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The feasibility of CT lung volume as a surrogate marker of donor–recipient size matching in lung transplantation

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Abstract

Donor–recipient size matching in lung transplantation (LTx) by computed tomography lung volume (CTvol) may be a reasonable approach because size matching is an anatomical issue. The purpose of this study is to evaluate the feasibility of CTvol as a surrogate marker of size matching in LTx by comparing CTvol and predicted total lung capacity (pTLC) to reference total lung capacity (TLC) values.

From January to December 2014, data from 400 patients who underwent plethysmography, pulmonary function testing (PFT), and chest computed tomography scans were reviewed retrospectively. Enrolled 264 patients were divided into 3 groups according to PFT results: Group I, obstructive pattern; Group II, restrictive pattern; Group III, normal range. The correlations between pTLC and TLC and between CTvol and TLC were analyzed, and the linear correlation coefficients were compared. The percentage error rates of pTLC and CTvol were calculated and absolute error rates were compared.

The correlation coefficient between CTvol and TLC in Group I was larger than that of pTLC and TLC (0.701 vs 0.432, $P=0.002$). The absolute percentage error rate between CTvol and pTLC was lower than that of pTLC in Group II (15.3% ± 11.9% vs 42.2% ± 28.1%, $P<0.001$).

CTvol showed similar or better correlation with TLC compared to the pTLC in normal participants and patients with obstructive or restrictive pulmonary diseases. CTvol showed a smaller error rate in patients with restrictive disease. The results suggest that CTvol may be a feasible method for size matching in LTx.

Abbreviations: CT = computed tomography, CTvol = computed tomography lung volume, FEV1 = forced expiratory volume in 1 second, FVC = forced vital capacity, LTx = lung transplantation, PFT = pulmonary function test, pTLC = predicted total lung capacity, TLC = total lung capacity.

Keywords: CT lung volume, lung transplantation, predicted total lung capacity, size matching, total lung capacity

1. Introduction

Size matching between a donor lung allograft and a recipient thorax is a major consideration in lung transplantation (LTx) because size mismatches may cause complications such as poor lung function and decreased long-term survival.[1–4]

Currently, predicted total lung capacity (pTLC) is widely used as a surrogate marker of functional lung volume (total lung capacity [TLC]) for lung size matching,[5,6] due to its clinical usefulness and the simplicity of calculation.[7,8] However, pTLC has well-known limitations and disadvantages when used to evaluate LTx candidates.[9,10]

With recent advances in computed tomography (CT) technology, multidetector row CT can provide accurate anatomical lung volume measurements.[11–14] Size matching by CT lung volume (CTvol) may be a reasonable approach because this method can provide a meaningful thoracic size during perioperative assessment for LTx, where size matching between recipient and donor is an anatomical issue.[11,15,16]

Therefore, this study evaluated the feasibility of CTvol as a surrogate marker of donor–recipient size matching in LTx by comparing CTvol and pTLC to reference TLC values.

2. Materials and methods

This study was designed as a retrospective observational study.

2.1. Patients

From January to December 2014, data from 400 patients who underwent plethysmography, pulmonary function testing (PFT), and chest CT scans were reviewed retrospectively. Patients with incomplete medical records (n = 75), previous thoracic surgery

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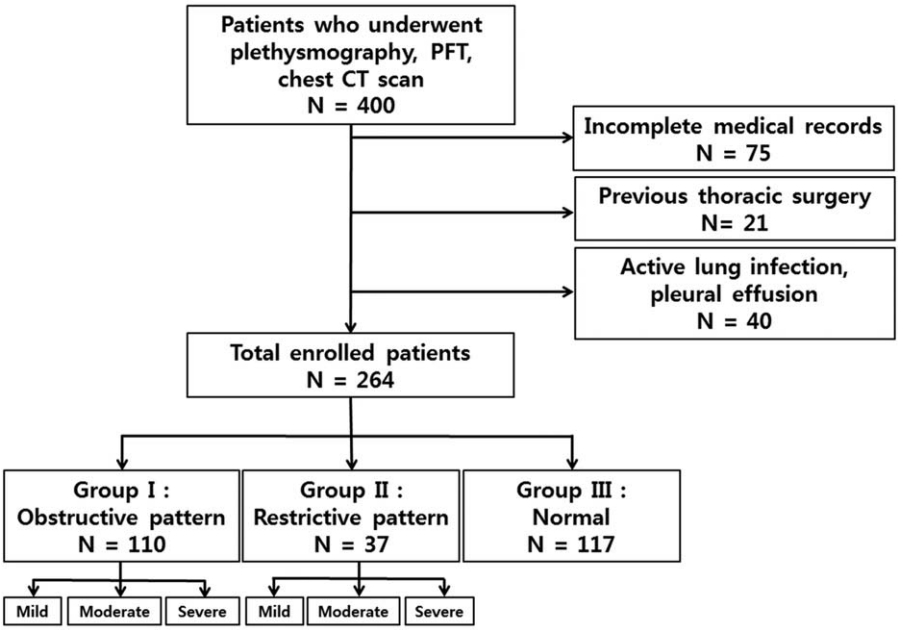

Figure 1. Flow chart of patient selection. On the basis of FEV1, FVC, and FEV1/FVC ratio by spirometry, lung disease patterns were classified into 3 groups: obstructive pattern (Group I), restrictive pattern (Group II), and normal (Group III). CT = computed tomography, FEV1 = forced expiratory volume in 1 second, FVC = forced vital capacity, PFT = pulmonary function test.

(n = 21), active infectious lung conditions (n = 32), and pleural effusion (n = 8) were excluded. Finally, 264 patients (M:F = 171:93) were enrolled (Fig. 1). This study received approval from the institutional review board at our institution. CT images and clinical data were retrospectively obtained from medical records, and the requirement for informed consent was waived due to the retrospective nature of this study.

2.2. pTLC calculation

pTLC was calculated using European Respiratory Society formulas, which are generally used for lung size matching during the LTx process as follows, where H represents height in meters[8,17]:

Males: $pTLC\ (mL) = (7.99H - 7.08) \times 1000$

Females: $pTLC\ (mL) = (6.60H - 5.79) \times 1000$

2.3. Measurement of total lung capacity and pulmonary function test

TLC was measured using whole-body plethysmography. For PFT, spirometry was used to measure the forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC). The FEV1/FVC ratio was calculated. Based on PFT results, patients were divided into 3 disease pattern groups as follows[18,19]:

1. Obstructive pattern (Group I): FEV1/FVC ratio <70%
2. Restrictive pattern (Group II): FEV1/FVC ratio ≥70% and FVC (%) <80
3. Within normal range (Group III): FEV1/FVC ratio ≥70% and FVC (%) ≥80

The Groups I and II were categorized according to the disease severity as mild, moderate, or severe disease: FEV1 >70% was considered as mild disease, 69% to 50% as moderate disease, and <49% as severe disease.[20]

2.4. Computed tomography protocol

One of the following 3 CT scanners was used for each participant in this study: a 128-slice multidetector CT (Somatom Definition AS+; Siemens Medical Solutions, Erlangen, Germany), a 64-slice multidetector CT (Somatom Sensation 64; Siemens Medical Solutions), or a 16-slice multidetector CT (Somatom Sensation 16; Siemens Medical Solutions). All the chest CT scans were performed using 120 kVp and 130 to 200 mAs at the end of inspiration in a supine position. The slice thickness of the chest CT was 3 or 5 mm. The acquired CT images were reviewed on the picture archiving and communication system (Centricity 2.0; GE Medical Systems, Mount Prospect, IL).

2.5. CT image analysis

Two radiologists (THK, CHP) working in the chest division, with over 20 and 8 years of experience, respectively, reviewed the CT images while blinded to the PFT results. If abnormal features, including active lung infection, previous thoracic surgery, or large amounts of pleural effusion, were noted, the chest CT images were excluded. The enrolled CT images were digitally analyzed (Aquarius iNtuition version 4.4.6; TeraRecon, Foster City, CA) to measure the CTvol. The CTvol was measured semiautomatically using a 3-dimensional autosegmentation technique with −200 to −1024 HU (Fig. 2).

2.6. Statistical analysis

The continuous data were demonstrated as mean ± standard deviation, and the categorical data were demonstrated as frequencies or percentages. The normality of the data distributions was tested with the Shapiro–Wilk test. A linear mixed model was utilized to analyze the differences between the pTLC, CTvol, and TLC. The post hoc analysis was performed using Bonferroni method. The correlation coefficients between the pTLC and the

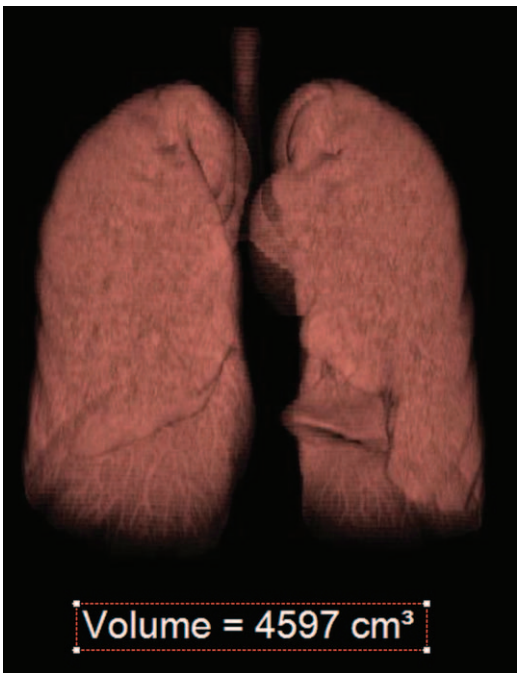

Figure 2. Measurement of CT lung volume using an autosegmentation technique. The lung parenchyma is semiautomatically extracted from CT images using a commercially available reconstruction program (Aquarius iNtuition version 4.4.6; TeraRecon). A 3-dimensional lung volume image is reconstructed using an automatic segmentation technique by a default range of −200 to −1024 HU. Then the CT lung volume is measured. CT = computed tomography.

TLC, and between the CTvol and the TLC were analyzed by the Pearson correlation analysis, based on the disease pattern and disease severity. The percentage error rate of the pTLC and CTvol was calculated as follows: $([\text{pTLC or CTvol} - \text{TLC}]/\text{TLC}) \times 100$; the absolute error rates of the pTLC and CTvol were compared using paired *t* tests. The interobserver reproducibility of the CTvol measurement was tested using the intraclass correlation coefficient. *P* values or Bonferroni-adjusted *P* values <0.05 were regarded as statistically significant. For the statistical analyses, a commercially available software was used (IBM SPSS Statistics for Windows, version 20.0; IBM Corp, Armonk, NY).

3. Results

The demographic data of the 264 enrolled patients (M:F = 171:93, mean age = 60.6 ± 14.4 years) are summarized in Table 1. There were 110 (42%) patients in Group I, 37 (14%) in Group II, and 117 (44%) in Group III. Among patients in Group I, 55 (50%), 37 (34%), and 18 (16%) patients had mild, moderate, and severe disease, respectively. In Group II, 29 (78%) and 7 (22%) had mild and moderate disease, respectively.

CTvol were successfully obtained in all participants, and the intraclass correlation coefficient for interobserver reproducibility was 0.999 ($P < 0.001$).

pTLC was significantly larger than TLC, whereas CTvol was significantly smaller than TLC overall (Table 2). In Group I, pTLC was not significantly different from TLC (5.92 ± 0.89 vs 5.73 ± 1.25, $P = 0.447$). In Group II, CTvol was not significantly different from TLC (3.57 ± 0.78 vs 3.98 ± 0.85, $P = 0.051$). In Group III, pTLC, CTvol, and TLC are all significantly different from each other (5.68 ± 1.06 vs 4.45 ± 1.05 vs 5.25 ± 1.18, $P < 0.001$, respectively) (Fig. 3).

The correlations between pTLC and TLC and between CTvol and TLC are listed in Table 3. The correlation coefficient between CTvol and TLC in Group I was significantly larger than that between pTLC and TLC (0.701 vs 0.432, $P = 0.002$). There were no statistical differences between Groups II and III (0.638 vs 0.530, $P = 0.248$ in Group II; 0.774 vs 0.759, $P = 0.392$ in Group III) (Fig. 4).

The absolute percentage error rates were not significantly different between CTvol and pTLC in Group I (15.4% ± 12.5% vs 16.0% ± 15.8%, $P = 0.701$) and Group III (16.4% ± 11.8% vs 14.3% ± 13.7%, $P = 0.180$). However, in Group II, the absolute percentage error rate of CTvol was significantly smaller than that of pTLC (15.3% ± 11.9% vs 42.2% ± 28.1%, $P < 0.001$) (Table 3; Fig. 5).

Analysis of correlation coefficient between CTvol and TLC according to disease severity revealed significantly higher values for pTLC and TLC (0.850 vs 0.509, $P = 0.026$) among Group I participants with severe disease. In Group II, the absolute percentage error rates between CTvol and pTLC were significantly lower in patients with mild (14.4% ± 11.9% vs 39.3% ± 26.6%, $P < 0.001$) and moderate (18.7% ± 12.3% vs 52.9% ± 32.5%, $P < 0.001$) disease. There was no patient with severe disease in Group II (Table 4).

Table 1

Demographic data for each disease group.

Characteristics	All	Group I	Group II	Group III
Number of participants	264	110	37	117
Male:female	171:93	86:24	19:18	66:51
Age, y	60.6 ± 14.4	67.9 ± 9.4	57.9 ± 17.4	54.7 ± 14.5
Height, cm	164.6 ± 8.4	165.1 ± 7.6	163.4 ± 8.8	164.6 ± 9.0
Body weight, kg	63.7 ± 11.1	63.5 ± 10.2	60.6 ± 11.1	64.8 ± 11.8
Body mass index, kg/m^2	23.4 ± 3.3	23.3 ± 3.1	22.7 ± 3.6	23.8 ± 3.2
Pulmonary function test	All	Obstructive pattern	Restrictive pattern	Within normal range
FEV1/FVC ratio, %	68.3 ± 15.4	53.6 ± 11.5	82.0 ± 7.3	77.4 ± 6.9
FVC, L	3.32 ± 0.97	3.26 ± 0.88	2.44 ± 0.65	3.66 ± 0.94
FVC, %	91.1 ± 17.7	90.9 ± 16.7	68.4 ± 9.4	98.6 ± 13.8
FEV1, L	2.26 ± 0.85	1.75 ± 0.62	2.02 ± 0.56	2.82 ± 0.76
FEV1, %	82.5 ± 24.2	70.4 ± 20.6	76.7 ± 11.0	102.4 ± 19.0

FEV1 = forced expiratory volume in 1 second, FVC = forced vital capacity.

Table 2

Comparison of pTLC, CTvol, and TLC in Groups I, II, and III.

	N (%)	pTLC	CTvol	TLC	*P*
Volume, L					
All	264 (100)	5.75±0.99*	4.52±1.15*	5.27±1.30	<0.001
Group I	110 (42)	5.92±0.89	4.91±1.14*	5.73±1.25	<0.001
Group II	37 (14)	5.53±1.01*	3.57±0.78	3.98±0.85	<0.001
Group III	117 (44)	5.68±1.06*	4.45±1.05*	5.25±1.18	<0.001

CTvol = computed tomography lung volume, pTLC = predictive total lung capacity, TLC = total lung capacity.
* Statistically significant, adjusted *P* value <0.05 on the post hoc analysis with TLC.

4. Discussion

This study evaluated the feasibility of CTvol as a surrogate marker for donor–recipient size matching in LTx. In patients with severe obstructive pattern lung disease, CTvol showed significantly higher correlation with TLC, compared to pTLC. In patients with restrictive lung disease, the CTvol also showed significantly lower absolute error rates compared to error rates in pTLC.

Lung size matching between donors and recipients in LTx is an anatomical issue[21]; however, until now, pTLC was widely used for lung size matching as a surrogate marker of functional lung volume (TLC) because pTLC is easily calculated using a small number of simple formulas.[7] Then pTLC differences within 25% between a donor and a recipient are considered acceptable.[16,22] However, pTLC has well-known limitations and disadvantages when applied to LTx candidates. First, pTLC differs among races. Second, because underlying lung diseases in LTx candidates may affect thoracic cavity volumes,[2,14,23] it is difficult to estimate lung volumes using formulas developed for use in healthy populations. Third, pTLC is estimation of TLC, whereas size matching is an anatomical comparison between the donor's lung and the recipient's thorax.[21,24]

In contrast, radiologic estimation of lung volume can provide information about both anatomical and functional lung volume. With recent advances in CT technology, volumetric CT data obtained from multidetector row CT can provide accurate lung volume measurements.[11,13,14,25–27]

We postulated that CTvol may be a reliable method for matching donor–recipient lung sizes; because the recipients typically undergo preoperative chest CT during workup for LTx, precise anatomical lung volumes could also be measured at that time. The present study evaluated whether CTvol could be a better method than pTLC for size matching in LTx.

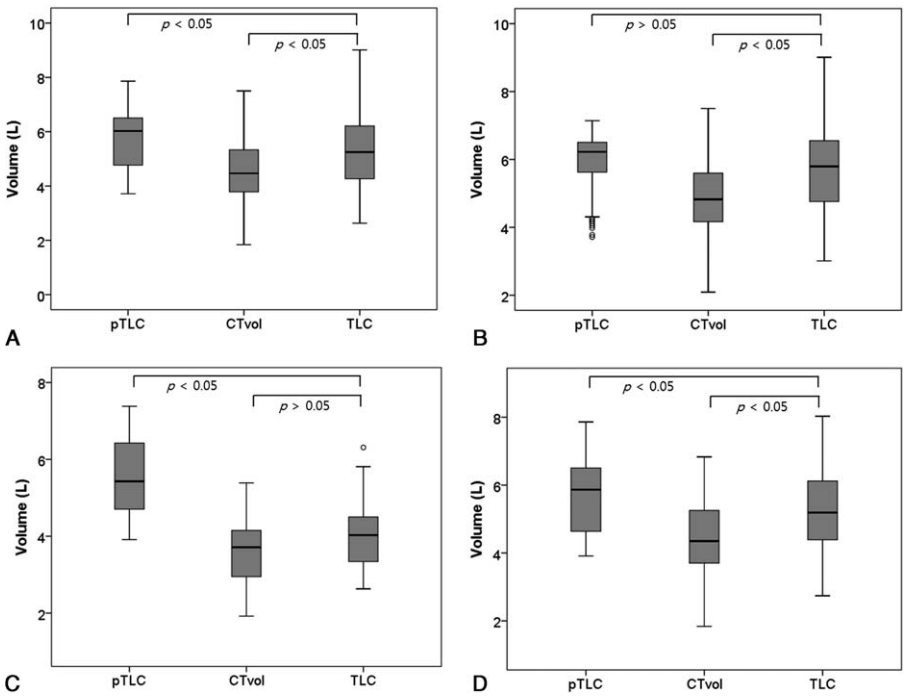

Figure 3. Comparison of lung volume (L) measured by pTLC and CTvol with TLC, in all participants in Groups I, II, and III (A–D). Among all participants (A), pTLC is significantly larger than TLC; CTvol is significantly smaller than TLC (5.75±0.99 and 4.52±1.15 vs 5.27±1.30, $P<0.001$). In Group I (B), pTLC is not statistically different from TLC (5.92±0.89 vs 5.73±1.25) and CTvol is significantly smaller than TLC (4.91±1.14 vs 5.73±1.25, $P<0.001$). In Group II (C), CTvol is not statistically different from TLC (3.57±0.78 vs 3.98±0.85) and pTLC is significantly larger than TLC (5.53±1.01 vs 3.98±0.85, $P<0.001$). In Group III (D), parameters of pTLC, CTvol, and TLC are significantly different from each other (5.68±1.06 vs 4.45±1.05 vs 5.25±1.18, $P<0.001$). CTvol = computed tomography lung volume, pTLC = predictive total lung capacity, TLC = total lung capacity.

Table 3

Comparison of correlation coefficient and absolute error rate with pTLC:TLC and CTvol:TLC among Groups I, II, and III.

PFT pattern	N (%)	pTLC and TLC	CTvol and TLC	*P*
Correlation coefficient (95% confidence interval)				
Group I	110 (42)	0.432 (0.264, 0.571)	0.701 (0.588, 0.783)	0.002
Group II	37 (14)	0.530 (0.242, 0.725)	0.638 (0.388, 0.793)	0.248
Group III	117 (44)	0.759 (0.667, 0.825)	0.774 (0.687, 0.836)	0.392
Absolute percentage error rate				
Group I	110 (42)	16.0±15.8	15.4±12.5	0.701
Group II	37 (14)	42.2±28.1	15.3±11.9	<0.001
Group III	117 (44)	14.3±13.7	16.4±11.8	0.180

CTvol = computed tomography lung volume, PFT = pulmonary function test, pTLC = predictive total lung capacity, TLC = total lung capacity.

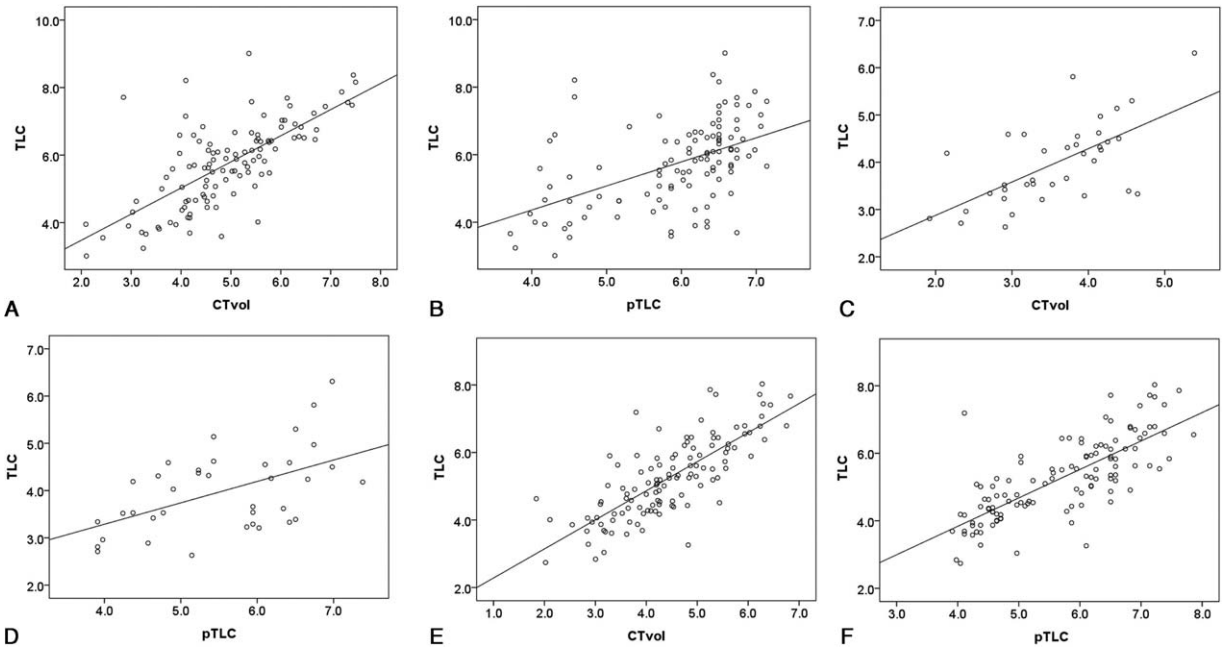

Figure 4. Comparison of correlation with TLC: pTLC versus CTvol. (A, B) In Group I, the correlation coefficient of CTvol is significantly higher than that of pTLC (0.701 vs 0.432, $P=0.002$). (C, D) In Group II, the correlation coefficient of CTvol is not statistically different from that of pTLC (0.638 vs 0.530, $P=0.248$). (E, F) In Group III, the correlation coefficient of CTvol is not statistically different from that of pTLC (0.774 vs 0.759, $P=0.392$). CTvol = computed tomography lung volume, pTLC = predictive total lung capacity, TLC = total lung capacity.

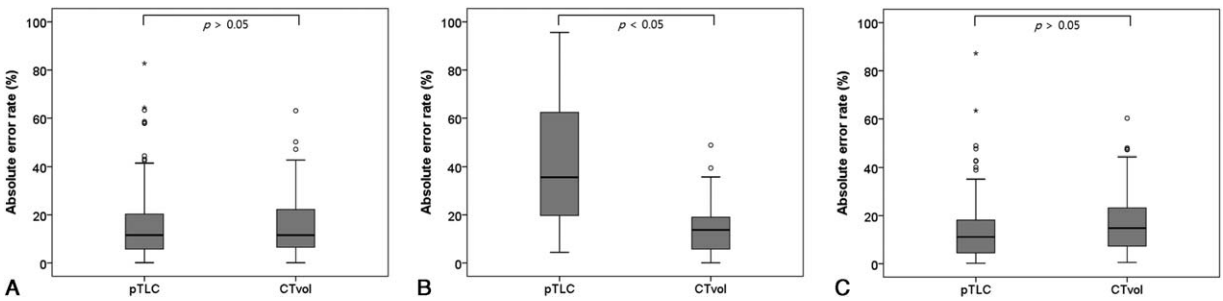

Figure 5. Comparison of absolute error rates of pTLC and CTvol. (A) In Group I, the absolute error rate of CTvol is not statistically different from that of pTLC (15.4% ±12.5% vs 16.0%±15.8%, $P=0.701$). (B) In Group II, the absolute error rate of CTvol is significantly smaller than that of pTLC (15.3%±11.9% vs 42.2%±28.1%, $P<0.001$). (C) In Group III, the absolute error rate of CTvol is not statistically different from that of pTLC (16.4%±11.8% vs 14.3%±13.7%, $P=0.180$). CTvol = computed tomography lung volume, pTLC = predictive total lung capacity.

Table 4

Comparison of correlation coefficient and absolute error rate with pTLC:TLC and CTvol:TLC among Groups I, II, and III, considering disease severity.

Pattern	Severity	N (%)	pTLC and TLC	CTvol and TLC	*P*
Obstructive (Group I)			Correlation coefficient (95% confidence interval)		
	Mild	55 (50)	0.615 (0.413, 0.755)	0.722 (0.560, 0.826)	0.160
	Moderate	37 (34)	0.383 (0.062, 0.626)	0.613 (0.354, 0.779)	0.098
	Severe	18 (16)	0.509 (0.040, 0.783)	0.850 (0.620, 0.940)	0.026
	Absolute percentage error rate				
	Mild	55 (50)	13.3±13.0	15.9±12.4	0.211
	Moderate	37 (34)	21.1±19.6	15.0±13.4	0.086
	Severe	18 (16)	13.7±13.0	14.5±11.5	0.815
Restrictive (Group II)			Correlation coefficient (95% confidence interval)		
	Mild	29 (78)	0.615 (0.311, 0.797)	0.696 (0.433, 0.843)	0.300
	Moderate	8 (22)	0.275 (−0.547, 0.814)	0.244 (−0.569, 0.803)	0.477
	Severe	0 (0)			
	Absolute percentage error rate				
	Mild	29 (78)	39.3±26.6	14.4±11.9	<0.001
	Moderate	8 (22)	52.9±32.5	18.7±12.3	0.035
	Severe	0 (0)			

CTvol = computed tomography lung volume, pTLC = predictive total lung capacity, TLC = total lung capacity.

In this study, pTLC was larger than TLC and CTvol was smaller than TLC overall. This result indicates that pTLC tends to overestimate lung volume, whereas routine CT images were obtained at submaximal inspiration, which were performed in the supine position while the patient followed the audio recording that stated "Inhale and hold your breath."

Obstructive pattern lung disease results in increased lung volume compared to the normal lung volume. Bellemare et al[10] showed significantly increased chest cavity volume in obstructive disease.[10,16] In the present study, the absolute error rate of CTvol was not statistically different from that of pTLC, but the correlation coefficient between CTvol and TLC was significantly higher than that of pTLC among patients with severe obstructive pattern lung disease. This is likely because the increased TLC simply comes close to fixed pTLC, but CTvol reflects the proportional increase of TLC associated with obstructive pattern lung disease in a 1:1 manner.[28] The correlation coefficients between CTvol and TLC were higher among patients with severe obstructive pattern lung disease, who are usually candidate for LTx, than among those with mild disease.

In restrictive lung disease, the chest wall shrinks and results in decreased lung volume.[10] In this study, patients with restrictive disease, the absolute percentage error rate of CTvol was significantly smaller than that of pTLC. This is because the decreased TLC is far from fixed pTLC, more significantly in moderate degree group than in mild degree group. Because most LTx candidates have severe lung disease, the potential for lung volume mismatch is high. However, the results of this study also suggest that CTvol can reflect these changes in patients with restrictive lung disease.

These results indicate that lung diseases affect the actual intrathoracic cavity volume; therefore, performing lung size matching in LTx candidates using equations designed for use in healthy individuals might have limitations, because these equations do not consider the effects of lung disease. However, CTvol can reflect these changes, resulting in consistent correlation coefficients and absolute error rates regardless of disease pattern and disease severity. Our study showed that CTvol can more accurately reflect TLC than pTLC, and can also simultaneously provide anatomical lung volume for all of the disease patterns assessed in this study.

This study has several limitations. First, the current study was a retrospective observational study conducted in a single institution. Two hundred sixty-four patients were enrolled; however, there were a relatively small number of patients with restrictive pattern or severe disease. Second, CT scans were performed using 3 different CT machines. However, CT parameters were all similar including tube voltage, tube current, slice thickness, and reconstruction algorithm. Furthermore, total CTvol was less influenced by various CT parameters, unlike CT emphysema index.[29] Third, CTvol could vary with the degree of inspiration, and patients' breathing during CT was not controlled by spirometric gating.[30] We assumed that majority of patients performed reasonable inspiration as directed by the audio-recorded instructions. Breath-holding education with maximal inspiration during CT scan would likely reduce this variability and differences between TLC and CTvol.

In conclusion, CTvol showed similar or better correlation with TLC compared to the pTLC in normal participants and patients with obstructive or restrictive pattern pulmonary diseases. CTvol showed a smaller error rate in patients with restrictive disease. The results suggest that CTvol may be a feasible method for size matching in LTx.

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