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Abstract

We evaluated the respiratory functions of patients with pulmonary emphysema who underwent lung volume reduction surgery (LVRS) by the mean transit time (MTT) with Xe-133 lung ventilation scintigraphy, forced expiration volume in 1 sec (FEV1.0), residual volume (RV), distance walked in 6 min (6-min walk), and the Hugh-Jones classification (H-J classification) before and after LVRS. In 69 patients with pulmonary emphysema (62 men, 7 women; age range, 47-75 years; mean age, 65.4 years +/- 6.1, preoperative H-J classification, III (two were II)-V) who underwent LVRS, all preoperative and postoperative parameters (MTT 3 weeks after LVRS and the others 3 months after LVRS) were judged statistically by the Wilcoxon signed-ranks test and Odds ratio. Every postoperative parameter was improved with a significant difference ($P < 0.05$) compared to preoperative parameters. MTT at 3 weeks after LVRS was not associated with %FEV1.0 and the H-J classification at 3 months after LVRS, but was associated with RV and a 6-min walk at 3 months after LVRS. MTT was useful for the clinical evalution of aerobic capability after LVRS.

KEYWORDS: lung volume reduction surgery (LVRS), respiratory functions, Xe-133 lung ventilation scintigraphy, pulmonary emphysema

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Original Article

Functional Evaluation of Lung by Xe-133 Lung Ventilation Scintigraphy before and after Lung Volume Reduction Surgery (LVRS) in Patients with Pulmonary Emphysema

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We evaluated the respiratory functions of patients with pulmonary emphysema who underwent lung volume reduction surgery (LVRS) by the mean transit time (MTT) with Xe-133 lung ventilation scintigraphy, forced expiration volume in 1 sec (FEV1.0), residual volume (RV), distance walked in 6 min (6-min walk), and the Hugh-Jones classification (H-J classification) before and after LVRS. In 69 patients with pulmonary emphysema (62 men, 7 women; age range, 47-75 years; mean age, 65.4 years ± 6.1, preoperative H-J classification, III (two were II)-V) who underwent LVRS, all preoperative and postoperative parameters (MTT 3 weeks after LVRS and the others 3 months after LVRS) were judged statistically by the Wilcoxon signed-ranks test and Odds ratio. Every postoperative parameter was improved with a significant difference ($P < 0.05$) compared to preoperative parameters. MTT at 3 weeks after LVRS was not associated with %FEV1.0 and the H-J classification at 3 months after LVRS, but was associated with RV and a 6-min walk at 3 months after LVRS. MTT was useful for the clinical evalution of aerobic capability after LVRS.

Key words: lung volume reduction surgery (LVRS), respiratory functions, Xe-133 lung ventilation scintigraphy, pulmonary emphysema

Although bronchodilators, respiratory rehabilitation, and home oxygen treatment have been provided for patients suffering from pulmonary emphysema, dramatic improvements have not been obtained because pulmonary emphysema is a disease of a chronic advanced nature [1].

In recent years it has been proved that dyspnea is remarkably improved by surgical treatment [1]. Resecting a segment of the most emphysematous part of the lung can improve the motion of the diaphragm. This operation is called lung volume reduction surgery (LVRS). Many years passed between the first surgical treatment for pulmonary emphysema being performed by Brantigan *et al.* [2, 3] in the 1950s and the performance

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of LVRS. Since 1991, Wakabayashi *et al.* [4] have reported laser pneumoplasty of unilateral lung under video-assisted thoracoscopic surgery (VATS), and attention has been attracted again.

Cooper *et al.* [5, 6] have improved the method of Brantigan. Lung volume reduction of both sides by median sternotomy has been reported, and 2 methods are now used together [7, 8].

Although there were have been reports of evaluations before and after LVRS using lung perfusion scintigraphy, visual evaluations have been used, as quantitative evaluation was difficult. We attempted a quantitative evaluation, paying attention to the Mean Transit Time (MTT) in lung ventilation scintigraphy. We measured the MTT of patients who underwent LVRS.

We then considered changes in parameters of the forced expiration volume in 1 sec (FEV1.0), residual volume (RV), the distance walked in 6 min (6-min walk), and the Hugh-Jones classification (H-J classification) before and after LVRS. We assessed the association of MTT after LVRS with the other parameters after LVRS. Finally, we considered why MTT was not improved after LVRS.

Materials and Methods

Patients and Surgical Methods. We retrospectively evaluated the findings for a cohort of 69 of 80 patients who underwent LVRS at our institution (62 men, 7 women; age range, 47-75 years; mean age, 65.4 years ± 6.1, preoperative H-J classification, III (some were II)-V). All of the patients underwent LVRS between August 1994 and March 2002. Eleven patients were excluded from the study due to incomplete scintigraphic study or lack of clinical follow-up data. We explained the nuclear medical examination to the patients in advance and obtained informed consent.

Fifty-nine of these 69 underwent bilateral LVRS, which was performed by means of median sternotomy [7]. Ten underwent unilateral nonsegmental wedge resection by VATS. Of the segments of excised lung, 45 were bilateral upper lobe, 12 bilateral lower lobe, 10 unilateral lung, and 2 something other. It was counted as a bilateral upper lobe excision when a bilateral partial upper lobe resection was performed. We disregarded the weight of the lungs from which we were excised.

Imaging Protocol. We used a triple-headed SPECT unit (GCA9300 A/DI, Toshiba Medical, Shibaura, Japan), carried out bolus inhalation of Xe-133 gas 370 MBq from the maximum expiration status to total lung capacity, carried out repetitive breathing for 3-5 min after the patient held his or her breath for approximately 10 sec within the closed circuit, and acquired a washout image for 5-8 min with room air.

MTT was computed by the height-over-area method from the washout curve (Fig. 1). The merits of this method are its simplicity and the lack of influence of uneven RI accumulation in the lung field, although the influence of the background cannot be eliminated.

All examinations were carried out before and 3 or 4 weeks after surgery.

The mean MTT of 6 Donors (4 male, 2 female) for lung plantation without lung disease, as normal data, was found to be 54.8 ± 8.1 sec (42.6-65.8 sec). The mean age of these donors was 35.0 ± 12.8 years (24-56), and the mean FEV1.0 was 3.29 ± 0.80 L (2.24-4.3 L).

We adopted a clinical cut-off value of 90 sec by MTT.

Clinical parameters. All patients underwent respiratory-function studies in room air so that lung volume could be measured. FEV1.0 (% FEV1.0) was measured based on the volume of expiration that can be expired in 1 sec after the maximum inhalation-of-air state. RV (% RV) was calculated by subtracting the vital capacity from the total lung capacity. The distance walked in 6 min was measured before and after surgery, and almost cases were measured in room air. The H-J

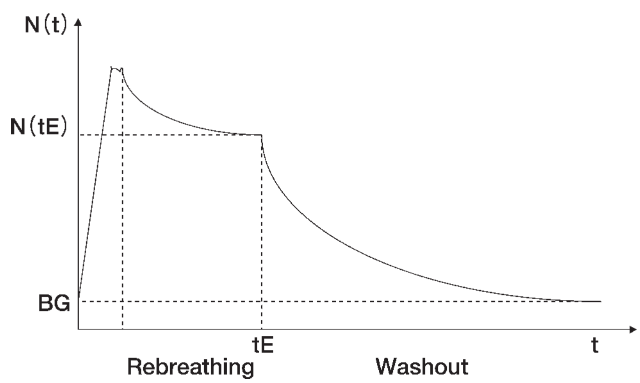


Fig. 1 MTT (sec) is computed by the height-over-area method from the washout curve. (From A New Textbook of Clinical Nuclear Medicine (3rd Edition) (Modified)).

$$T = \frac{\int_{tE}^{5'30''} N(t)dt}{N(tE)}$$

T, Mean transit time (MTT); tE, The start of washout; N (t), The count of an interested resion.

classification was judged clinically for the category in the attached Table 1 [9].

Study Design. We adopted each parameter of MTT, FEV1.0, RV, 6-min walk, and H-J classification before and after LVRS. The value of postoperative MTT was that at 3 weeks after LVRS under hospitalization. We adopted the value 3 months after LVRS for outpatients as the postoperative value of the other parameters because at 3 weeks after surgery, there were some patients with postoperative changes affecting lung function, the 6-min walk, and the H-J classification. However, MTT was measured under static conditions without maximum inspiration and expiration. We adopted a clinical cut-off values of % FEV 1.0, % RV, 6-min walk, and H-J classification of 50%, 200%, 400 m, and III by H-J classification, respectively at 3 months after LVRS. These cut-off levels were determined so as to refer to the threshold value of indication for operation.

Statistical Technique. A statistical analysis was performed using the Wilcoxon signed-ranks test for differences in value before and after surgery for every parameter. We used χ^2 analysis and Odds ratio[s] for the association between MTT and other parameters. A P value of less than 0.05 was considered statistically significant.

Results

Each postoperative parameter was significantly improved ($P < 0.05$) as compared to those before LVRS (Figs. 2A–E). MTT at 3 weeks after LVRS was not associated with %FEV1.0, and the H-J classification (n. s.) 3 months after LVRS. Odds ratios were 1.17 and 1.17, but were associated with %RV and 6-min walk 3 months after LVRS ($P < 0.05$), Odds ratios were 6.83 and 2.93, respectively. (Tables. 2A–D).

Thirty-six of 45 patients who underwent bilateral partial upper lobectomy and 11 of 12 patients who underwent bilateral partial lower lobectomy, and both patients who underwent bilateral partial upper and lower lobectomy were improved. But only 6 of 10 patients who underwent unilateral LVRS were improved (Table 3A).

We examined the group for which MTT did not improve after surgery. There appeared to be 3 reasons why MTT had not improved (Table 3B). The most frequent reason, n = 7, was that the patient could not fully inhale the Xe-133 gas in a closed circuit. The second reason was that the segment MTT prolonged in lung ventilation scintigraphy was not excised (n = 3) (It is thought that the vasculature shrinkage of lungs was maintained in lung perfusion scintigraphy). Another reason is that neither a patient's clinical condition nor the respiratory function parameter improved in a simple way (n = 3).

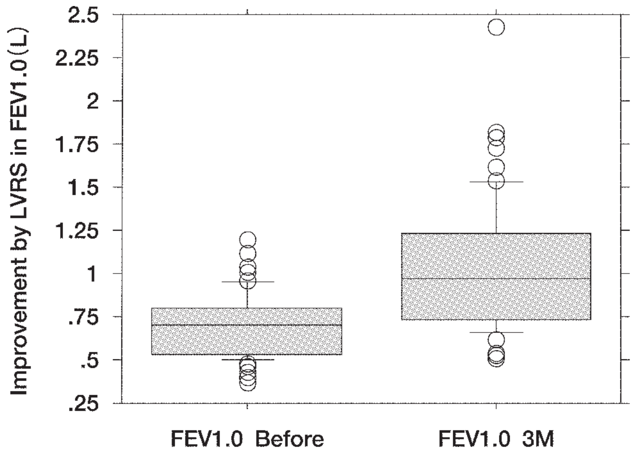
Case Presentation. Case 1 was a 69-year-old male whose H-J classification was III before LVRS. In lung ventilation scintigraphy before surgery, there were prolonged Xe-133 retentions seen in the bilateral apical lung field ventilation scintigraphy before LVRS (Figs. 3A and B). In postoperative lung ventilation scintigraphy, Xe-133 retention in lung ventilation scintigraphy and H-J classification (I) were remarkably improved (Figs. 3C and D). The patient's postoperative MTT (82.5 s→29.4 s) was remarkably improved compared to the preoperative value. His postoperative FEV1.0 (0.85 L→1.83 L), and 6-min walk (410 m→490 m) were remarkably improved compared to preoperative values. His postoperative RV was slightly improved compared to the preoperative value (3.31 L→2.97 L).

Case 2 was a 72-year-old male who had H-J classification IV before LVRS. Prolonged Xe-133 retention was seen at the bilateral lungs in preoperative lung ventilation scintigraphy, and vasculature shrinkage of the right lung was comparatively maintained in lung perfusion scintigraphy (Figs. 4A and B). Partial resection of the left lung was then performed. In the postoperative lung ventilation scintigraphy, however, Xe-133 retention of the patient's lung was not improved. His postoperative degree of H-J classification was III. His postoperative MTT (105.0 s→118.0 s) was not improved compared to that of preoperative lung ventilation scintigraphy (Figs. 4C and D). His postoperative FEV1.0 (0.73 L→0.86 L),

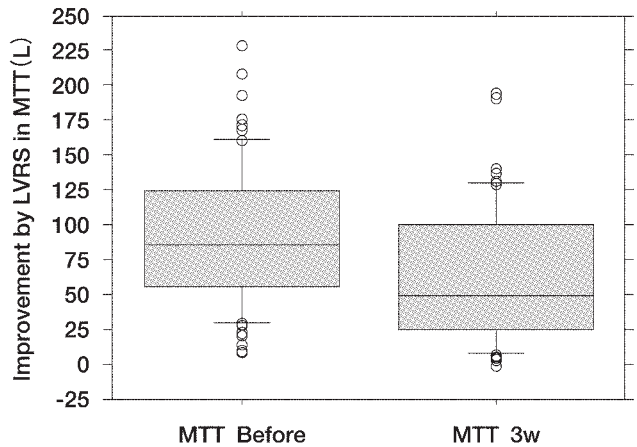
Table I Fletcher-Hugh-Jones classification [9]

I	Is the patient's breathing as good as that of other men of his own age and build at work, when walking,and when climbing hills or stairs?
II	Is the patient able to walk with normal men of his own age and build on the level but is unable to keep up on hills or stairs?
III	Is the patient unable to keep up with normal men on the level, but is able to walk about one mile or more at his own speed?
IV	Is the patient unable to walk more than about 100 yards on the level without a rest?
V	Is the patient breathless when talking or undressing, or unable to leave his house because of breathlessness?

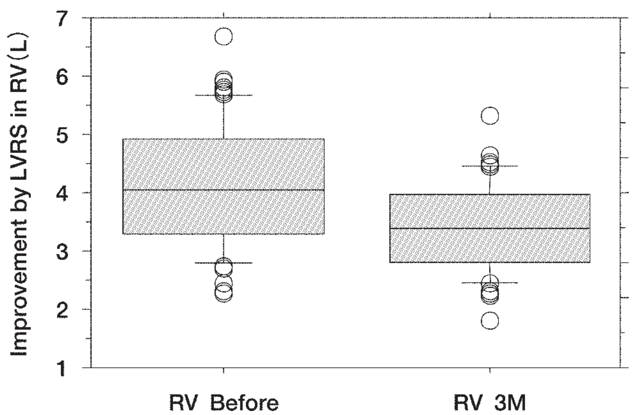
From Proc R Soc Med (1952) 45:577–584 (Modified).



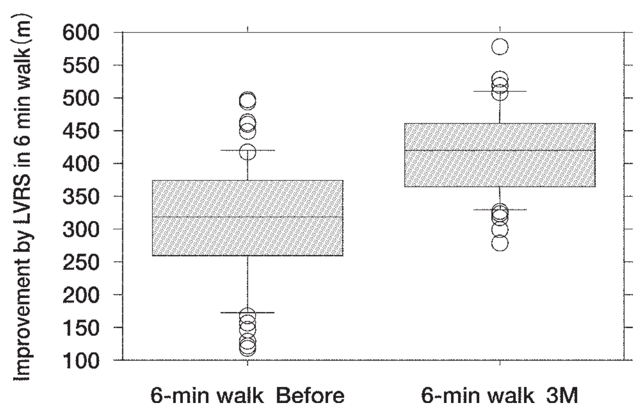
A, Improvement by LVRS in FEV1.0. Wilcoxon signed-ranks test $P < 0.001$ (n = 69).



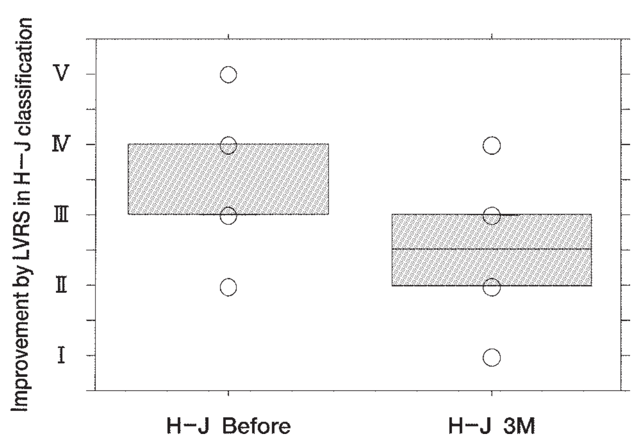
B, Improvement by LVRS in MTT. Wilcoxon signed-ranks test $P < 0.001$ (n = 69).



C, Improvement by LVRS in RV. Wilcoxon signed-ranks test $P < 0.001$ (n = 69).



D, Improvement by LVRS in 6-min walk. Wilcoxon signed-ranks test $P < 0.001$ (n = 65).



E, Improvement by LVRS in H-J classification. Wilcoxon signed-ranks test $P < 0.001$ (n = 65).

Fig. 2 Each postoperative parameter was improved with a significant difference ($P < 0.05$) as compared to those before LVRS (**A**–**E**).

Table 2A Odds ratio for %FEV1.0 associated with MTT

	%FEV1.0 < 50	%FEV1.0 ≧ 50
MTT ≧ 90 (sec)	15	6
MTT < 90 (sec)	30	14

X^2, n.s. Odds ratio = 1.167.
FEV1.0, forced expiratory volume in 1 sec; MTT, mean transit time.

Table 2B Odds ratio for %RV associated with MTT

	%RV ≧ 200	%RV < 200
MTT ≧ 90 (sec)	7	14
MTT < 90 (sec)	3	41

X^2, $P = 0.0056$. Odds ratio = 6.833.
RV, residual volume; MTT, mean transit time.

Table 2C Odds ratio for 6-min walk associated with MTT

	6-min walk < 400	6-min walk ≧ 400
MTT ≧ 90 (sec)	11	10
MTT < 90 (sec)	12	32

X^2, $P = 0.0477$. Odds ratio = 2.933.
6-min walk, walking distance in 6 min; MTT, mean transit time.

Table 2D Odds ratio for Hugh-Jones classification associated with MTT

	H-J = III, IV, V	H-J = I, II
MTT ≧ 90 (sec)	10	9
MTT < 90 (sec)	20	21

X^2, n.s. Odds ratio = 1.167.
H-J, Hugh-Jones classification; MTT, mean transit time.

Table 3A Clinical results of LVRS categolized by excised lungs

	Bilateral partial upper lobectomy n = 45	Bilateral partial lower lobectomy n = 12	Partial excision of unilateral lung n = 10	Unilateral partial upper lobectomy and partial lower lobectomy n = 2
Improved	36	11	6	2
Not-improved	9	1	4	0

Table 3B About the reason which MTT has not improved after LVRS

	Bilateral partial upper lobectomy n = 45	Bilateral partial lower lobectomy n = 12	Partial excision of unilateral lung n = 10	Unilateral partial upper lobectomy and partial lower lobectomy n = 2
Inadequate inhalation	6	0	1	0
Target area is not excised.	2	1	1	0
Clinically no improvement	1	0	2	0

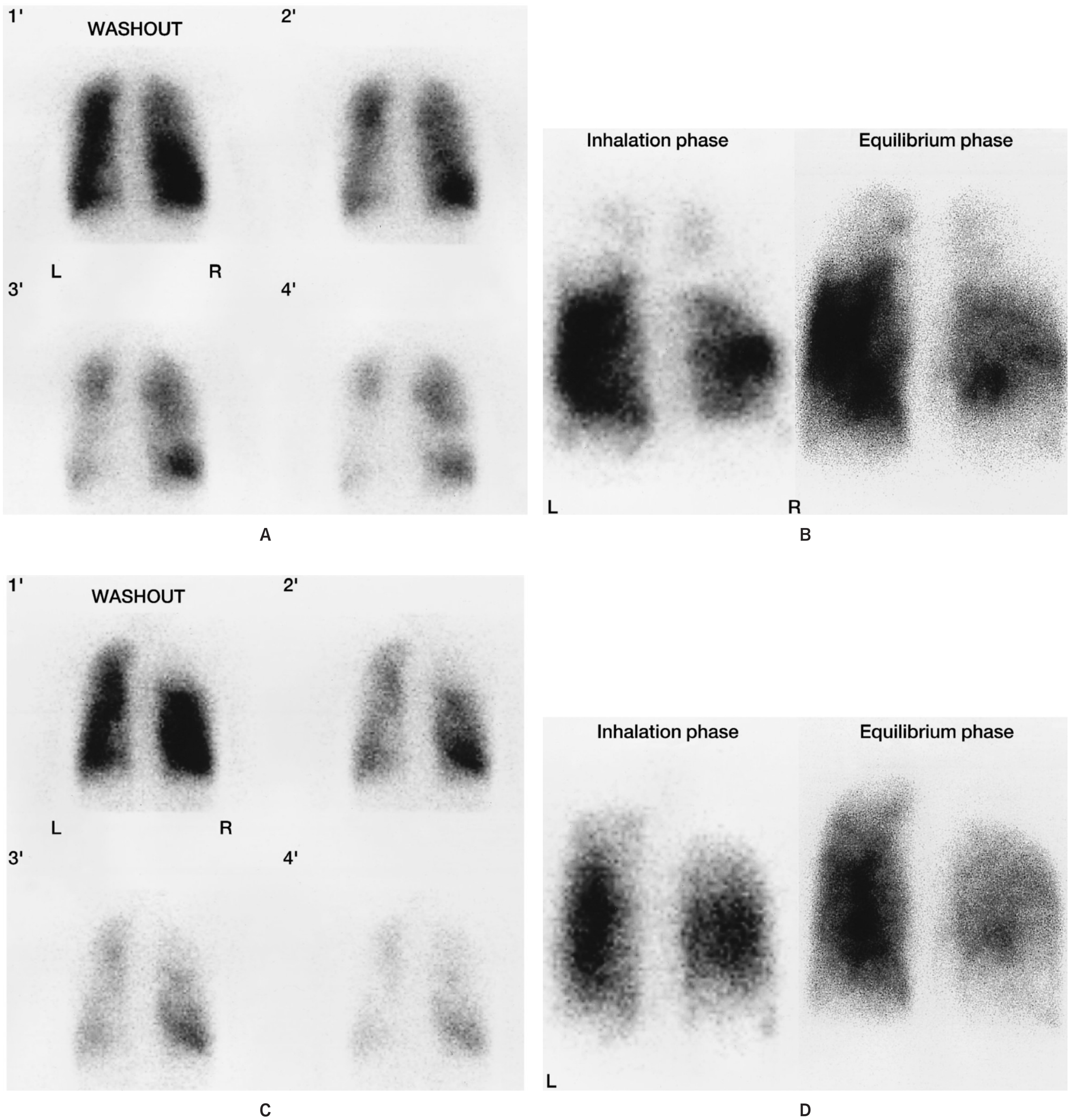


Fig. 3 69-year-old male; both postoperative performance status and MTT in lung ventilation scintigraphy were remarkably improved compared to preoperative measurements. His H-J classification before operation was grade III. Before the LVRS, Xe-133 retention was regarded at the bilateral apex lung (**A**, **B**). Partial excision from the bilateral apex lung was carried out. Xe-133 retention decreased remarkably at lung ventilation scintigraphy after surgery, during which a total of 96 g was resected from his lung, and the H-J classification also improved to grade I (**C**, **D**). His postoperative FEV1.0 and 6-min walk were remarkably improved compared to preoperative values. His postoperative RV was slightly improved compared to the preoperative value.

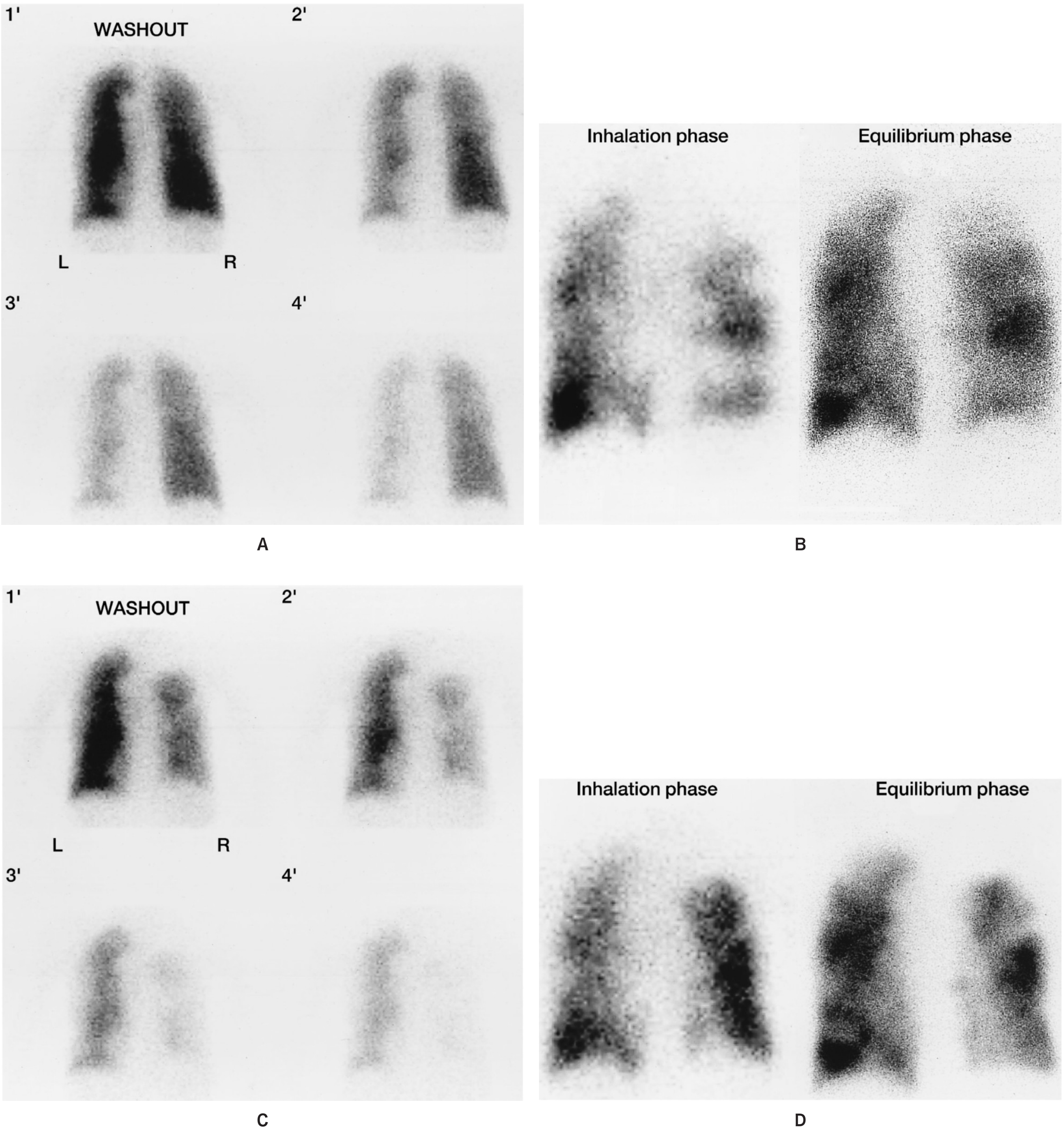


Fig. 4 72-year-old male; both postoperative performance status and MTT in lung ventilation scintigraphy were not improved compared to the preoperative measurements. His H-J classification before operation was grade IV. Before the LVRS, Xe-133 retention was determined at the bilateral lungs. Because vascular shrinkage of his right lung was comparatively maintained in lung perfusion scintigraphy, partial resection of the left lung was performed (**A**, **B**). During the postoperative lung ventilation scintigraphy, however, Xe-133 retention of the patient's lung was not improved. His postoperative degree of H-J classification was grade III. His postoperative MTT was not improved compared to that of preoperative lung ventilation scintigraphy (**C**, **D**). His postoperative FEV1.0 and 6-min walk were slightly improved compared to preoperative values. His postoperative RV was improved compared to the preoperative value.

and 6-min walk (260 m→280 m) were slightly improved compared to preoperative values. His postoperative RV was improved compared to preoperative values (5.02 L→ 3.91 L).

Discussion

There have been many reports of lung perfusion scintigraphy evaluations before and after LVRS [1], but they have been visual and not quantitative. We attempted a quantitative evaluation by MTT in Xe-133 lung ventilation scintigraphy. MTT at 3 weeks after LVRS was associated with %RV and 6-min walk at 3 months after LVRS. MTT was found to be useful for the clinical evaluation of aerobic capability after LVRS. The 6-min walk index has been used as an index of rehabilitation after LVRS at many institutions. For this parameter, reflecting aerobic capability. In contrast, MTT at 3 weeks after LVRS was not associated with %FEV1.0 and H-J classification at 3 months after LVRS. We therefore did not think that MTT, in addition to T1/2 [11], could serve as an index of central respiratory tract resistance. MTT at 3 week after LVRS was significantly improved ($P < 0.05$) compared with preoperative data. We therefore hypothesized that, similar to the results of Nezu, MTT appears to reflect reduced airway resistance due to the recovery of elastic recoil pressure opening terminal bronchioles [10].

Peripheral respiratory tract resistance is increasing in the patient with pulmonary emphysema because normal alveolar elastic tension decreases by destroying alveolar structure, lapsing into hyperinflation. When TLC, FRC, and RV decrease by LVRS, expiratory pressure increases because of diaphragmatic motion openning terminal bronchioles to recovery of elastic recoil pressure, and it reduces the peripheral respiratory tract resistance. These factors lead to an improvement of respiratory function parameters. If ventilation-and-perfusion defects exist in the bilateral apex lung in lung ventilation and perfusion scintigraphy, elastic recoil pressure improvements become stronger and it may become an index of good adaptation [14, 15].

Determination of the target area for excision is most important in LVRS for pulmonary emphysema. MTT measured for every segment of both lungs has a high probability of being useful for pinpointing a segment where prolonged Xe-133 retention is seen (or a segment where Xe-133 is not taken in at all), and a segment that has not contributed to gas exchange, which should be excised. The most frequent reason for no improvement after LVRS (n = 7) was found to be that the patient could not fully inhale Xe-133 gas in a closed circuit. In this group, preoperative and postoperative MTT may not necessarily have reflected clinical improvement. Priority will be given to the results of lung perfusion scintigraphy in this group. Three cases were not improved by LVRS because the segment MTT extended in the lung was not resected. Chest CT has conventionally been used for determining the segments to be excised. However, previous studies correlating chest CT findings with histologic analysis have shown that CT is not always sensitive in patients with an obstructive lung disease [13]. Dynamic Xe-133 SPECT is a useful tool for accurately assessing the extent and location of air trapped in lung lesions without superimposition of lung tissues [12].

There have been many reports of resecting a segment with vasculature shrinkage destroyed from chest CT and lung perfusion scintigraphy [14]. Regarding determination of the segment to be excised, the segment considered not to have contributed to gas exchange for which prolonged Xe-133 retention is noted in lung ventilation scintigraphy is added to the target area at our facility. But when lung vasculature shrinkage is maintained on lung perfusion scintigraphy, the segment is excepted as a candidate for excision.

This study was retrospective, however, and there were deviations in the cases collected. In addition, the examination of every parameter involved a comparison of mid-term prognosis instead of long-term prognosis.

In summary, we examined patients who underwent LVRS using preoperative and postoperative Xe-133 ventilation scintigraphy and a respiratory function test. MTT at 3 weeks after LVRS was found to be associated with RV and 6-min walk at 3 months after LVRS, and was useful for the clinical evaluation of aerobic capability after LVRS.

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