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Clinical Research

Impact of Sarcopenia on Early Postoperative Complications in Early-Stage Non–Small-Cell Lung Cancer

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Background: Risk assessment for pulmonary resection in patients with early-stage non–small-cell lung cancer (NSCLC) is important for minimizing postoperative morbidity. Depletion of skeletal muscle mass is closely associated with impaired nutritional status and limited physical ability. We evaluated the relationship between skeletal muscle depletion and early postoperative complications in patients with early-stage NSCLC.
Methods: Patients who underwent curative lung resection between 2016 and 2018 and who were diagnosed with pathological stage I/II NSCLC were included, and their records were retrospectively analyzed. The psoas volume index (PVI, cm^3/m^3) was calculated based on computed tomography images from routine preoperative positron emission tomography-computed tomography. Early postoperative complications, defined as those occurring within 90 days of surgery, were compared between the lowest sex-specific quartile for PVI and the remaining quartiles.
Results: A strong correlation was found between the volume and the cross-sectional area of the psoas muscle (R^2=0.816). The overall rate of complications was 57.6% among patients with a low PVI and 32.8% among those with a normal-to-high PVI. The most common complication was prolonged air leak (low PVI, 16.9%; normal-to-high PVI, 9.6%), followed by pneumonia (low PVI, 13.6%; normal-to-high PVI, 7.9%) and recurrent pleural effusion (low PVI, 11.9%; normal-to-high PVI, 6.8%). The predictors of overall complications were low PVI (odds ratio [OR], 2.18; 95% confidence interval [CI], 1.07–4.09; p=0.03), low hemoglobin level (OR, 0.686; 95% CI, 0.54–0.87; p=0.002), and smoking history (OR, 3.93; 95% CI, 2.03–7.58; p<0.001).
Conclusion: Low PVI was associated with a higher rate of early postoperative complications in patients with early-stage NSCLC.

Keywords: Sarcopenia, Non–small-cell lung carcinoma, Postoperative complications

Introduction

Lung cancer is the most common cause of death from cancer worldwide. In 2013, the estimated global incidence of lung cancer was 1.8 million, and the estimated number of fatalities was 1.6 million [1]. Mortality from lung cancer has slightly decreased in Korea since 2002, but lung cancer remains the leading cause of death from cancer and a major health threat in Korea. The overall 5-year relative survival rate of lung cancer has improved from 11.2% for men and 14.7% for women among patients diagnosed between 1993 and 1997 to 19.3% for men and 28.2% for women among patients diagnosed between 2008 and 2012 [2,3]. The standard treatment for patients with stage I non–small-cell lung cancer (NSCLC) is anatomical surgical resection and appropriate mediastinal lymph node dissection; this treatment renders a chance of cure, with overall documented 5-year survival of up to 75% after surgery [4,5]. Perioperative management has improved over the past decades, but postoperative morbidity still occurs as the patient population ages and the complexity of the procedure increases alongside the more prevalent use of neo-

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adjuvant therapies. Common respiratory complications after lobectomy include prolonged air leak, reported in 15% to 18% of cases, and pneumonia, reported in up to 6% [6].

Sarcopenia is a recently-defined geriatric syndrome that is characterized by an age-related decline in skeletal muscle mass combined with diminished muscle strength or reduced physical performance [7]. Sarcopenia is recognized as a predictor of poor surgical outcomes because it is associated with poor nutritional status and limited physical activity. Sarcopenia has been found to be associated with prolonged hospitalization and greater requirements of postoperative transfusion in elderly patients with femur fractures [8]. Studies in the field of thoracic surgery have also been performed, and while the effect of body mass index (BMI) as a predictor of surgical outcome remains unclear, Weig et al. [9] demonstrated that lean muscle mass was a more accurate predictor of postoperative outcome than BMI and that the lean psoas muscle area was a reliable predictor of surgical outcomes after lung transplantation. The psoas muscle area at the level of the third lumbar vertebra (L3) is commonly measured to assess sarcopenia [10-12]. Assessment of the psoas muscle in patients with lung cancer is hindered since routine preoperative chest computed tomography (CT) usually does not include the lower lumbar area. Additionally, the area of the psoas muscle at L3 is not representative of the actual volume of the psoas muscle in every patient.

The purpose of this study was to assess the relationship between the area and the volume of the psoas muscle at L3 and to assess the feasibility of a psoas muscle volume index as a predictor of early postoperative complications after curative resection of early-stage NSCLC.

Methods

Patient cohort

Patients who underwent curative surgery for stage I/II NSCLC between January 2016 and December 2018 were retrospectively enrolled from our institution's batabase (Seoul St. Mary's Hospital, Seoul, Republic of Korea) of electronic medical records. We excluded patients who had undergone neoadjuvant therapy, who had pathologic stage III/IV cancer, who had undergone prior surgery for metachronous lung cancer, or for whom imaging studies were unavailable. The baseline clinical characteristics and preoperative bloodwork, including a carcinoembryonic antigen assay, as well as pulmonary function tests and imaging studies performed within 30 days prior to surgery were reviewed. Early postoperative complications, defined as morbidity occurring within 90 days of surgery, were analyzed together as overall complications. Additionally, respiratory complications, including prolonged (>5-day) air leak, recurrent pleural effusion, pneumonia, and bronchopleural fistula were analyzed.

This study was approved by the Institutional Review Board of Seoul St. Mary's Hospital (approval no., KC19RESI0452). The requirement of informed consent from individual patients was waived because the study was a retrospective database review.

Image analysis

The psoas muscle area was measured at the region of L3 where the transverse process was most well-visualized on axial CT images taken from routine preoperative positron emission tomography-CT (PET-CT) scans. The psoas muscle volume was calculated semi-automatically from the level of the diaphragm to the symphysis pubis using image analysis software (Fujifilm SYNAPSE VINCENT; Fujifilm Medical, Tokyo, Japan). Subcutaneous and visceral fat tissues were identified, and the psoas muscle mass was calculated based on programmed Hounsfield units with an estimated threshold from –200 to –50 and exclusion of the fatty tissues (Fig. 1).

Since muscle mass can vary according to height and body weight, the calculated measurements must be normalized. Although there is no consistent method for the normalization of psoas muscle volume, we chose to use the cube of the height. In studies of human dynamics and physics, normalizing volume by the cube of height is the most widely accepted option of the various possible normalization methods [13]. Thus, to normalize the cross-sectional area, we defined the psoas area index (PAI) as the psoas muscle area at L3 divided by the square of height (m^2), and to normalize the volume, we defined the psoas volume index (PVI) as the psoas muscle volume divided by the cube of height (m^3).

Low-psoas volume index versus normal-to-high psoas volume index groups

Another key determinant of muscle mass is sex. We stratified the study cohort by sex for the analysis and identified low-PVI (PVI values in the lowest quartile) and normal-to-high–PVI (PVI values in the remaining quartiles) groups for each sex. We chose the lowest quartile as a separator because there is as yet no well-known threshold for

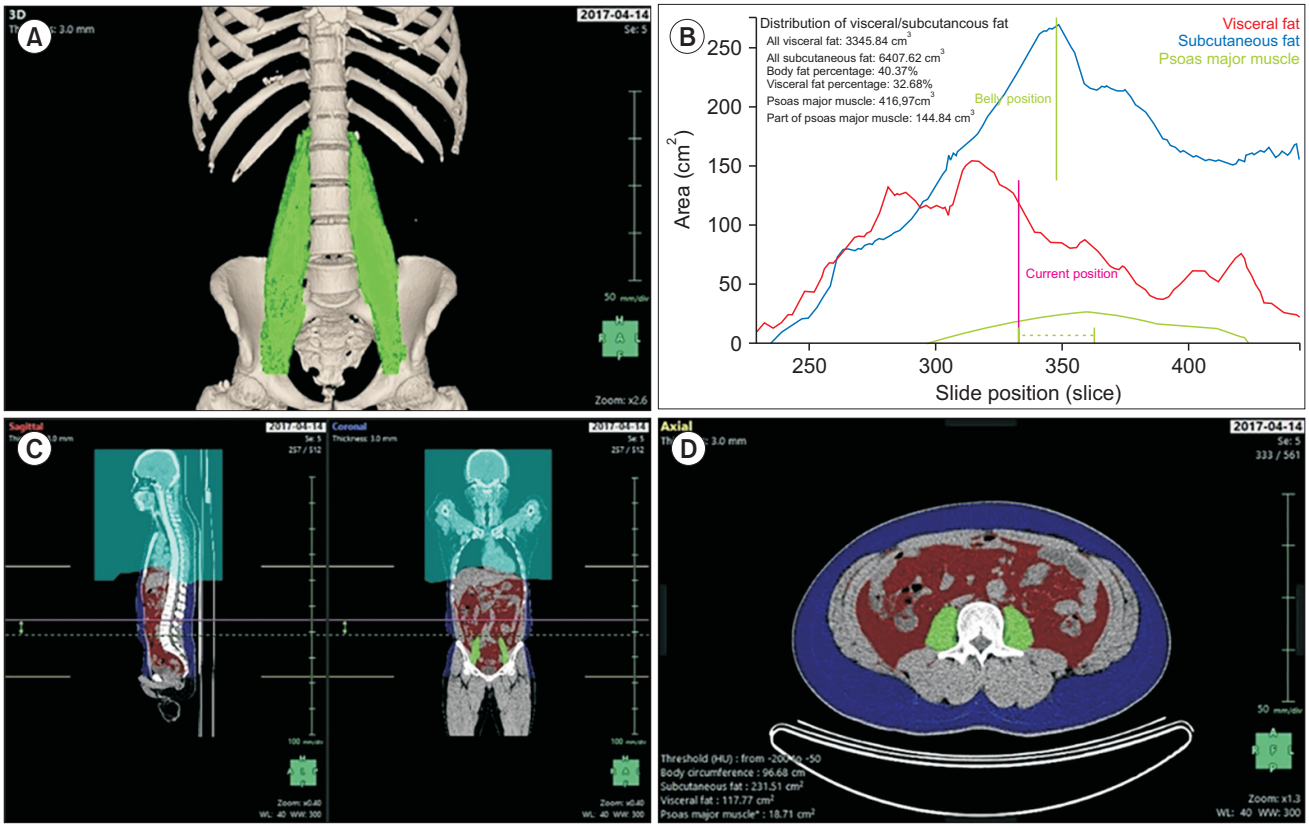

Fig. 1. (A–D) Semi-automatic measurement of psoas muscle area and volume using image analysis software (Fujifilm SYNAPSE VINCENT; Fujifilm Medical, Tokyo, Japan).

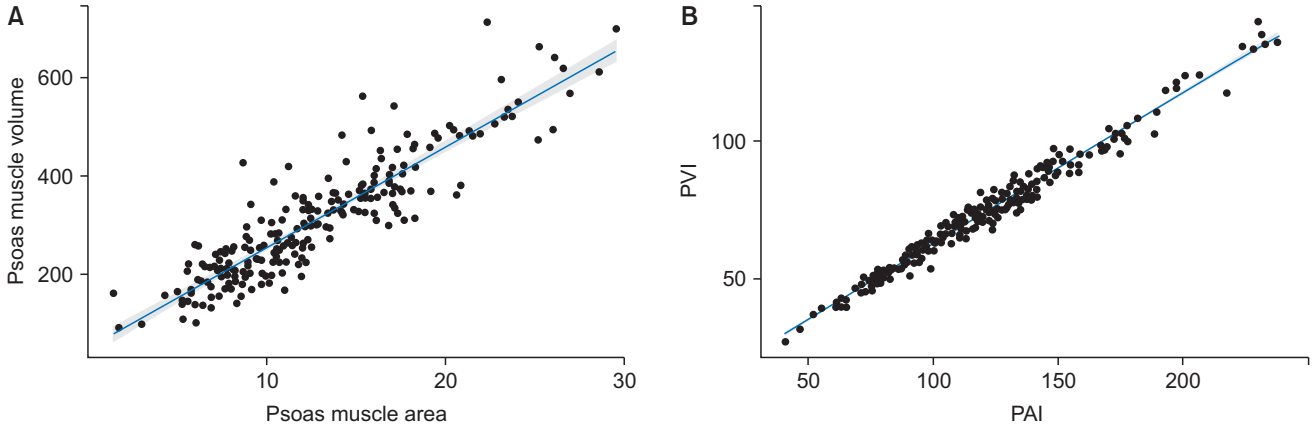

Fig. 2. Scatter plots. (A) The psoas muscle area and volume in the total cohort (R^2=0.816) and (B) the PAI and PVI (R^2=0.743) were positively correlated. PAI, psoas area index; PVI, psoas volume index.

defining sarcopenia by the psoas muscle volume.

Statistical analysis

The primary endpoint of this study was the relationship between PVI and all early (within 90 days of surgery) postoperative complications and between PVI and respiratory complications. As the secondary endpoint, we explored the relationship between PVI and preoperative pulmonary function, immunological status (neutrophil-to-lymphocyte ratio), and nutritional status via the Geriatric Nutritional Risk Index (GNRI). The GNRI was calculated using serum

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albumin concentration and body weight as 14.87×serum albumin concentration (g/dL)+41.7×(preoperative weight/ideal weight [kg]); ideal body weight was calculated as 22×the square of height (m^2) [14,15]. The baseline characteristics were summarized using standard statistical methods, with data presented as mean±standard deviation for continuous variables and as frequencies with percentages for categorial variables. Distributions of continuous variables were compared using the Student t-test or the Mann-Whitney U-test depending on the result of the test of normality. Categorial variables were compared using the chi-square or Fisher exact test. The relationships between the PVI and PAI were assessed using Pearson correlation coefficients. The risk factors for overall complications and respiratory complications were analyzed using univariate and multivariate logistic regression. Statistical significance was indicated by a 2-sided p-value of <0.05, and variables determined to have statistical significance in the univariate analysis were incorporated into a multivariate model. All statistical analyses were performed with IBM SPSS Statistics for Windows ver. 24.0 (IBM Corp., Armonk, NY, USA), and the graphics were constructed using R ver. 3.4.1 (R Project for Statistical Computing, Vienna, Austria).

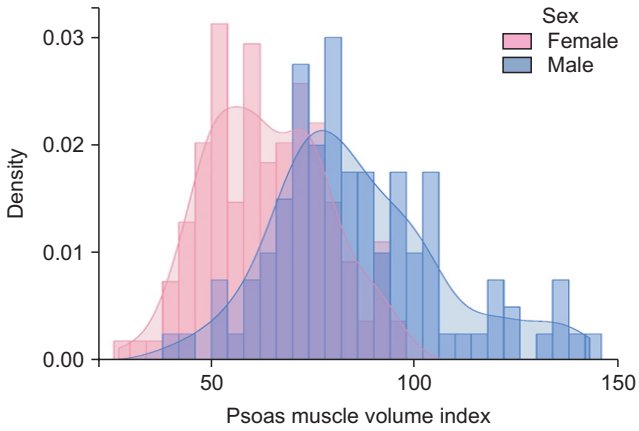

Fig. 3. Distribution of the psoas volume index (volume/height cubed, cm^3/m^3) by sex.

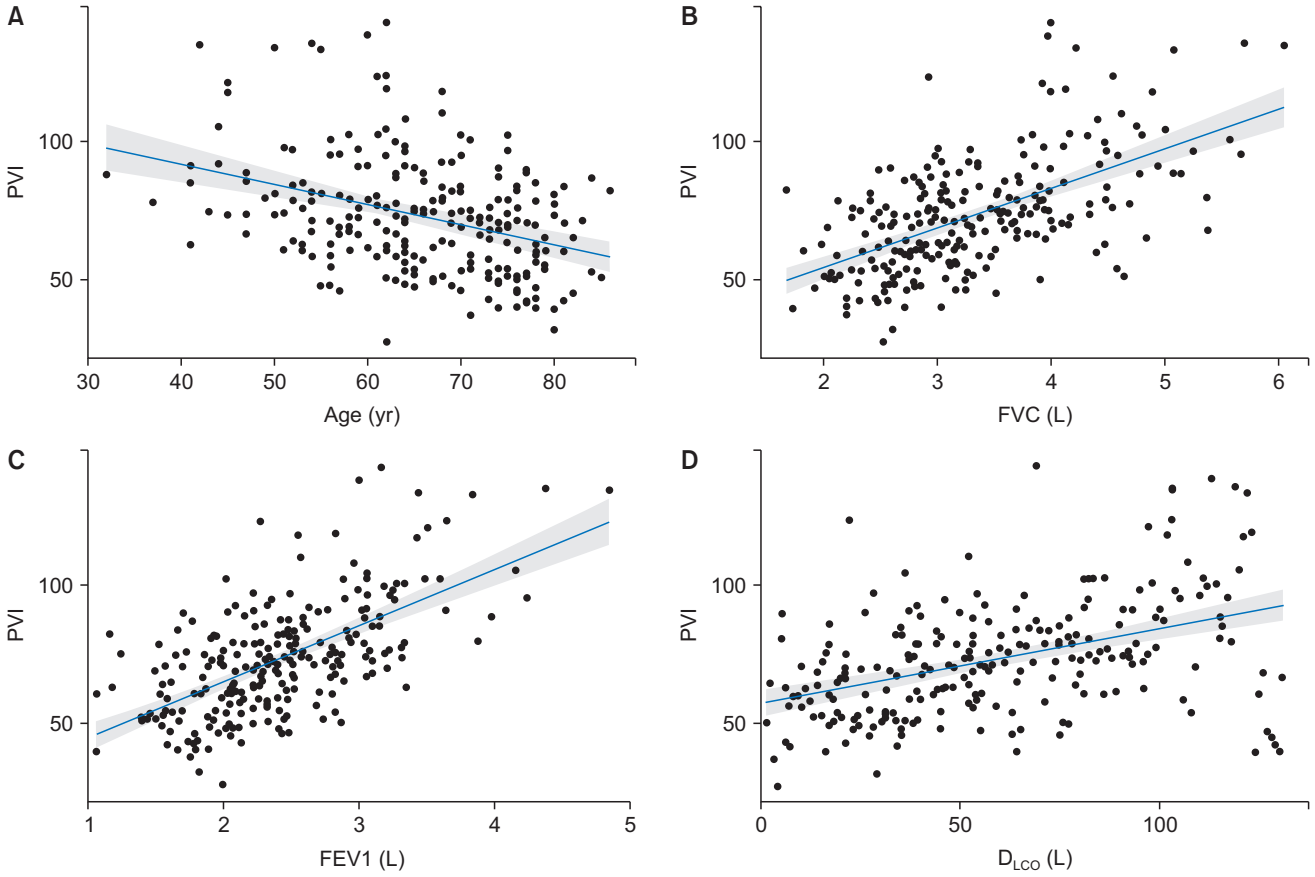

Fig. 4. Relationship between the PVI and (A) age (R^2=–0.368, p<0.001); (B) FVC (L) (R^2=0.588, p<0.001); (C) FEV1 (L) (R^2=0.619, p<0.001); and (D) D_{LCO} (L) (R^2=0.435, p<0.001). PVI, psoas volume index; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; D_{LCO}, diffusing capacity of carbon monoxide.

Table 1. Basic characteristics in the low-PVI and normal-to-high–PVI groups

Characteristic	Low-PVI (n=59)	Normal-to-high–PVI (n=177)	p-value
Age (yr)	72.3±7.28	63.4±10.54	<0.001
Sex, male	25 (42.4)	75 (42.4)	>0.999
Body mass index (kg/m^2)	23.06±3.79	24.36±3.18	0.006
Psoas area index (cm^2/m^2)	3.96±1.14	5.44±1.63	<0.001
PVI (cm^3/m^3)	52.86±11.08	79.92±19.02	<0.001
Pulmonary function tests			
FVC (L)	3.02±0.82	3.42±0.85	0.002
FVC (%)	91.93±12.82	95.50±13.75	0.08
FEV1 (L)	2.08±0.48	2.53±0.64	<0.001
FEV1 (%)	90.54±16.68	94.26±15.17	0.113
D_{LCO} (L)	13.84±3.24	18.27±4.60	<0.001
D_{LCO} (%)	82.66±15.86	94.95±16.19	<0.001
Comorbidities			
Hypertension	28 (47.5)	75 (42.4)	0.495
Diabetes mellitus	7 (11.9)	28 (15.8)	0.459
Chronic obstructive pulmonary disease	8 (13.6)	10 (5.6)	0.084
History of tuberculosis	5 (8.5)	16 (9.0)	0.895
Blood laboratory results			
White blood cells (10^6/L)	6,132.4±1,989.51	6,281.2±1,728.37	0.582
Neutrophils (10^6/L)	3,655.5±1,736.05	3,660.7±1,512.23	0.982
Lymphocytes (10^6/L)	1,820.4±499.12	2,006.8±653.71	0.046
Hemoglobin (g/dL)	12.39±1.32	13.40±1.30	<0.001
C-reactive protein (mg/dL)	0.35±0.97	0.25±1.03	0.501
Albumin (g/dL)	4.05±0.37	4.24±0.30	<0.001
Carcinoembryonic antigen	4.28±11.01	3.55±3.55	0.026
Neutrophil-lymphocyte ratio	2.14±1.15	2.18±2.03	0.881
Geriatric Nutritional Risk Index	103.45±8.15	108.76±7.82	<0.001
Smoking history			0.815
No	38 (64.4)	111 (62.7)	
Yes	21 (35.6)	66 (37.3)	
Amount smoked (pack-years)	11.47±19.12	10.27±18.23	0.670
Surgical approach			0.101
Video-assisted thoracoscopic surgery	56 (94.9)	175 (98.9)	
Open	3 (5.1)	2 (1.1)	
Extent of resection			0.188
Sublobar	5 (8.5)	27 (15.3)	
Lobectomy	54 (91.5)	150 (84.7)	
Mediastinal lymph nodes			0.236
None	2 (3.4)	9 (5.1)	
Sampling	9 (15.3)	14 (7.9)	
Dissection	48 (81.4)	154 (87.0)	
Intraoperative characteristics			
Anesthesia time (min)	215.1±59.58	185.1±44.13	<0.001
Operation time (min)	165.4±59.13	141.0±41.85	0.001
Blood loss (mL)	161.7±286.85	99.0±144.86	0.029
Postoperative hospital stay (day)	5.9±3.59	5.7±5.48	0.796
Pathology			0.299
Adenocarcinoma	49 (83.1)	160 (90.4)	
Squamous cell carcinoma	8 (13.6)	13 (7.3)	
Other	2 (2.4)	4 (2.3)	

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Table 1. Continued

Characteristic	Low-PVI (n=59)	Normal-to-high–PVI (n=177)	p-value
Grade			0.581
Well	19 (34.5)	61 (36.5)	
Moderately	26 (47.3)	85 (50.9)	
Poorly	10 (18.2)	21 (12.6)	
Lymphatic invasion	23 (39.0)	53 (30.1)	0.208
Vascular invasion	7 (11.9)	16 (9.1)	0.535
TNM staging (AJCC 8th edition)			0.826
Stage 0	1 (1.7)	2 (1.1)	
Stage IA1	10 (16.9)	26 (14.7)	
Stage IA2	14 (23.7)	59 (33.3)	
Stage IA3	10 (16.9)	32 (18.1)	
Stage IB	12 (20.3)	32 (18.1)	
Stage IIA	2 (3.4)	3 (1.7)	
Stage IIB	7 (11.9)	19 (10.7)	
Stage IIIA	3 (5.1)	4 (2.3)	
T stage (AJCC 8th edition)			0.840
Tis, T1 (mi)	5 (8.5)	15 (8.5)	
T1a	6 (10.2)	13 (7.3)	
T1b	15 (25.4)	60 (33.9)	
T1c	11 (18.6)	35 (19.8)	
T2a	13 (22.0)	34 (19.2)	
T2b	3 (5.1)	4 (2.3)	
T3	4 (6.8)	13 (7.3)	
T4	2 (3.4)	3 (1.7)	
N stage (AJCC 8th edition)			0.249
N0	54 (91.5)	169 (95.5)	
N1	5 (8.5)	8 (4.5)	
Adjuvant chemotherapy	4 (6.8)	23 (13.0)	0.194

Values are presented as mean±standard deviation or number (%).
PVI, psoas volume index; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; D_{LCO}, diffusing capacity for carbon monoxide; TNM, tumor-node-metastasis; AJCC, American Joint Committee on Cancer.

Results

General characteristics of patients and psoas muscle profile

A total of 236 patients with pathologic stage I/II NSCLC who underwent curative pulmonary resection during the study period were eligible. Video-assisted thoracoscopic surgery was the predominant surgical approach (n=231, 97.9%). Common characteristics of the patients included adenocarcinoma (n=175, 74.2%), pathologic stage IA1-3 according to the 8th edition of tumor-node-metastasis staging system (n=151, 64.0%), pathologic stage N0 according to the same system (n=223, 94.5%), and lobectomy (n=204, 86.4%).

We assessed the relationship between psoas muscle area and volume based on the semi-automatic CT measurements of the psoas muscle area and volume at L3 (Fig. 2). A strong correlation between the 2 parameters (R^2=0.816, p<0.001) was found and persisted after normalization (R^2=0.743; p<0.001 for PAI and PVI).

Characteristics of the low- and normal-to-high–psoas volume index groups

The distribution of PVI by sex is shown in Fig. 3. We divided the cohort into 2 groups, according to the threshold separating the lowest quartile for sex-specific PVI (men, 71.37; women, 51.87) from the higher quartiles. The age at operation showed a weakly negative correlation with the PVI (R^2=–0.368, p<0.001) (Fig. 4A). The 2 groups are compared in Table 1. The PAI (cm^2/m^2) was 3.96±1.14 in the low-PVI group and 5.44±1.63 in the normal-to-high–PVI group. The PVI (cm^3/m^3) was 52.86±11.08 in the low-PVI group and 79.92±19.02 in the normal-to-high–PVI group.

In the low-PVI group, the patients were older (p<0.001)

and had a lower BMI (p=0.006), lower hemoglobin and albumin levels (p<0.001 for both), and poorer nutritional status, as reflected by a lower GNRI (p<0.001), than the patients in the normal-to-high group. Patients in the low-PVI group also had lower forced vital capacity (p=0.002), lower forced expiratory volume in 1 second (FEV1, p<0.001), and lower diffusing capacity for carbon monoxide (D_{LCO}, p<0.001) than those in the normal-to-high–PVI group (Fig. 4). There were no significant differences in the distribution of sex, history of tuberculosis or malignancy, type of operation, pathologic profile or stage of tumor, or length of postoperative hospital stay.

Early postoperative complications

The rate of all complications for the entire cohort was 39%, and the rate of respiratory complications was 27.1%. More complications were present in the low-PVI group (p=0.001) (Table 2), and postoperative atrial fibrillation (p=0.046) and vocal cord palsy (p=0.049) were significantly more frequent among patients with low PVI. Although statistically insignificant, prolonged air leaks, postoperative pneumonia, recurrent pleural effusion, and wound infection were also more frequently observed in the low-PVI group.

Table 2. Distribution of early postoperative complications within 90 days after surgery

Variable	Low-PVI (n=59)	Normal-to-high–PVI (n=177)	p-value
Overall	34 (57.6)	58 (32.8)	0.001
Prolonged air leak[a]	10 (16.9)	17 (9.6)	0.125
Postoperative pneumonia	8 (13.6)	14 (7.9)	0.196
Recurrent pleural effusion	7 (11.9)	12 (6.8)	0.267
Postoperative atrial fibrillation	5 (8.5)	4 (2.3)	0.046
Postoperative vocal cord palsy	3 (5.1)	1 (0.6)	0.049
Postoperative bleeding	2 (3.4)	1 (0.6)	0.155
Wound infection	2 (3.4)	1 (0.6)	0.155
Chylothorax	1 (1.7)	4 (2.3)	>0.999
Postoperative pulmonary thromboembolism	1 (1.7)	3 (1.7)	>0.999
Pulmonary infarction/ torsion	1 (1.7)	1 (0.6)	0.438
Pericardial effusion	0	2 (1.1)	>0.999
Postoperative pneumothorax	0	4 (2.3)	0.575
Other	2 (3.4)	1 (0.6)	0.155

Values are presented as number (%).
PVI, psoas volume index.
[a]Prolonged air leak was defined as a leak lasting more than 5 days.

Risk factors for overall and respiratory complications

Univariate and multivariate logistic regression analyses were performed to identify potential risk factors for overall complications and for respiratory complications. On the univariate analysis for overall complications, male sex (OR, 2.078; p=0.007), low PVI (OR, 2.79; p=0.001), smoking history (OR, 1.019; p=0.002), and longer operation time (OR, 1.008; p=0.006) were associated with increased risk of complications, while high hemoglobin level (OR, 0.745; p=0.004), high albumin level (OR, 0.401; p=0.538), and high D_{LCO} (OR, 0.972; p=0.001) were associated with decreased risk (Table 3). Multivariate analysis found that low PVI (OR, 2.180; p=0.031) and preoperative hemoglobin level (OR, 0.686; p=0.002) were the strongest predictors of early postoperative complications.

We performed the same analyses focusing on only respiratory complications (Table 4). Univariate analysis showed an association between complication risk and male sex (OR, 2.593; p=0.001), low PVI (OR, 2.119; p=0.019), chronic obstructive pulmonary disease (OR, 3.796; p=0.008), smoking history (OR, 2.545; p=0.002), and longer operation time (OR, 1.010; p=0.001). High D_{LCO} (OR, 0.970; p=0.002) was associated with a lower risk of respiratory morbidities. On multivariate analysis, only male sex (OR, 2.166; p=0.017) and a longer operation time (OR, 1.008; p=0.018) were associated with increased risk, and high D_{LCO} (OR, 0.974; p=0.008) remained associated with a decreased risk of respiratory morbidities in the early postoperative period.

Discussion

Outcomes after lung cancer surgery and predictors thereof have been extensively reported [16], and several well-known predictors have been identified, namely age, male sex, pneumonectomy, low FEV1, and pre-existing comorbidities [17-19]. With the changing profiles of patient populations, efforts to define preoperative risk factors have been increasingly focused on patient characteristics, mainly cardiac and respiratory reserve. As the population ages, much interest has been placed in assessing frailty and its relation to surgical outcomes. Frailty is characterized by decreased reserve and resistance to stressors resulting from cumulative declines across multiple physiological systems, causing vulnerability to adverse outcomes [20]. Decreased muscle mass is a result of frailty, and it is also a clinical marker in the assessment of frailty [21].

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Table 3. Risk factors for overall complications in the early postoperative period, defined as those occurring within 90 days of surgery (n=92, 39%)

Variable	Univariate		Multivariate	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.021 (0.995–1.047)	0.113		
Sex (ref: female)	2.078 (1.219–3.542)	0.007		
Body mass index	0.973 (0.896–1.057)	0.518		
PVI group (ref: normal-to-high PVI)	2.790 (1.525–5.106)	0.001	2.180 (1.072–4.094)	0.031
Pulmonary function tests				
FVC (L)	1.087 (0.802–1.475)	0.591		
FVC (%)	0.985 (0.966–1.004)	0.128		
FEV1 (L)	0.492 (0.568–1.313)	0.492		
FEV1 (%)	0.984 (0.967–1.001)	0.071		
D_{LCO} (L)	0.954 (0.900–1.011)	0.113		
D_{LCO} (%)	0.972 (0.956–0.989)	0.001		
Comorbidities (ref: no disease)				
Hypertension	1.143 (0.675–1.936)	0.619		
Diabetes mellitus	1.817 (0.883–3.741)	0.105		
Chronic obstructive pulmonary disease	2.658 (0.991–7.129)	0.052		
History of tuberculosis	1.193 (0.482–2.954)	0.703		
Blood laboratories				
Hemoglobin	0.745 (0.611–0.908)	0.004	0.686 (0.541–0.870)	0.002
C-reactive protein	1.060 (0.822–1.368)	0.653		
Albumin	0.401 (0.177–0.909)	0.029		
Carcinoembryonic antigen	0.983 (0.932–1.037)	0.538		
Neutrophil-lymphocyte ratio	1.086 (0.939–1.257)	0.266		
Geriatric Nutritional Risk Index	0.968 (0.937–1.001)	0.054		
Smoking history (ref: no history)	2.325 (1.349–4.007)	0.002	3.925 (2.032–7.582)	<0.001
Amount smoked (pack-years)	1.019 (1.004–1.035)	0.011		
Surgical approach (ref: video-assisted thoracoscopic surgery)	2.393 (0.392–14.605)	0.344		
Extent of resection (ref: sublobar)	1.753 (0.772–3.979)	0.180		
Intraoperation				
Anesthesia time	1.008 (1.002–1.014)	0.005		
Operation time	1.008 (1.002–1.014)	0.006		
Blood loss	1.001 (0.999–1.002)	0.296		

OR, odds ratio; CI, confidence interval; ref, reference; PVI, psoas volume index; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; D_{LCO}, diffusing capacity of carbon monoxide.

Among several candidates for predictors of surgical outcome, reduced muscle mass has been an interesting target, and its usefulness as a clinical marker for outcomes has been assessed in various settings. Sarcopenia is the progressive loss of skeletal muscle mass and strength associated with aging that has previously been shown to predict poor outcomes in patients who undergo abdominal, vascular, lung, and esophageal surgery [22-25].

The levels and methods that most precisely reflect muscle mass have yet to be standardized. Since Mourtzakis et al. [26] showed that CT imaging of the muscle mass at L3 was as effective as dual-energy absorptiometry and superior to bioelectrical impedance analysis, the L3 muscle index has been used to assess sarcopenia. We also used L3 as the target level for measuring the psoas muscle area.

As far as we know, this is the first study to evaluate the relationship between area and volume in the psoas muscle and to explore the feasibility of the PVI as a predictor after lung cancer surgery. Volume can be more accurate for evaluating muscle mass than a single axial image, and we therefore used SYNAPSE 3D reconstruction software (Fujifilm Medical) to extract the entire psoas muscle volume in semi-automatic mode [27]. CT is ideal for identifying and quantifying skeletal muscle mass because it provides precise differentiation among fat, muscle, and other tissues. However, since routine preoperative chest CT in our lung cancer patients did not cover the lower lumbar area, we used CT images from routine preoperative PET-CT instead. It was possible to extract psoas muscle density from these images and to reconstruct and calculate the volume.

Table 4. Risk factors for early (within 90 days) postoperative respiratory complications (n=64, 27.1%)

Variable	Univariate		Multivariate	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.011 (0.983–1.039)	0.451		
Sex (ref: female)	2.593 (1.440–4.668)	0.001	2.166 (1.150–4.077)	0.017
Body mass index	0.950 (0.867–1.041)	0.272		
PVI group (ref: normal-to-high PVI)	2.119 (1.130–3.975)	0.019		
Pulmonary function tests				
FVC (L)	1.365 (0.981–1.900)	0.065		
FVC (%)	0.996 (0.975–1.017)	0.713		
FEV1 (L)	1.185 (0.755–1.859)	0.461		
FEV1 (%)	0.991 (0.972–1.009)	0.319		
D_{LCO} (L)	0.974 (0.915–1.038)	0.421		
D_{LCO} (%)	0.970 (0.952–0.989)	0.002	0.974 (0.955–0.993)	0.008
Comorbidities (ref: no disease)				
Hypertension	1.006 (0.564–1.794)	0.984		
Diabetes mellitus	2.013 (0.953–4.254)	0.067		
Chronic obstructive pulmonary disease	3.796 (1.426–10.107)	0.008		
History of tuberculosis	1.747 (0.688–4.437)	0.241		
Blood laboratories				
Hemoglobin	0.825 (0.670–1.016)	0.071		
C-reactive protein	1.085 (0.837–1.407)	0.539		
Albumin	0.529 (0.221–1.267)	0.153		
Carcinoembryonic antigen	0.990 (0.937–1.046)	0.721		
Neutrophil-lymphocyte ratio	1.092 (0.944–1.263)	0.235		
Geriatric Nutritional Risk Index	0.968 (0.934–1.003)	0.073		
Smoking history (ref: no history)	2.545 (1.413–4.582)	0.002		
Smoking (pack-years)	1.014 (0.999–1.029)	0.063		
Approach (ref: video-assisted thoracoscopic surgery)	1.817 (0.297–11.134)	0.518		
Extent of resection (ref: sublobar)	1.135 (0.482–2.675)	0.772		
Intraoperation				
Anesthesia time	1.010 (1.004–1.016)	0.001		
Operation time	1.010 (1.004–1.016)	0.001	1.008 (1.001–1.015)	0.018
Blood loss	1.001 (0.999–1.002)	0.235		

OR, odds ratio; CI, confidence interval; ref, reference; PVI, psoas volume index; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; D_{LCO}, diffusing capacity of carbon monoxide.

We found a strong correlation between psoas muscle area and volume, and we analyzed the risk factors for overall and respiratory complications. Because the muscle mass distribution is the most strongly affected by sex, we first normalized psoas area and volume (PAI, PVI) by height and then categorized the PVI by sex. As there is still no consensus regarding sex-specific cut-off values for sarcopenia, we arbitrarily defined a low PVI as the lowest quartile value.

Sarcopenia, as represented by a low PVI in this study, was found to be a negative prognostic factor for overall early postoperative complications. Sarcopenia is attributed to the aging process, but it has also been shown to be accelerated with malnutrition and chronic illness. The depletion of skeletal muscle mass leads to a decline in physical activity, which in turn leads to more profound sarcopenia. This vicious cycle leads to functional decline and increased susceptibility to comorbidities. Therefore, well-planned preoperative and rehabilitation programs that include physical exercise and nutritional support should help reduce complications in fragile patients. Other risk factors were found to include hemoglobin levels and smoking, which are well-known risk factors.

Interestingly, our study also showed that BMI was not a statistically significant risk factor. BMI does not account for the proportion of adipose tissue versus lean muscle mass, and it might not be an appropriate parameter to describe sarcopenia and frailty. Earlier research has shown that decreased BMI with preservation of muscle mass did not have a deleterious impact on survival [28].

Our results confirmed a significant correlation between sarcopenia and impaired pulmonary function. The association between low FEV1 and sarcopenia has been noted by others, as have the associations between low PVI and low FEV1, low forced vital capacity, and low D_{LCO} [9,27]. Pulmonary function is influenced by the interactions among the lungs, chest wall, and respiratory muscles. Among these, the respiratory muscle mass is positively correlated with the whole-body muscle mass, including the psoas muscle. Further research is warranted concerning the relationship between low skeletal muscle mass and D_{LCO}.

Another interesting result is that nutritional status was significantly correlated with sarcopenia. The GNRI, which is a function of serum albumin concentration and body weight, reflects nutritional status; a cross-sectional study of Chinese participants revealed that elderly patients with a low GNRI were more likely to have low muscle mass (OR, 3.904 for men and 4.486 for women; $p<0.001$ and $p=0.001$, respectively) [29]. These findings emphasize the need for nutritional support in addition to exercise training in sarcopenic patients to optimize their status.

This study had several limitations. First, it was a retrospective study conducted in a single institution. Second, it was a cross-sectional study based on PET-CT images that were taken at a single point in time before surgery. Trends or changes therefore could not be evaluated, and it is possible that patients with decreasing muscle mass would have worse outcomes. Third, because we used CT data from PET-CT images instead of contrast-enhanced abdominal CT, underestimation or overestimation of muscle mass was possible. However, the effect of this bias was minimized because we used the same imaging modalities for all patients. Therefore, the directionality of the conclusion should remain the same even if the magnitude of the effect changes slightly in further studies. Fourth and most importantly, because there was still no consensus definition of sarcopenia at the time of our study, we used the lowest quartile of the PVI.

In conclusion, the volume of the psoas muscle is a useful predictor of overall complication risk in the early postoperative period after curative resection in stage I/II NSCLC.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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