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ORIGINAL ARTICLE

National perioperative outcomes of pulmonary lobectomy for cancer: the influence of nutritional status[†]

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Abstract

OBJECTIVES: Nutritional assessment is not included yet as a major recommendation in lung cancer guidelines. The purpose of this study was thus to assess the influence on surgical outcome of the nutritional status of patients with primary lung cancer undergoing lobectomy.

METHODS: We queried Epithor, the national clinical database of the French Society of Thoracic and Cardiovascular Surgery, and identified a retrospective cohort of 19 635 patients having undergone lobectomy for a primary lung cancer in the years 2005–11. Their nutritional status was categorized according to the WHO definition: underweight (BMI < 18.5): 857 patients (4.4%), normal (18.5 ≤ BMI < 25): 9391 patients (47.8%), overweight (25 ≤ BMI < 30): 6721 patients (34.2%), obese (BMI ≥ 30): 2666 patients (13.6%). Operative mortality, pulmonary, cardiovascular, infectious and surgical complications rates were collected and analysed for these various BMI groups.

RESULTS: In the normal-weight category, operative mortality, pulmonary, surgical, cardiovascular and infectious complications rates were 2.7, 14.6, 13.8, 5.5 and 4.1%, respectively. When compared with that of normal BMI patients, adjusted operative mortality was significantly lower in overweight (2.3%; odd ratio (OR): 0.72 [95% confidence interval (CI): 0.59–0.89]; *P* = 0.002) and obese patients (1.9%, OR: 0.54 [95% CI: 0.40–0.74]; *P* < 0.001), and significantly higher in underweight patients (4.1%, OR: 1.89 [95% CI: 1.30–2.75]; *P* = 0.001). Underweight patients experienced significantly more pulmonary (21.1%; *P* < 0.001), surgical (23.2%; *P* < 0.001) and infectious (5.1%; *P* = 0.05) complications (*P* < 0.0001). Among surgical complications, prolonged air leaks (17.6%; *P* < 0.001) and bronchial stump dehiscence (1.5%; *P* = 0.001) were significantly more frequent in underweight patients than in normal BMI patients. Obesity was not associated with increased incidence of postoperative complications, except for arrhythmia (5.6%; *P* < 0.05), deep venous thrombosis and pulmonary embolism (1.5%; *P* = 0.005). Moreover, a statistical protective effect of obesity was observed regarding surgical complications (7.1%; *P* < 0.001).

CONCLUSIONS: Despite having an increased risk of some postoperative cardiovascular complications, obese patients should undergo surgical standard of care therapy for appropriately stage-specific lung cancer. In underweight patients, in addition to preoperative rehabilitation including a nutritional program, attention should be given to aggressive prophylactic respiratory therapy in the perioperative period, and specific intraoperative actions to prevent prolonged air leaks and bronchial stump dehiscence.

Keywords: Lobectomy • Lung cancer • Body mass index • Nutritional status

INTRODUCTION

Assessment of nutritional status is not addressed or even mentioned in the current recommendations on the physiological evaluation of patients with lung cancer who are being considered for curative-intent therapy, including the latest ones established by the American College of Chest Physicians [1]. Indeed, the effect of obesity or malnutrition on postoperative complications of patients with lung cancer has seldom been studied, and remains unclear. Although several preoperative risk-scoring systems exist [2], body mass index (BMI) has not been included in the majority of them, since it was not considered an independent predictor for outcomes.

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Recently, two European institutional publications have concluded that malnutrition and obesity represented additional risk factors for cancer patients requiring pneumonectomy [3, 4]. Conversely, two other European institutional studies commented on the absence of an association between low BMI and postoperative death or poor surgical outcome in patient cohorts having undergone a lobectomy for cancer [5, 6]. Lastly, a nation-based analysis disclosed that obese patients in the United States had an increased risk of postoperative pulmonary complications but not other morbidity, or mortality after lobectomy [7].

The purpose of this observational study was thus to try to clarify this issue while assessing the impact on the postoperative outcome of the nutritional status of lung cancer patients referred for lobectomy, querying a nationally representative clinical database. It aimed at facilitating informed patient consent and identifying those individuals who may benefit from specific perioperative interventions to possibly decrease the risk of postoperative complications.

MATERIALS AND METHODS

The Institutional Review Board of the French Society of Thoracic and Cardiovascular Surgery (FSTCVS) approved the study (approval number 2013-1-5-16-57-9-ThPa). Patient consent has been obtained for entry into the database, and patients were aware that these data would be used for research purposes.

The French National Database Epithor

Epithor, the FSTCVS database, was created in 2002 as a voluntary and free initiative of general thoracic surgeons. At present, about 100 private and public institutions contribute daily to this database, including more than 180 000 procedures recorded to date, which represents more than 70% of all thoracic surgical procedures performed in France annually. Its technical characteristics have been previously described in detail [8, 9].

Epithor is a government-recognized clinical database, financially supported by the National Cancer Institute (Institut National du Cancer) for data-quality monitoring. Epithor is labelled by the French National High Authority for Health (Haute Autorité de Santé), a governmental agency designed to improve the quality of patient care and to guarantee equity within the health care system, as a methodologically correct tool to assess professional surgical practices. Participating in Epithor is now part of the required criteria for medical accreditation and thoracic surgery unit certification in France.

Completeness and accuracy of the data are facilitated by the use of hierarchic pull-down menus and the absence of free text spaces. The software incorporates routine utilities for data consistency, alerting to aberrant or contradictory values in some fields. Each patient's file includes some mandatory items to initialize and close the process. Fifty variables are collected per patient, covering information about patients' personal characteristics, medical history, pulmonary function, surgical procedures, cancer staging and outcomes. Data are sent through the Internet to the national database; patients are anonymous.

Each participating centre has to implement and download the national database at least every 2 months to avoid becoming temporarily unauthorized to access the database. The software includes functions allowing participating surgeons to benchmark their activity against the national picture almost in a real-time context. Moreover, participants have to check the quality of the local database for missing values by comparing its completeness with that of the national database. This comparison is expressed through a quality score ranging from 0 to 100%. A score exceeding 80% is mandatory to have the local data incorporated in the national database. The accuracy of data collection is checked in regular external onsite audits initiated in 2010.

Patient population

From 1 January 2005 to 31 December 2011, 134 981 patients were registered in Epithor, among whom 29 873 received surgery with the main diagnosis of primary lung cancer. We selected those 19 856 patients having undergone a lobectomy. After discarding data fields with too many inconsistent or missing values and patients with unknown information on variables otherwise suitable for study, a group of 19 635 patients having undergone a lobectomy for a primary lung cancer was selected for further analysis. From this population, patients were divided into four cohorts on the basis of their body mass index (BMI) according to the WHO classification [10]: underweight (BMI <18.5 kg/m^{-2}), normal (18.5 kg/m^{-2}≤BMI< 25 kg/m^{-2}), overweight (25 kg/m^{-2}≤BMI<30 kg/m^{-2}) and obese (BMI≥30 kg/m^{-2}).

Clinical variables

Baseline demographics, comorbidities, procedure and outcome were recorded in every case. Categorical variables with missing data exceeding a proportion of 5% were included within an extra 'missing value' category. Otherwise, missing data were considered as real missing value. Patient-related variables used were considered categorical: age (≤55, 56–65, >65) (completeness of the information for this variable: 100%), gender (completeness: 100%), American Society of Anesthesia scores (≤2, ≥3) (completeness: 99.8%), World Health Organization performance status (≤2, ≥3) (completeness: 93.6%), Medical Research Council Dyspnea score (≤2, ≥3) (completeness: 88.7%) and number of comorbid diseases (0, 1–2, ≥3) (completeness: 100%). The number of comorbid diseases per patient was thus considered a categorical variable because recent consistent data based on Epithor suggested the superiority of this variable on the types of individual comorbidities in a predictive model for operative mortality [9]. Tobacco consumption within 5 weeks before surgery defined the active smoker category (completeness: 100%). Surgery-related variables included: side of the procedure (left or right) (completeness: 99.9%), surgical approach (thoracotomy, VATS) (completeness: 100%), lobectomy type (right upper, middle, lower lobectomy, left upper and lower lobectomy) (completeness: 99.9%), standard or extended resections to the bronchial tree (sleeve), to the chest or mediastinal structures (completeness: 100%) and technique of lymphadenectomy (lymphadenectomy, sampling) (completeness: 99.9%). Additional information concerning pathological staging (completeness: 99.8%) in accordance with the International Association for the Study of Lung Cancer (IASLC) classification [11] (early I–II, locally advanced III, metastatic IV), and histology (carcinoid, adenocarcinoma, squamous cell carcinoma, other) (completeness: 99.9%) were also reported.

Outcome definition

The primary end-point was operative mortality defined as any patient who died within 30 days after the operation, or later if the patient was still in the hospital. Secondary end-points were pulmonary, cardiovascular, infectious and surgical complications. Pulmonary complications included atelectasis requiring bronchial aspiration by fibroscopy, confirmed or suspected pneumonia, respiratory failure requiring invasive (ARDS) or non-invasive mechanical ventilation. Cardiovascular complications included deep venous thrombosis and pulmonary embolism, atrial fibrillation, stroke, acute coronary events and acute heart failure. Infectious complications included septicaemia, isolated fever unrelated to pneumonia or any specific surgical complication and urinary tract infections. Surgical complications included vocal cord palsy, bronchial fistula, prolonged (>7 days) air leaks, haemothorax, chylothorax, empyema and wound abscess.

Statistical analysis

Descriptive data were expressed as counts and percentages for qualitative variables, and as means and (±) standard deviations for continuous variables. Comparisons of means were carried out using parametric tests (unpaired Student's *t*-tests, ANOVA) and χ^2 tests were performed for qualitative variables.

Binary logistic regression was used to construct models of association of each outcome studied (primary outcome: operative mortality; secondary outcomes: respiratory, cardiovascular, surgical and infectious complications) with the BMI group (normal as the reference modality, underweight, preobesity and obesity) as the explanatory variable. Potential confounding factors relevant to each model were selected from the univariate analyses, provided that they were associated with the studied outcome with a *P*-value <0.05. Each subset of selected variables was included in a final model and calibration of the logistic model was assessed using a Hosmer–Lemeshow goodness-of-fit test, to evaluate the discrepancy between observed and expected values. Adjusted odds ratios (OR) of having each type of outcome (including 95% confidence intervals) were estimated. All of the tests were two sided. Statistical significance was defined as $P < 0.05$. The statistical analyses were performed using PASW Statistics software version 17.0.2.

RESULTS

There were 5463 females and 14 172 males whose mean age was 63.2 ± 10.4 years. BMI values ranged from 10.8 to 60.6 kg/m^{-2}. Accordingly, 857 patients (4.4%) were allocated to the underweight group, 9391 patients (47.8%) in the normal BMI group, 6721 patients (34.2%) in the preobesity group and 2666 patients (13.6%) in the obesity group. Among the last patients, 2133 (80%) were mild (Class I), 420 (15.8%) moderate (Class II) and 113 (4.2%) morbid (Class III) obese patients. Their characteristics are detailed in Table 1. Besides their respective proportions in the whole surgical cohort, and their mean BMI values, the four BMI categories differed significantly regarding 11 of the 16 recorded variables.

Overall operative mortality was 2.5% ($n = 490$). When compared with normal BMI patients, preobese and obese patients had a significantly lower, whereas underweight patients had significantly higher, observed and adjusted operative mortality (Table 2). The observed operative mortality rates in class I, class II and class III obese patients were 1.88% ($n = 40$), 1.90% ($n = 8$) and 1.77% ($n = 2$), respectively.

The overall postoperative complication rate was 34.1%; 6698 patients developed 10 003 complications. When compared with normal BMI patients, the overall operative complication rate was significantly higher in underweight patients (46.7%: $P < 0.001$) and significantly lower in preobese and obese patients (31.3 and 31.5% respectively; $P < 0.001$).

Pulmonary complications developed in 14.6% of patients and were the most common (2865 patients with pulmonary complications), followed by surgical complications (11.7%, $n = 2291$), cardiac complications (6%; $n = 1173$) and infectious complications (4%, $n = 781$). Unspecific events occurred in 969 patients (4.9%). The statistical relationship between these complications and each BMI

Table 1: Patient demographics and characteristics

Variables	Normal	Underweight	Overweight	Obesity	*P*
N (%)	9391 (47.8)	857 (4.4)	6721 (34.2)	2666 (13.6)	
Male, *n* (%)	6392 (68.1)	436 (50.9)	5366 (79,8)	1978 (74.2)	**<0.001**
Age >65, *n* (%)	3595 (38.3)	214 (25.0)	3278 (48.8)	1262 (47.3)	**<0.001**
Performance status ≥2, *n* (%)	736 (7.8)	113 (13.2)	479 (7.1)	262 (9.8)	**<0.001**
MRC Dyspnea score ≥2, *n* (%)	914 (9.7)	119 (13.9)	783 (11.6)	472 (17.7)	**<0.001**
ASA score ≥3, *n* (%)	2196 (23.4)	296 (34.6)	1762 (26.3)	935 (35.1)	**<0.001**
Comorbidities ≥3, *n* (%)	1002 (10.7)	60 (7.0)	1169 (17.4)	526 (19.7)	**<0.001**
Active smokers, *n* (%)	3339 (35.6)	383 (44.7)	1924 (28.6)	558 (20.9)	**<0.001**
Side R, *n* (%)	5531 (59.2)	490 (57.4)	3853 (57.6)	1524 (57.4)	0.142
VATS, *n* (%)	326 (3.5)	38 (4.4)	227 (3.4)	78 (2.9)	0.191
Upper lobectomy, *n* (%)	6047 (64.7)	578 (67.8)	4122 (61.7)	1586 (59.7)	**<0.001**
Extended lobectomy, *n* (%)	1343 (14.3)	156 (18.2)	870 (12.9)	336 (12.6)	**<0.001**
Radical lymphadenectomy, *n* (%)	8653 (92.1)	801 (93.5)	6238 (92.8)	2453 (92.0)	0.210
Operative time (mean ± SD)	133 ± 56	135 ± 58	133 ± 52	134 ± 55	0.543
Early-stage disease, *n* (%)	6100 (65.0)	570 (66.5)	4409 (65.6)	1763 (66.1)	0.572
Histology adenocarcinoma, *n* (%)	5154 (54.9)	479 (55.9)	3459 (51.5)	1289 (48.3)	**<0.001**
Induction therapy, *n* (%)	1021 (10.9)	108 (12.6)	639 (9.5)	211 (7.9)	**<0.001**

Bold values: $P < 0.05$ was significant.

Table 2: Observed and adjusted operative mortality

	Operative death		P*	OR a	95% CI	P**
	Yes (N = 490)	No (N = 19 145)				
BMI, N (%)						
Normal	249 (2.7)	9142 (97.3)	**0.002**	1		
Underweight	35 (4.1)	822 (95.9)		1.89	[1.30–2.75]	**0.001**
Overweight	156 (2.3)	6565 (97.7)		0.72	[0.59–0.89]	**0.002**
Obesity	50 (1.9)	2616 (98.1)		0.54	[0.40–0.74]	**<0.001**

*Unadjusted analysis.
**Adjusted analysis. Co-variables: male gender, age, performance status, ASA score, comorbidities, active smokers, right side, extended lobectomy, early-stage disease, histology non adenocarcinoma, operative time.
Bold values: $P < 0.05$ was significant.
BMI: body mass index; OR a: adjusted odd ratio; CI: confidence interval.

Table 3: Pulmonary complications

	Pulmonary complications		P*	OR a	95% CI	P**
	Yes (N = 2865)	No (N = 16 770)				
BMI, N (%)						
Normal	1369 (14.6)	8022 (85.4)	**<0.001**	1		
Underweight	181 (21.1)	676 (78.9)		1.67	[1.39–2.00]	**<0.001**
Overweight	913 (13.6)	5808 (86.4)		0.84	[0.77–0.93]	**<0.001**
Obesity	402 (15.1)	2264 (84.9)		0.95	[0.84–1.08]	0.420

*Unadjusted analysis.
**Adjusted analysis. Co-variables: male gender, age, performance status, ASA score, comorbidities, active smokers, right side, open surgical approach, upper lobectomy, extended lobectomy, histology non-adenocarcinoma, operative time.
Bold values: $P < 0.05$ was significant.
BMI: body mass index; OR a: adjusted odd ratio; CI: confidence interval.

Table 4: Surgical complications

	Surgical complications		P*	OR a	95% CI	P**
	Yes (N = 2296)	No (N = 17 339)				
BMI, N (%)						
Normal	1293 (13.8)	8098 (86.2)	**<0.001**	1		
Underweight	199 (23.2)	658 (76.8)		1.96	[1.65–2.33]	**<0.001**
Overweight	616 (9.2)	6105 (90.8)		0.62	[0.56–0.69]	**<0.001**
Obesity	188 (7.1)	2478 (92.9)		0.47	[0.40–0.55]	**<0.001**

*Unadjusted analysis.
**Adjusted analysis. Co-variables: male gender, MRC dyspnea score, upper lobectomy, histology adenocarcinoma, operative time.
Bold values: $P < 0.05$ was significant.
BMI: body mass index; OR a: adjusted odd ratio; CI: confidence interval.

patient's category is disclosed in Tables 3–6. When compared with normal BMI patients, underweight patients experienced significantly more pulmonary, surgical and infectious complications. Obese patients had more overall cardiovascular complications, but this finding did not reach statistical significance. Preobese patients experienced significantly less pulmonary, surgical and infectious

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Table 5: Cardiovascular complications

	Cardiovascular complications		P*	OR a	95% CI	P**
	Yes (N = 1173)	No (N = 18 462)				
BMI, N (%)						
Normal	513 (5.5)	8878 (94.5)	**<0.001**	1		
Underweight	30 (3.5)	827 (96.5)		0.71	[0.48–1.03]	0.07
Overweight	437 (6.5)	6284 (93.5)		1.07	[0.93–1.22]	0.35
Obesity	193 (7.2)	2473 (92.8)		1.17	[0.98–1.40]	0.08

*Unadjusted analysis.
**Adjusted analysis. Co-variables: male gender, age, ASA score, comorbidities, active smokers, operative time.
Bold values: $P < 0.05$ was significant.
BMI: body mass index; OR a, adjusted odd ratio; CI: confidence interval.

Table 6: Infectious complications

	Infectious complications		P*	OR a	95% CI	P**
	Yes (N = 781)	No (N = 18 854)				
BMI, N (%)						
Normal	383 (4.1)	9008 (95.9)	0.09	1		
Underweight	44 (5.1)	813 (94.9)		1.39	[1.01–1.93]	**0.05**
Overweight	241 (3.6)	6480 (96.4)		0.79	[0.67–0.93]	**0.01**
Obesity	113 (4.2)	2553 (95.8)		0.92	[0.74–1.15]	0.48

*Unadjusted analysis.
**Adjusted analysis. Co-variables: male gender, age, performance status, ASA score, comorbidities, operative time.
Bold values: $P < 0.05$ was significant.
BMI: body mass index; OR a: adjusted odd ratio; CI: confidence interval.

Table 7: Single complications

Complications	Normal N = 9391	Underweight N = 857	Overweight N = 6721	Obesity N = 2666	P
Prolonged air leaks, n (%)	913 (9.7)	151 (17.6)[a]	389 (5.8)[a]	103 (3.9)[a]	**<0.001**
Atelectasis, n (%)	692 (7.4)	99 (11.6)[a]	480 (7.1)	231 (8.7)	**<0.001**
Pneumonia, n (%)	647 (6.9)	76 (8.9)	409 (6.1)	149 (5.6)	**0.001**
Arrhythmia, n (%)	401 (4.3)	20 (2.3)[a]	339 (5.0)	150 (5.6)[a]	**<0.001**
Ventilatory support, n (%)	356 (3.8)	57 (6.7)[a]	203 (3.0)[a]	94 (3.5)	**<0.001**
ARDS, n (%)	192 (2.0)	33 (3.9)[a]	103 (1.5)	34 (1.3)[a]	**<0.001**
Haemothorax, n (%)	185 (2.0)	19 (2.2)	102 (1.5)	26 (1.0)[a]	**0.002**
Recurrent nerve palsy, n (%)	126 (1.3)	16 (1.9)	80 (1.2)	34 (1.3)	0.404
Pulmonary embolism and DVT, n (%)	76 (0.8)	5 (0.6)	77 (1.1)	40 (1.5)[a]	**0.005**
Bronchial fistula, n (%)	51 (0.5)	12 (1.5)[a]	25 (0.4)	11 (0.4)	**0.001**
Coronary events, n (%)	23 (0.2)	5 (0.6)	24 (0.4)	8 (0.3)	0.262

[a]Difference statistically significant (reference group: Normal). To correct for multiple outcome testing, the threshold for significance level was 0.05/3 = 0.017.
Bold values: $P < 0.05$ was significant.
ARDS: acute respiratory distress syndrome; DVT: deep vein thrombosis.

complications. Obese patients underwent significantly less surgical complications.

Table 7 lists the most frequent single complications, ranked by decreasing frequency as they occurred in the normal BMI patient' group. Prolonged air leaks, atelectasis, ARDS and need for ventilator support, as well as bronchial stump fistula, occurred significantly more frequently in underweight patients when compared with normal BMI patients. Arrhythmia, deep venous thrombosis and pulmonary embolism occurred significantly more frequently in obese patients. A statistical protective effect of overweight and obesity was observed for prolonged air leaks and some respiratory complications.

DISCUSSION

Our study identified underweight patients as a particularly high-risk surgical population. The role of nutrition in predicting the outcome of operations for lung cancer has been already suspected [12], and even recently emphasized for pneumonectomy [4]. The increase in major infectious and pulmonary complications after resection can be explained by the combination of immunodeficiency and weakness of respiratory muscles in malnourished patients with lung cancer [13]. The benefit of intensive nutritional support with branched-chain amino acids and herbal medication for the improvement of appetite has been recently suggested in reducing the risks of lung cancer surgery [14], but still needs to be studied in large-scale randomized trials. Of note was also the high proportion of active smokers in underweight patients in our cohort, which might have contributed to the higher incidence of pulmonary complications. Thus, in underweight patients, in addition to comprehensive preoperative rehabilitation including a nutritional program and a tobacco-cessation program, attention should be given to aggressive prophylactic respiratory therapy, even if no firm conclusions can be reached about their respective effectiveness from current bodies of evidence [15]. In contrast, the observation of increased surgical complications has seldom been reported. Impaired healing capabilities are understandably involved in the occurrence of prolonged air leaks and bronchial fistulas. Malnutrition has been already presumed as one possible factor contributing to the development of some rare complications such as bronchopleural fistula [12]. This important effect of malnutrition has not been missed in our large-sized cohort. It may thus justify some prophylactic practices in this subgroup of patients such as the adoption of the fissureless technique for performing upper lobectomies [16], selective use of sealants and buttressing of the fissural staple lines [17] and routine use of regional flaps to reinforce the bronchial stump [18].

Almost 50% of patients of this surgical cohort were overweight or obese. Obese patients accounted for 14% of all patients, a prevalence known to be very low compared with that (25–30%) in the USA, Canada, the UK and Eastern European Countries. This prevalence was close to that observed in the general population in France [19], and this similarity suggests the absence of a stringent selection among obese surgical candidates. In contrast, a selection bias is strongly suspected in multi-institutional lung cancer surgery series coming from the US that report on very dissimilar rates: 3.7% in the Healthcare Cost and Utilization Project Nationwide Inpatient Sample (HCUP-NIS) database [7], 4.8% in the Florida Cancer Data System [20] and 25.3% in the Society of Thoracic Surgeons national database [21]. These discrepancies render direct comparisons with our national figures hazardous. In any case, it is commonly assumed that obese patients are at higher risk of surgical complications than those who are not obese. Nonetheless, obesity was not associated in the present study with increased incidence of overall postoperative morbidity or mortality in patients after lobectomy for lung cancer, although those patients were significantly older and presented with more comorbid conditions than those with normal BMI values. Moreover, our study did not disclose any highest postoperative mortality risks in the morbid (class III) obese patients, when compared with class I and class II obese patients. This counterintuitive fact has already been reported for lung cancer patients [7, 21, 22]. Conversely to Launer et al. [7], we observed an equal prevalence of respiratory complications in obese patients when compared with normal BMI patients. In addition, the ARDS rate was significantly lower in obese patients. Of note, we confirmed in this cohort the well-recognized observation of consistently lower smoking rates in obese patients, which is possibly part of the explanation. Likewise, we substantiated a protective effect of obesity on early mortality and overall morbidity compared with outcomes of normal BMI patients. This phenomenon has already been reported and is known as the 'obesity paradox'. Hypotheses to explain the obesity paradox include protective peripheral body fat, reduced inflammatory response, genetics and a decline in cardiovascular disease risk factors, but probably unknown factors contribute too [23]. On the other hand, we observed an increased risk, even if not statistically significant, of cardiovascular complications. Coronary events did not occur more frequently in this group of patients, and this finding challenges the evidence-base thought that increased body mass is a predictor of increased coronary disease risk, independent of cardiovascular risk factors [24]. One may assume that this results from an accurate selection of candidates for surgery, according to current guidelines [1]. Conversely, arrhythmia, deep venous thrombosis and pulmonary embolism were significantly more frequent, highlighting the potential interest in additional prophylactic measures such as perioperative intermittent pneumatic compression of the lower limbs besides early mobilization, compression elastic stockings and routine use of weight-adjusted low-molecular-weight heparin, and targeting this patient's subset for amiodarone prophylaxis [25].

The main limitation of this study is the use of BMI as a proxy of overall body fat content and a surrogate of the nutritional status, without any focus on its possible recent variations in each individual, or the adjunct of additional biomarkers such as plasmatic albumin. Furthermore, in overweight patients, BMI does not discriminate between fat mass and lean mass, and as a result, BMI does not adequately reflect adiposity. Therefore, it might be that some so-called overweight individuals have a preserved lean body mass actually, which would offer a possible explanation for the protective effect in this category. However, we believe that these limitations are favourably compensated by its ease of measurement and excellent correlation to mortality and morbidity.

To conclude, our results, based on the best available data—clinical, large-sized-, risk- and case-mix-adjusted, nationally benchmarked and audited 30-day patient outcomes show that nutritional status does have an independent impact on early postoperative outcomes. Despite having an increased risk of some postoperative cardiovascular complications, obese patients should undergo surgical standard of care therapy for appropriately stage-specific lung cancer. In underweight patients, in addition to preoperative rehabilitation including a nutritional program, attention should be given to aggressive prophylactic respiratory therapy in the peri-

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operative period and specific intraoperative actions to prevent some surgical complications such as prolonged air leaks and bronchial stump fistula.

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APPENDIX. CONFERENCE DISCUSSION

Dr M. Ferguson *(Chicago, IL, USA)*: This paper focuses on a very important topic, prediction of surgical risk prior to major lung surgery. Although a variety of risk scoring systems have been devised, BMI and nutritional status have not been part of such systems. This study clearly demonstrates that BMI is a strong and independent determinant of surgical risk for major lung resection, and I think this is a very important contribution to our knowledge base. As you point out, the findings are not intuitive despite reports in other disease states that echo these findings.

Your manuscript refers to nutritional status, but really you are studying BMI. Better measures for assessing nutritional status and risk have been identified, including waist circumference and core muscle mass. Sarcopenic obesity, that is, obesity accompanied by the loss of muscle mass, is associated with poorer outcomes in cancer patients compared to other obese categories. This illustrates the complexity of defining body composition using single measurements.

Our institutional findings are similar to those that you report. The incidence of all categories of complications was elevated in underweight patients and decreased inversely with increasing BMI. We found, however, that at the extremes of obesity, there appeared to be an uptick in the incidence of complications. This would not be unexpected as the risks must outweigh the benefits at some point along the obesity continuum. So my first question is, did you explore these extreme categories to determine whether the seeming protective effect of obesity was lost at some point?

Second, weight loss is an important component of frailty, and frailty is an independent determinant of outcomes after major surgery. Is there any way to determine in your database whether underweight patients were chronically underweight or whether they had suffered recent weight loss? Do you think there would be a difference between these two groups of patients in terms of outcomes?

Finally, the measures you propose for avoiding surgical complications in the underweight patients are quite reasonable. However, nutritional interventions in underweight patients have not been efficacious in the time frame necessary for cancer treatment. Assuming that we can't reverse underweight or sarcopenic status preoperatively, how do you suggest we approach decision-making in these higher risk patients?

Dr Thomas: We do not check the results in class 2 or class 3 obese patients, for a simple reason. This is that the proportion of patients with class 3 or class 2 obesity was very, very low. Indeed, among 2600 obese patients; only 100 were class 3 obese and 400 class 2 obese patients. The shape of the obese patient in France is very different to the obese patient in the United States. The proportion of obese patients in this series was 14%, which is very similar to the incidence of obesity in the general population. I think that in the US it is close to 25%, and within this category you have a roughly similar distribution among the different classes of obesity. I think this is the main difference between our respective populations.

We were not able to segregate those patients having chronically low weight. Because of the nature of the database, this information was not present, but certainly for a prospective study it would be very interesting.

The third question deals with the nutritional programme. For sure, we do not have much time to prepare the patient, but I don't think that the aim of the nutritional preparation is to gain weight. Perhaps we have to look at it in a similar way to the management of oesophageal cancer patients, which is immune-nutrition seven days before and seven days after the operation. Besides, you can see in this population that almost 50% of the underweight patients were active smokers, and a very strong recommendation from the French guidelines is to stop tobacco consumption before surgery even if it takes five weeks, and during these five weeks there is an opportunity to improve the nutritional condition of the patients.

Dr F. Venuta *(Rome, Italy)*: I have a couple of questions. Was there any difference in the incidence of thoracoscopic procedures between the three groups? I didn't get it. Maybe you said it.

Dr Thomas: No, there was no difference, and overall the prevalence of VATS procedures was very low at that time, around 3% of the cases. It is now increasing, but at that time it was 3% with no difference between groups.

Dr Venuta: And another question. Do you have any information about whether the increase of weight in some of the patients started after they quit smoking?

Dr Thomas: No, we didn't get this information. But this correlation, active smoking and underweight, and no smoking status and obesity, is very commonly reported in every paper dealing with this topic.

Dr N. Chaudhuri *(Leeds, UK)*: It must be reassuring to many of our patients in the Western world that obesity has a protective effect on them. But my question is (and I might have missed it in your paper), did you compare the lung function in these patients as an independent variable?

Dr Thomas: Yes. I didn't show these figures on the slide in the interests of time, but we compared the lung function with the FEV1 and (in those patients in whom it was measured) the DLCO, and there was no difference between the groups.

Dr S. Cassivi *(Rochester, MN, USA)*: I wonder if I can get a comment from you on the fact that you have used BMI clearly as a surrogate for nutrition, but what about as a surrogate for socioeconomic status? In your group you found that those with low BMI had poorer outcomes, and perhaps that has some correlation with socioeconomic status. And the interesting sociologic study would be the fact that Mark Ferguson showed in the United States that that also starts to show poorer outcomes at the higher end, too, where I think in the United States obesity, or supreme obesity, is also a marker of poor socioeconomic status and the implications that that might have.

Dr M. Mueller *(Vienna, Austria)*: You stated that you suspect a tissue healing problem in these underweight patients, but you did not see more local infections or wound infections in your patients, only more pulmonary complications. Do you think this is smoking-related or do you have any other Western medical-based ideas why this is so?

Dr Thomas: I have no clear explanation. It is true, that there was no difference in terms of the healing of the thoracotomy, for example, or wound infection, but clearly there were differences in terms of chronic air leaks and bronchial dehiscence. I have no clear explanation, but, for sure, I think that we have to apply surgical procedures that may improve their situation in those patients. I mean the use of the fissure-less technique, buttressing of the staple line, muscle flap reinforcement of the bronchus, and so on.

THORACIC