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Decreased 6-minute walk distance after pulmonary resection increases the risk of postoperative hospital re-admission: a retrospective cohort study

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Abstract

Background The purpose of this study was to determine the association between a decline in 6-minute walk distance after pulmonary resection and prognosis, including hospital re-admission and mortality.

Methods This study was a retrospective cohort study, and included 99 patients who underwent pulmonary resection between April 2015 and February 2018 and a 6-minute walk test before and after surgery. The subjects were divided into two groups: those with a ≥30-m decrease in 6-minute walk distance (the decreased group) and those with a < 30-m decrease (the unchanged group). The number of days until hospital re-admission or mortality after discharge was investigated and compared. A Cox proportional hazards model was used to examine the factors affecting hospital re-admission.

Results The unchanged group contained 46 subjects, and the decreased group contained 53 subjects. There was no statistically significant difference in clinicopathologic background between the two groups, except for operating time. There were five hospital re-admissions in the unchanged group and 14 in the decreased group, with a significant increase in the decreased group ($P = 0.04$). There was no significant difference in overall survival between the two groups; however, overall survival tended to be lower in the decreased group ($P = 0.07$). The results of the Cox proportional hazards model identified a decrease in 6-minute walk distance of 30 m as an independent influencing factor affecting hospital re-admission (hazard ratio, 3.05; 95% confidence interval, 1.02–9.15; $P = 0.04$).

Conclusions The results suggest that a reduction of greater than 30 m in 6-minute walk distance before and after pulmonary resection is associated with an increased risk of hospital re-admission.

Keywords 6-minute walk distance, Pulmonary resection, Hospital re-admission

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Background

Due to improved surgical techniques, pulmonary complications after pulmonary resection have decreased. However, the rates of complications, including pneumonia and air leak, remain significant at 3.3% and 11.1%, respectively, and the hospital re-admission rate after pulmonary resection is as high as 8.9% [1]. Moreover, patients who are readmitted to the hospital may experience a worse prognosis [2, 3]. Thus, research has been conducted to identify the clinicopathological factors associated with hospital re-admission. Factors that influence hospital re-admission after pulmonary resection include male gender, weight loss, complicated diabetes, complicated hypertension, and the development of postoperative pulmonary complications [4, 5].

There has also been a recent focus on exercise tolerance. Assessment of exercise tolerance includes the 6-minute walk test (6-MWT), shuttle walk test, and cardiopulmonary exercise test (CPET). Among these, the 6-MWT is frequently performed in clinical settings because it does not require special equipment and can be completed in a relatively short period. Thus, the 6-MWT is often used to assess exercise tolerance before and after pulmonary resection. In patients undergoing pulmonary resection, the 6-minute walk distance (6-MWD) has been reported to decrease from 514 m preoperatively to 469 m postoperatively [6]. In addition, a preoperative 6MWD of 450 m or less has been associated with the development of postoperative pneumonia [7].

Previous studies have shown that in patients who have undergone pulmonary resection, the 6-MWD decreases after surgery and the preoperative 6-MWD is associated with postoperative complications [6, 7]. However, it is unclear whether a decrease in 6-MWD after pulmonary resection affects prognosis, such as hospital re-admission or mortality. Thus, to predict the prognosis of patients undergoing pulmonary resection, clarifying this relationship would be useful and would provide critically meaningful information for perioperative physical therapy. Therefore, the purpose of this study was to determine the association between a decline in 6-MWD after pulmonary resection and prognosis, including hospital re-admission and mortality.

Methods

Patients and study setting

This study was a retrospective cohort study. We enrolled patients who underwent pulmonary resection at Matsue Red Cross Hospital (Matsue, Japan) from April 2015 to February 2018 and who underwent a 6-MWT before and after surgery. The exclusion criteria were preoperative gait disturbance, discontinuation of physical therapy due to postoperative complications, circulatory instability, and nonconsent. We included 170 patients, of whom 71 were excluded and 99 were included in the analysis (Fig. 1). The unchanged group was defined as patients with a difference of 30 m between the preoperative and postoperative 6-MWD. Conversely, the decreased group was defined as patients with a difference of 30 m. We used 30 m as the cutoff because the minimum clinically important difference (MCID) in 6-MWD is 30 m in chronic obstructive pulmonary disease (COPD) [8]. The MCID is not clear in lung cancer but is estimated to be between 22 m and 32 m [9]. All patients received mobilization, respiratory muscle training, and resistance training from a physical therapist during the perioperative period. The preoperative 6-MWT was performed within 2 days before surgery and the postoperative 6-MWT was performed at a mean of 6.2 ± 3.2 days after surgery.

This study was approved by the Ethics Committee of Matsue Red Cross Hospital (approval No. 569, July 2023). In accordance with the decision of the Ethics Committee, we published information about the study and ensured that patients had the opportunity to opt out of participation.

Patient characteristics

We retrospectively collected information about the patients from the electronic medical records. Data included performance status (PS), non–small-cell lung cancer (NSCLC) staging, percentage of predicted vital capacity (%VC), forced expiratory volume in 1 s (FEV1%), left ventricular ejection fraction (LVEF), blood test results (e.g., hemoglobin, blood urea nitrogen, and creatinine), operation procedure, operating time, and anesthesia time.

6-MWT

We performed the 6-MWT before and after surgery to determine the patient's exercise tolerance. The 6-MWT was performed indoors along a flat, straight, 30-m walking course according to the American Thoracic Society guidelines [10]. Participants were provided with standardized instructions and encouragement during the test. Participants were monitored throughout the test with portable pulse oximetry. Patients were allowed to stop and rest during the test but were instructed to resume walking as soon as they felt able to do so.

Data collection on hospital re-admissions and mortality

We collected data on hospital re-admission and mortality as information on prognosis, and we calculated the duration from surgery to hospital re-admission or mortality from the data. We defined hospital re-admission as an emergency hospitalization, excluding hospitalizations scheduled for chemotherapy or other reasons. We included mortality for deaths from all causes. In addition, patients whose progress was unknown during the

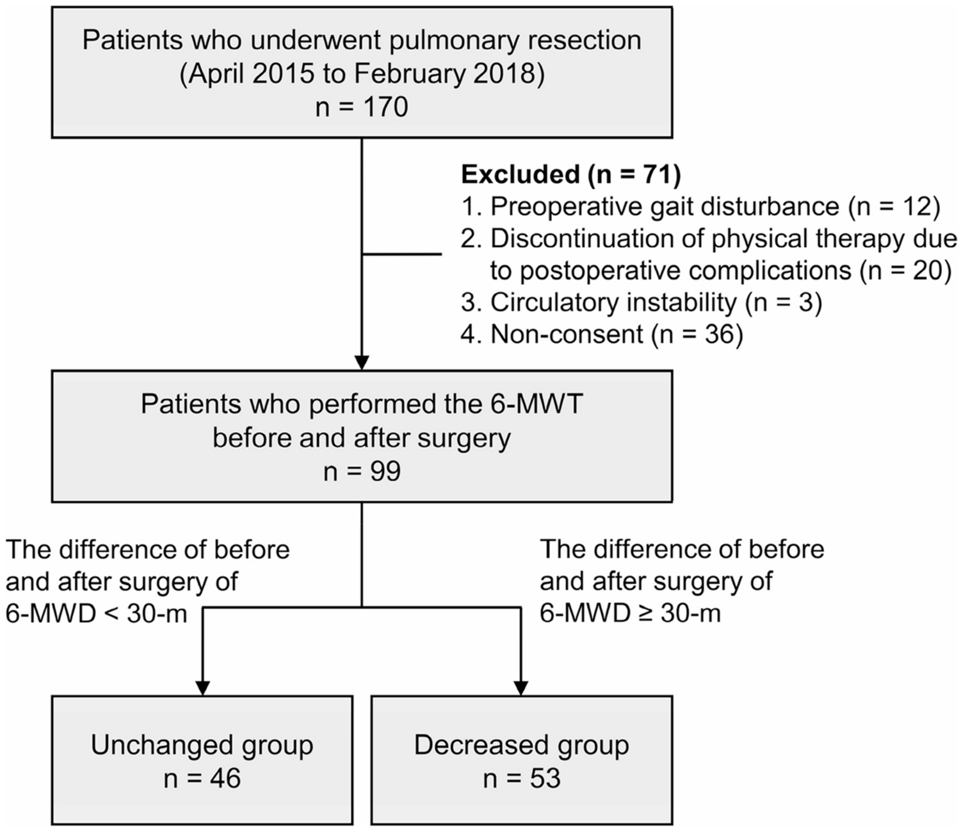

Fig. 1 Patient flow diagram

follow-up were considered as dropout cases, and we counted the number of days until the last day of data collection in the dropout cases. The follow-up period was 1 year from surgery for hospital re-admission and 5 years from surgery for death. We collected all data in November 2023.

Statistical analysis

We used *t*-test and chi-square test to compare the background factors between the unchanged and decreased groups. We used the log-rank test to compare prognosis, and we performed the Cox proportional hazards regression analysis to identify the factors affecting prognosis. The independent variables were age, gender, NSCLC staging, ventilatory impairment, operating time, and a decrease of at least 30 m in 6-MWD. We selected age, gender, and NSCLC staging because they might influence prognosis [11]. In addition, we chose ventilatory impairment because it may increase the risk of postoperative complications [7] and affect hospital re-admission [2, 3]. Operating time was added as an adjustment factor. Cox proportional hazards regression analysis was conducted using two models. Model 1 assessed time to all-cause hospital re-admission, while Model 2 focused on time to hospital re-admission specifically due to cardiopulmonary complications.

We performed all statistical analyses using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of the R commander designed to add statistical functions frequently used in biostatistics [12]. We used $P < 0.05$ as the level of significance.

Results

Patient characteristics

There were no significant differences between the two groups in age, gender, BMI, PS, NSCLC staging, pulmonary function, LVEF, or blood data. There was also no significant difference between the two groups in the percentage of procedures performed. However, the percentage of thoracotomy was higher in the decreased group than in the unchanged group. The operating time was significantly prolonged in the decreased group (Table 1). Fourteen patients underwent surgery for stage IV or metastatic lung cancer. The reasons for surgery were as follows: six cases underwent surgery to resect lung metastases, seven cases underwent surgery for diagnostic purposes (biopsy), and one case underwent surgery for thymoma resection combined with diagnostic purposes (biopsy).

Table 1 Patient characteristics in the unchanged and decreased groups

Variable	Total		Unchanged group		Decreased group		*P* Value
	(*N* = 99)		46.6	(46)	53.3	(53)	
Age, mean (SD), y	70.2	(8.1)	68.9	(8.7)	71.3	(7.3)	0.152
Gender							
Male	68.7	(68)	73.9	(34)	64.2	(34)	0.386
Female	31.3	(31)	26.1	(12)	35.8	(19)	
BMI, mean (SD), kg/m^2	23.3	(2.8)	23.5	(3.1)	23.2	(2.6)	0.541
PS							
0	83.8	(83)	82.6	(38)	84.9	(45)	0.890
1	14.2	(14)	15.2	(7)	13.2	(7)	
2	2	(2)	2	(1)	2	(1)	
NSCLC staging							
0	6.1	(6)	6.5	(3)	5.7	(3)	0.800
IA	39.4	(39)	41.3	(19)	37.7	(20)	
IB	18.2	(18)	15.2	(7)	20.8	(11)	
IIA	7.1	(7)	8.7	(4)	5.7	(3)	
IIB	5.1	(5)	4.3	(2)	5.7	(3)	
IIIA	6.1	(6)	2.2	(1)	9.4	(5)	
IV	3	(3)	2.2	(1)	3.8	(2)	
Metastatic	11.1	(11)	13	(6)	9.4	(5)	
Unknown	4	(4)	6.5	(3)	1.9	(1)	
%VC, mean (SD), %	99.4	(14.5)	99.6	(14.6)	99.1	(14.7)	0.863
FEV_1%, mean (SD), %	73.1	(9.4)	71.9	(9.3)	74	(9.5)	0.276
LVEF, mean (SD), %	64.5	(5.7)	65.1	(5.9)	64	(5.6)	0.381
Hgb, mean (SD), g/dl	13.7	(2.5)	13.9	(3.3)	13.5	(1.4)	0.471
BUN, mean (SD), mg/dl	15.5	(4.9)	15.2	(4.6)	15.8	(5.1)	0.510
Cr, mean (SD), mg/dl	0.8	(0.3)	0.8	(0.2)	0.8	(0.3)	0.553
Procedure							
VATS	80.8	(80)	87	(40)	75.5	(40)	0.202
Thoracotomy	19.2	(19)	13	(6)	24.5	(13)	
Resection range							
Segmentectomy	38.4	(38)	39.1	(18)	37.7	(20)	0.064
Lobectomy	60.6	(60)	60.9	(28)	60.3	(32)	
Pneumonectomy	1	(1)	0	(0)	2	(1)	
Operating time, mean (SD), m	276.5	(109.1)	245.4	(96.9)	303.4	(112.7)	< 0.001
Postoperative pulmonary complications							
Yes	19.2	(19)	19.6	(9)	18.9	(10)	> 0.99
No	80.8	(80)	80.4	(37)	81.1	(43)	

Data are presented as % (*n*) unless indicated otherwise. *BMI* body mass index, *BUN* blood urea nitrogen, *Cr* creatinine, *FEV* forced expiratory volume, *Hgb* hemoglobin, *LVEF* left ventricular ejection fraction, *NSCLC* non–small-cell lung cancer, *PS* performance status, *SD* standard deviation, *VATS* video-assisted thoracic surgery, *VC* vital capacity

6-MWD

The preoperative 6-MWD was 443.7 ± 98.7 m in the unchanged group and 467.7 ± 80.4 m in the decreased group, with no significant difference ($P = 0.19$). The postoperative 6-MWD was 447.6 ± 101.8 m in the unchanged group and 370.0 ± 107.9 m in the decreased group. The decreased group had a significantly shorter 6-MWD ($P < 0.01$). The mean time to the first walking practice after surgery was similar for both groups, at 1.2 ± 0.6 days after surgery. In addition, the number of days to perform 6-MWT after surgery was similar in both groups, at 6.2 ± 3.2 days after surgery.

Cumulative incidence of hospital re-admission

The mean follow-up period was 311.3 ± 107.7 days. There were five hospital re-admissions in the unchanged group and 14 in the decreased group, with a significant increase observed in the decreased group ($P = 0.04$) (Fig. 2). Pneumonia was the most common cause of hospital re-admission, with one case in the unchanged group and four cases in the decreased group. There were 10 cases of hospital re-admission because of cardiopulmonary complications (Table 2).

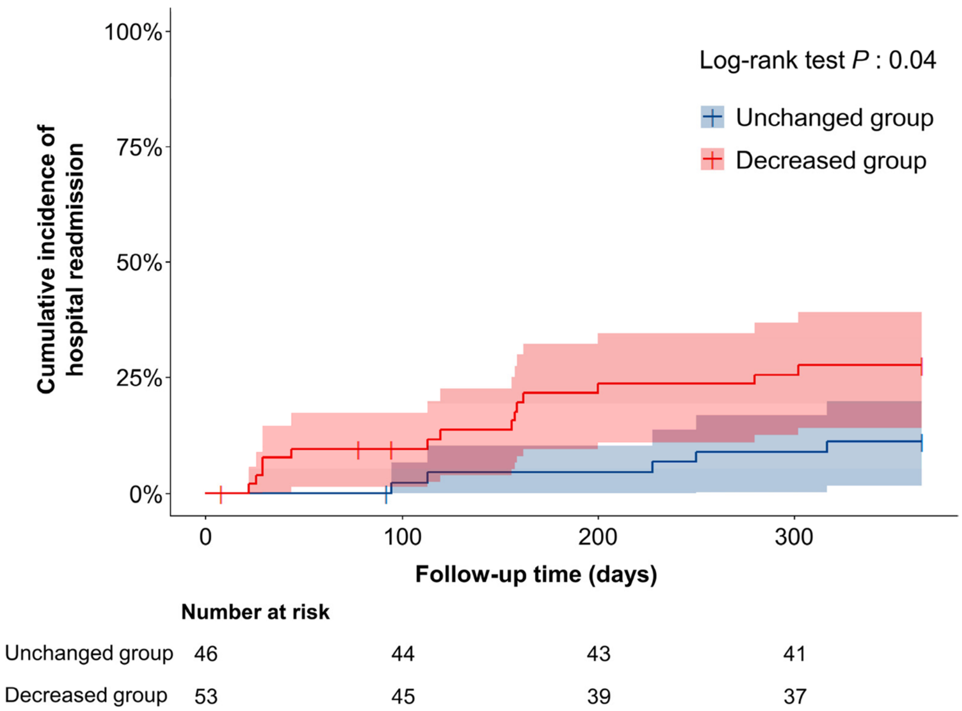

Fig. 2 Cumulative incidence of hospital re-admission. There were five hospital re-admissions in the unchanged group and 14 in the decreased group, with a significant increase in the decreased group ($P=0.04$)

Table 2 Causes of hospital re-admission

Cause	Total ($n=19$)	Unchanged group ($n=5$)	Decreased group ($n=14$)
Cardiopulmonary complications			
Pneumonia	5	1	4
Pleural fluid	2	0	2
Pyothorax	1	0	1
Interstitial pneumonia	1	1	0
Aortic dissection	1	0	1
Others			
Lung metastasis	1	1	0
Acid fast infection	1	0	1
Pyelonephritis	1	0	1
Shingles	1	0	1
Skull tumor	1	0	1
Nausea	1	0	1
Metastatic brain tumor	1	1	0
Wound abnormality	1	1	0
Subarachnoid hemorrhage	1	0	1

Data are presented as number

Overall survival

The mean follow-up period was 1,555.5 ± 498.0 days. Overall survival was not significantly different between the two groups; however, it tended to be lower in the decreased group ($P=0.07$) (Fig. 3). A total of 18 patients died, five in the unchanged group and 13 in the decreased group. The 5-year survival rates were 87.6% in the unchanged group and 70.9% in the decreased group.

Cox proportional hazards regression

The results of the Cox proportional hazards regression with hospital re-admission as the dependent variable revealed a decrease in 6-MWD of 30 m as an independent predictor of hospital re-admission, even after adjusting for several variables (Model 1, hazard ratio [HR]: 3.05, 95% confidence interval [CI]: 1.02–9.15, $P=0.04$, Model 2, HR: 5.39, 95% CI: 1.05–27.64, $P=0.04$) (Table 3).

Discussion

We found that a decrease in the 6-MWD of more than 30 m following pulmonary resection, as compared with preoperative levels, is an independent predictor of increased postoperative hospital re-admission. To the best of our knowledge, this is the first study to demonstrate an association between changes in 6-MWD before and after pulmonary resection and hospital re-admission.

We discuss the reasons for using 6-MWT as a measure of physical function in this study. Several studies have examined the relationship between physical function and prognosis. In particular, maximal oxygen uptake has been shown to be associated with mortality and is considered a strong independent predictor of prognosis [13–15]. However, the measurement of maximal oxygen uptake requires CPET, which requires involves equipment and is time-consuming. As a result, many institutions have

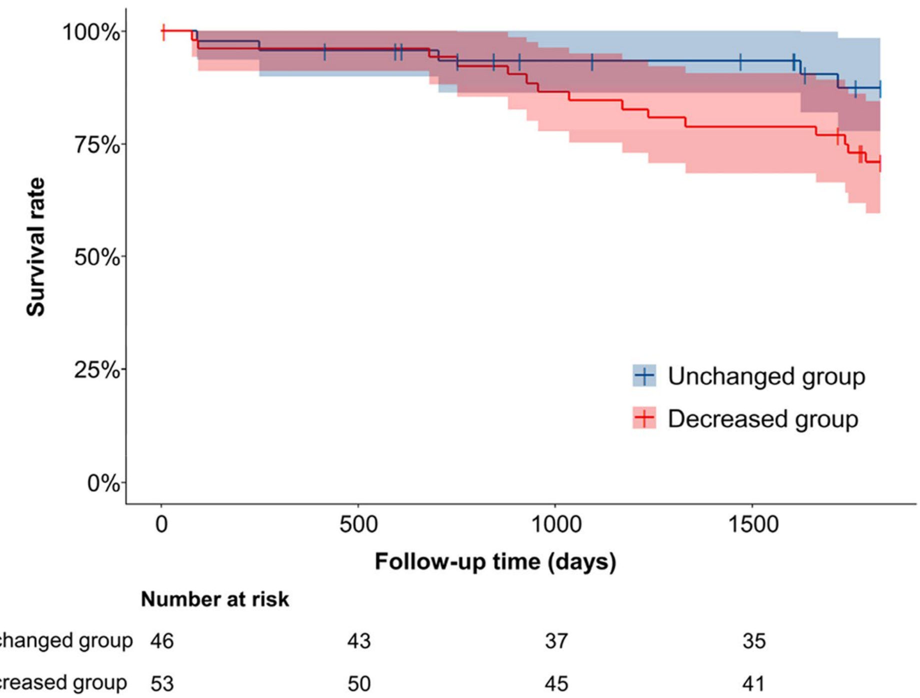

Fig. 3 Kaplan–Meier curves for overall survival. Overall survival was not significantly different between the two groups but tended to be lower in the decreased group ($P=0.07$)

Table 3 Cox proportional hazards regression analysis of hospital re-admission

	Model 1 (All-cause hospital re-admission)		**Model 2 (Hospital re-admission because of cardiopulmonary complications)**	
Characteristic	Hazard ratio (95% CI)	*P* Value	Hazard ratio (95% CI)	*P* Value
Age	0.99 (0.92–1.06)	0.81	1.00 (0.91–1.10)	0.14
Female (vs. male)	2.97 (0.81–10.78)	0.10	5.24 (0.62–43.91)	0.80
NSCLC staging III, IV, metastatic (vs. I, II)	1.82 (0.68–4.91)	0.26	1.40 (0.35–5.64)	0.76
Ventilatory impairment (vs. none)	1.12 (0.42–2.91)	0.82	1.43 (0.37–5.49)	0.25
Operating time	1.00 (0.99–1.01)	0.91	1.00 (0.99–1.00)	0.30
Decrease in 6-MWD ≥ 30 m (vs. < 30 m)	3.05 (1.02–9.15)	0.04	5.39 (1.05–27.64)	0.04

6-MWD 6-minute walk distance, *CI* confidence interval, *NSCLC* non–small-cell lung cancer

difficulty performing the test. In addition, because CPET requires maximal exercise, it is often not possible to perform the test on patients in the early postoperative period. Alternatively, the 6-MWT can be performed in a short time without the need for special equipment and can estimate maximal oxygen uptake [16]. We considered 6-MWT to be an alternative to CPET. Thus, we selected 6-MWT for this study. The 6-MWT was performed 6.2 ± 3.2 days after pulmonary resection. A previous study also performed the 6-MWT at 7 days postoperatively [6], which was considered an appropriate timing.

The 6-MWD has been studied in relation to the clinicopathological background and prognosis in several diseases. As reported by Hattori et al. [7], preoperative shortening of the 6-MWD is associated with the development of postoperative pneumonia. Marjanski et al. also found that a preoperative 6-MWD of 525 m before pulmonary resection was an independent factor in the prediction of postoperative survival [17]. In addition, Amir et al. and Durheim et al. reported that in patients with heart failure and COPD, 6-MWD is an important predictor of hospital re-admission and mortality [18, 19]. However, these reports measured 6-MWD at only a single time point. Although patients undergoing pulmonary resection often have good preoperative 6-MWD, some patients experience a significant decrease in 6-MWD postoperatively, and the change cannot be determined by measuring one time point alone. Thus, focusing on the amount of change in 6-MWD before and after surgery is necessary for predicting the prognosis and hospital re-admission of such patients. In this study, we investigated the association between the change in 6-MWD before and after pulmonary resection and hospital re-admission and found that a decrease in 6-MWD was associated with an increase in hospital re-admission. Even after performing multivariate adjustment, we identified a decrease in 6-MWD as a factor significantly influencing hospital re-admission, which suggests that a decrease in 6-MWD before and after pulmonary resection is an independent factor that influences hospital re-admission. The operating time was longer in the decreased group than in the unchanged group. This was thought to be because of the higher proportion of thoracotomy procedures in the decreased group. Considering the possibility that the longer operating time might affect re-admission, the operating time was included as an adjustment variable in the multivariate analysis.

Focusing on the amount of change in 6-MWD has high clinical applicability; many studies have examined the association between the amount of change in 6-MWD and various factors. For example, Granger et al. administered the 6-MWT in patients with lung cancer undergoing chemotherapy before and 10 weeks after the start of treatment and examined its association with function, physical activity, and symptoms [9]. They estimated that the MCID in the 6-MWD reduction was between 22 m and 42 m. Polkey et al. also examined the association between the change in 6-MWD and mortality in patients with COPD over a 1-year period and found that a decrease in 6MWD of 30 m was associated with an increased risk of mortality in COPD patients [8]. Thus, attempts have been made to calculate the MCID of 6-MWD changes in various diseases. However, no association between 6-MWD change and re-admission or mortality has been examined before or after lung resection, and the MCID has not yet been established. We used 30 m as the criterion in this study to sort the invariant and decreased groups, based on the reports of Granger et al. and Polkey et al. [8, 9]. Inferences from the results suggest that this criterion had some validity. Although a more accurate determination of the MCID will be required in the future, our results suggest that it is possible to estimate the risk of postoperative hospital re-admission by focusing on the amount of change in 6-MWD before and after lung resection.

Previous studies have reported an association between 6-MWD and mortality [17]. In this study, although we noted a trend for an association between a decrease in 6-MWD and mortality, this was not significant. We speculated that the low incidence of mortality events was the reason for the lack of a significant association. There were two reasons for the lack of mortality: first, the sample size was small, and second, most patients in this study were in the early stages of lung cancer. However, there was a trend toward increased mortality in the group with a decreased 6-MWD, and it is possible that a decrease in 6-MWD after pneumonectomy leads to increased mortality. We expect future studies to overcome these limitations. This study is a retrospective study involving only 99 cases, and the reliability of the results is limited. Therefore, larger cohort studies or prospective studies are needed.

Preventing a decrease in 6-MWD before and after pulmonary resection could lead to improved prognosis. Future interventional studies should be conducted to examine rehabilitation programs that can prevent a decrease in 6-MWD. In addition, determining the MCID of the change in 6-MWD before and after pulmonary resection could assist in setting clear goals during rehabilitation.

Conclusions

The results of this study suggest that a decrease of greater than 30 m in 6-MWD before and after pulmonary resection is associated with an increased risk of hospital re-admission.

Abbreviations

%VC	Percentage of predicted vital capacity
6-MWD	6-minute walk distance
6-MWT	6-minute walk test
CI	Confidence Interval
CPET	Cardiopulmonary exercise test
COPD	Chronic obstructive pulmonary disease
FEV1%	Forced expiratory volume in 1 second
HR	Hazard ratio
LVEF	Left ventricular ejection fraction
MCID	Minimum clinically important difference
NSCLC	Non–small-cell lung cancer
PS	Performance status

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Authors' contributions

H.M. wrote the main manuscript text and prepared Figs. 1, 2 and 3. All authors reviewd the manuscript.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Matsue Red Cross Hospital (approval No. 569, July 2023). In accordance with the decision of the Ethics Committee, an opt-out consent procedure was used due to the retrospective nature of the study. All procedures were performed in accordance with the ethical standards of the responsible committees for clinical study (institutional and national) and the Helsinki Declaration of 1964 and its later versions.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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