of the study.

SUPPLEMENTARY MATERIAL

Scanning this QR code will take you to the article title page to access supplementary material.

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