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## PHYSIOLOGY & REHABILITATION | RESEARCH ARTICLE

# Preoperative evaluation of six-minute walk test in patients with malignant pleural mesothelioma

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**Abstract:** *Objective:* Surgical treatment of malignant pleural mesothelioma (MPM) is accompanied by high morbidity and mortality. The aim of this retrospective study was to characterize preoperative physical fitness and relate it to pulmonary functions, oxygenation, and postoperative outcomes in patients with MPM who underwent surgical resection with perioperative rehabilitation. *Methods:* A total of 18 patients were retrospectively reviewed. Preoperative exercise capacity was evaluated by the 6-min walk test (6MWT). Oxygen saturation of a peripheral artery (SpO<sub>2</sub>) was measured during the 6MWT. *Results:* The 6-min walk distance was significantly correlated with inspiratory capacity and % of predicted diffusing capacity of the lung for carbon monoxide. The minimum SpO<sub>2</sub> during the 6MWT correlated with % of predicted vital capacity and total lung capacity and postoperative days of extubation. There were a total of 14 major complications in six patients. The incidence of major complications was associated with longer stays in intensive care unit and hospital but not with preoperative physical status or pulmonary functions. *Conclusion:* Our results indicate that the 6MWT is useful to assess preoperative physical status in patients with resectable MPM.

**Subjects:** Physiology; Pulmonary Medicine; Thoracic Surgery

**Keywords:** malignant pleural mesothelioma; rehabilitation; 6-min walk distance; 6-min walk test; surgery; desaturation

### ABOUT THE AUTHORS

Motoki Nagaya, is the chief physical therapist of the Pulmonary Rehabilitation Team at the Department of Rehabilitation, Nagoya University Hospital in Japan. His work is focused on perioperative rehabilitation and appropriate management of patient with thoracic and abdominal cancers who underwent surgical resection. The corresponding author, Dr Satoru Ito, MD, PhD, is associate professor at Respiratory Medicine and Allergology, Aichi Medical University in Japan. His research themes are pulmonary rehabilitation, respiratory physiology, airway diseases specifically asthma and COPD, and basic science such as mechanobiology. The current article is one of our research works investigating relations between preoperative physical fitness and postoperative outcomes in patients with thoracic malignant diseases who underwent invasive surgery.

### PUBLIC INTEREST STATEMENT

Malignant pleural mesothelioma is an aggressive and fatal disease associated with asbestos exposure. Surgery for malignant pleural mesothelioma is an invasive procedure associated with high morbidity and mortality rates. Therefore, perioperative rehabilitation has been expected to promote early mobilization and reduce postoperative complications in patients who undergo thoracic surgery. To provide proper perioperative care, we have evaluated preoperative pulmonary functions and physical fitness of patients with malignant pleural mesothelioma as our perioperative rehabilitation program. The six-minute walk test is a simple, safe, and inexpensive field test that can be used to evaluate the functional exercise capacity of patients. Results of our article suggest that the six-minute walk test is useful to assess preoperative physical status in patients with resectable malignant pleural mesothelioma.

## 1. Introduction

Malignant pleural mesothelioma (MPM) is a rare, aggressive, and fatal disease commonly associated with asbestos exposure (Hasegawa, 2014; Robinson, Musk, & Lake, 2005). In Japan, the incidence of MPM is expected to peak between 2015 and 2020 due to previous heavy use of asbestos (Murayama, Takahashi, Natori, & Kurumatani, 2006). MPM often invades adjacent structures such as the chest wall, diaphragm, and mediastinum (Schipper et al., 2008). Thus, pulmonary functions and levels of physical fitness are reduced in patients with advanced MPM (Jones, Eves, Haykowsky, Freedland, & Mackey, 2009; Nowak, Stockler, & Byrne, 2004). Multimodal therapy including chemotherapy, radiotherapy, and surgery has been proposed as the treatment strategy (Hoda et al., 2016). There are two types of surgical treatment for MPM; extrapleural pneumonectomy (EPP) and pleurectomy/decortication (P/D). However, the rates of major postoperative complications after EPP and P/D remain high due to their invasiveness, the impaired physical status of patients, and the aggressiveness of the surgical treatment (de Perrot et al., 2008; Hasegawa, 2014; Rena & Casadio, 2012; Zellos, Jaklitsch, Al-Mourgi, & Sugarbaker, 2007).

The 6-min walk distance (6MWD) measured by the 6-min walk test (6MWT) is a simple, safe, and inexpensive field test that can be used to evaluate the functional exercise capacity of patients who undergo thoracic surgery (ATS, 2002; Butland, Pang, Gross, Woodcock, & Geddes, 1982; Ha, Mazzone, Ries, Malhotra, & Fuster, 2016; Hattori et al., 2017; Hayashi, Fukumoto et al., 2017; Holden, Rice, Stelmach, & Meeker, 1992; Inoue et al., 2016; Marjanski et al., 2015; Pierce, Copland, Sharpe, & Barter, 1994). Previous studies have explored the changes in 6MWD after surgical treatment for MPM (Ambrogi, Baldi, Schillaci, & Mineo, 2012; Tanaka et al., 2017). However, the relationships between the preoperative 6MWD and pulmonary functions or postoperative outcomes in patients with resectable MPM are still unknown.

The purpose of the present study was to characterize the preoperative exercise capacity and physical fitness and to relate them to clinical variables, oxygenation, pulmonary function parameters, and postoperative outcomes in patients who underwent surgical treatment for MPM with perioperative rehabilitation. To estimate exercise capacity, we conducted the 6MWT and measured 6MWD and oxygen saturation of a peripheral artery (SpO<sub>2</sub>) during the test.

## 2. Methods

### 2.1. Patients and design

Records of 26 consecutive patients who underwent scheduled surgery for MPM, either EPP or P/D, at the Department of Thoracic Surgery, Nagoya University Hospital, from July 2012 to April 2016 were retrospectively reviewed. All patients were provided similar perioperative in-hospital rehabilitation, which included mobilization, ambulation, breathing exercise, and muscle strengthening exercises, by specialized physical therapists according to the institutional protocol as daily practice (Inoue et al., 2016; Mizuno et al., 2016). In addition, physical status was routinely assessed before the surgery by the preoperative rehabilitation program (Hayashi, Fukumoto et al., 2017; Inoue et al., 2016; Mizuno et al., 2016). Of the 26 patients, 18 patients who performed the perioperative rehabilitation and whose preoperative pulmonary function and 6MWD were assessed were enrolled in this study. The study was approved by the Institutional Review Board of Nagoya University Hospital (approval No. 2015-0413). The requirement for written informed consent was waived due to the retrospective design of the study.

### 2.2. Demographic, clinical, and diagnostic data

Information about patients, including smoking history, comorbidities, preoperative induction chemotherapy with cisplatin and pemetrexed for three cycles, laboratory test results, intraoperative parameters, postoperative complications within 30 days, and survival was collected through a review of electronic medical records. The pathological stage was determined according to the seventh edition of the Union for International Cancer Control TNM staging system for MPM, and the tumor grades were classified according to the WHO classification of histological differentiation (Rusch &

Giroux, 2012). The performance status (PS) scores according to Eastern Cooperative Oncology Group (ECOG) were assessed. Nutritional status was assessed by the Controlling Nutritional Status (CONUT) score, which consists of the serum albumin level, total cholesterol level, and total lymphocyte count and ranges between 0 and 12 (Ignacio de Ulbarri et al., 2005). A higher CONUT score represents a poorer nutrition level. It has been reported that the cut-off CONUT score for a better likelihood of one-year survival is  $\geq 2$  in patients with MPM (Takamori et al., 2017). The severity of postoperative complications was classified using the Clavien-Dindo classification system (Dindo, Demartines, & Clavien, 2004). Grades III and IV of the Clavien-Dindo classification were defined as major complications. Prolonged air leak was defined as persistent air leak beyond five days (Seely et al., 2010).

### **2.3. Pulmonary function test**

Preoperative pulmonary functions were routinely measured using computerized equipment (Fudak77, Fukuda Sangyo, Tokyo, Japan) at the clinical laboratory 2 to 38 days before surgery. The following spirometric parameters, vital capacity (VC), inspiratory capacity, forced vital capacity (FVC), and forced expiratory volume in 1 s ( $FEV_1$ ), were measured. Lung volumes including residual volume (RV) and total lung capacity (TLC) were measured by means of the helium dilution technique. Diffusion capacity of the lung for carbon monoxide ( $DL_{CO}$ ), and its value corrected for alveolar volume ( $DL_{CO}/V_A$ ) were measured by the single-breath technique. Data are also calculated as the % of predicted values according to the method of the Japanese Respiratory Society (Japanese-Respiratory-Society, 2004).

### **2.4. Measurements of physical fitness**

The 6MWD was measured by the 6MWT according to guidelines of the American Thoracic Society (ATS, 2002) within four days before surgery. Briefly, all patients were tested under the standardized conditions by trained physical therapists (Hayashi, Fukumoto et al., 2017; Hayashi, Yokoyama et al., 2017; Inoue et al., 2016; Mizuno et al., 2016). Patients were instructed to walk as far as possible for 6 min, and the distance was recorded. The 6MWT is not assumed to be a routine tool for evaluation for surgical resection, and patients were allowed to refuse the assessment if they wished. During the 6MWT,  $SpO_2$  was measured using a pulse oximeter (Pulsox-Me300; Teijin Pharma Co., Tokyo, Japan) without supplemental oxygen. Desaturation was defined as a fall in  $SpO_2 \geq 4\%$  or  $SpO_2 < 90\%$  during the 6MWT (Poulain et al., 2003). Hand grip strength was measured using a digital dynamometer (Grip-D, Takei Co., Niigata, Japan). Muscle strength was measured twice on each side, and the highest value was chosen for evaluation. These physical parameters were routinely measured, if possible, as a part of the perioperative rehabilitation program.

### **2.5. Rehabilitation program**

Pre- and postoperative rehabilitation was performed by specialized physical therapists (Hayashi, Fukumoto et al., 2017; Inoue et al., 2016). The preoperative pulmonary rehabilitation protocol included measurements of 6MWD and hand grip strength, and orientation to the postoperative rehabilitation program and encouragement of early mobilization. Preoperative measurements were assessed one to four days before surgery. All patients performed the postoperative pulmonary rehabilitation, which consisted of positioning, stretching of respiratory muscles and thoracic cage, deep diaphragmatic breathing, coughing and huffing, and early mobilization from the first postoperative day. The rehabilitation program was provided until discharge of the patient.

### **2.6. Statistical analysis**

Data were expressed as means  $\pm$  SD, median (range), or number of patients. A *t*-test, Mann-Whitney U test, chi-square test, or Fisher's exact test was used to evaluate statistical significance. Correlations between variables were analyzed using Spearman's rank or Pearson's correlation coefficient. Statistical analyses were conducted using SPSS ver. 19 (SPSS Inc., Chicago, IL, USA).  $p < 0.05$  was considered statistically significant.

### 3. Results

The demographic and preoperative characteristics and pulmonary functions of the 18 patients included in this study are shown in Table 1. The patients were predominantly male (88.9%), and the tumors were epithelioid type (83.3%). Eleven patients (61.1%) received induction chemotherapy. The mean values of preoperative 6MWD were 465.9 m. Minimum SpO<sub>2</sub> during the 6MWT ranged from 86% to 97%, and five patients (27.8%) experienced desaturation during the 6MWT. Only three patients (16.7%) showed high (3≤) CONUT scores. Values of pulmonary function parameters varied and the mean % of predictive FEV<sub>1</sub> (78.7%) was less than 80%.

Intraoperative characteristics and postoperative outcomes are shown in Table 2. P/D was performed in 11 cases (61.1%). There was no in-hospital death or death within 30 days after surgery. The one-year survival rate was 77.8%. Postoperative complications are shown in Table 3. A total of 14 major (seven grade III and seven grade IV) complications occurred in six patients (33.3%).

Spearman's correlations between preoperative parameters for physical fitness, pulmonary functions, arterial blood gas analysis without supplemental oxygen, and surgery-related parameters are shown in Table 4. 6MWD significantly correlated with inspiratory capacity and % of predicted values of DL<sub>CO</sub>. The minimum SpO<sub>2</sub> during the 6MWT significantly correlated with percentages of predicted values of VC and TLC and postoperative days of extubation. PaO<sub>2</sub> significantly correlated with % of predicted value of DL<sub>CO</sub>.

**Table 1. Clinical characteristics and pulmonary function test results (n = 18)**

Variable	Number	Mean ± SD (range) or ratio
Age, years		65.8 ± 6.4 (52-76)
Male	N = 16	88.9%
Body mass index, kg/m <sup>2</sup>		23.4 ± 3.3 (18.3-29.7)
Smoking history, yes	N = 13	72.2%
Known asbestos exposure	N = 9	50.0%
Performance status, 0/1	N = 17/1	
Clinical stage, I/II/III	N = 7/6/5	
Histology, epithelioid/biphasic/sarcomatoid	N = 15/2/1	
Induction chemotherapy	N = 11	61.1%
Hand grip strength, kgf		33.8 ± 6.0 (21.5-42.3)
6MWD, m		465.9 ± 96.7 (316-651)
Minimum SpO <sub>2</sub> during 6MWT, % (N = 17)		93.6 ± 2.7 (86-97)
Desaturation during 6MWT*, yes	N = 5	27.8%
Controlling Nutritional Status score ≥3	N = 3	16.7%
Hemoglobin, g/dL		12.0 ± 1.8 (9.4-15.0)
VC, % predicted		84.3 ± 16.5 (46.8-117.6)
TLC, % predicted		86.6 ± 17.7 (57.3-116.8)
RV, % predicted		96.4 ± 26.5 (53.3-152.2)
FVC, % predicted		83.3 ± 16.9 (48.1-118.1)
FEV <sub>1</sub> , % predicted		78.7 ± 18.8 (45.1-108.5)
FEV <sub>1</sub> /FVC, %		74.3 ± 11.5 (42.1-91.5)
DLco, % predicted		93.4 ± 21.9 (56.5-130.3)
DLco/V <sub>A</sub> , % predicted		98.6 ± 21.4 (64.3-144.6)

Note: Data are given as mean ± SD (range) or number (%).

\*Desaturation was defined as a fall in SpO<sub>2</sub> ≥ 4% or SpO<sub>2</sub> < 90% during the 6-min walk test (6MWT). The Controlling Nutritional Status (CONUT) score consists of the serum albumin concentration, total peripheral lymphocyte count, and total cholesterol concentration.

**Table 2. Surgical parameters and postoperative outcome (n = 18)**

Variable	Number	Mean ± SD (range) or ratio (%)
Surgical technique		
Extrapleural pneumonectomy	N = 7	38.9%
Pleurectomy/decortication	N = 11	61.1%
Right-side surgery	N = 10	55.6%
Operation time, min		459.6 ± 159.0 (183–732)
Blood loss during surgery, g		2115 ± 1641 (197–5078)
Red blood cell transfusions, yes	N = 11	61.1%
Timing of extubation, 0/1/2 days after surgery	N = 8/9/1	
Length of postoperative ICU stay, days		2.2 ± 1.5 (0–6)
Postoperative day of first walking with support		3.7 ± 2.0 (1–10)
Hospital stay after surgery, days		26.3 ± 26.5 (8–102)
Readmission within 30 days after discharge	N = 1	5.6%
Death within 30 days after surgery	N = 0	0%
One-year survival rate	N = 14	77.8%

Note: Data are given as mean ± SD (range) or number (%).

**Table 3. Total postoperative complications**

Complication	Minor		Major	
	Grade I	Grade II	Grade III	Grade IV
Respiratory failure <sup>a</sup>	N = 0	N = 0	N = 4 (2)	N = 4 (2)
Pneumonia	N = 0	N = 1 (0)	N = 0	N = 2 (2)
Empyema	N = 0	N = 0	N = 1 (0)	N = 1 (1)
Atrial fibrillation	N = 0	N = 3 (2)	N = 1 (1)	N = 0
Prolonged air leak <sup>b</sup>	N = 1 (0)	N = 0	N = 1 (0)	N = 0
Wound infection	N = 0	N = 2 (1)	N = 0	N = 0
Recurrent nerve paralysis	N = 1 (0)	N = 0	N = 0	N = 0

Notes: Postoperative complications were graded as either minor (Grade I and II) or major (Grade III and IV) by the Clavien-Dindo classification system. Data are given as number (EPP cases).

<sup>a</sup>Respiratory failure involves four Grade IV complications (two CO<sub>2</sub> capture and storage, one acute respiratory distress syndrome, and one alveolar hemorrhage) and four Grade III complications (expectoration discharge disorder).

<sup>b</sup>Prolonged air leak involves one Grade I complication (persistent air leak for 13 days) and one Grade III complication (treated with drainage and intrapleural OK432).

Clinical data and pulmonary function parameters of patients with and without major postoperative complications defined as Clavien-Dindo grade III or IV are compared in Table 5. There was no significant difference in 6MWD, minimum SpO<sub>2</sub> during the 6MWT, pulmonary functions, or ratio of induction chemotherapy between the groups. Postoperative days of first walking with support and length of ICU and hospital stays after surgery were significantly longer in patients with major complications than in those without.

Data of patients who underwent EPP and P/D are compared in supplemental Table S1. Preoperative hand grip strength of the EPP group was significantly less than that of the P/D group. Hospital stays after EPP were significantly longer than those after P/D.

**Table 4. Correlation between preoperative physical parameters and clinical parameters or postoperative outcomes**

Variables	6MWD (n = 18)		Minimum SpO <sub>2</sub> during 6MWT (n = 17)		Hand grip strength (n = 16)		PaO <sub>2</sub> (n = 18)		PaCO <sub>2</sub> (n = 18)	
	ρ	p-value	ρ	p-value	ρ	p-value	ρ	p-value	ρ	p-value
Minimum SpO <sub>2</sub> during 6MWT	-0.122	0.640 (n = 17)	-	-	-	-	-	-	-	-
Hand grip strength	-0.006	0.983 (n = 16)	-0.230	0.392 (n = 16)	-	-	-	-	-	-
PaO <sub>2</sub>	0.352	0.152	-0.054	0.838	0.085	0.753	-	-	-	-
PaCO <sub>2</sub>	0.277	0.266	-0.289	0.260	0.296	0.266	-0.180	0.476	-	-
VC, % predicted	0.216	0.390	0.619	0.008*	-0.306	0.249	0.344	0.163	-0.392	0.107
TLC, % predicted	0.138	0.584	0.493	0.044*	-0.417	0.108	0.373	0.127	-0.395	0.105
Inspiratory capacity	0.507	0.032*	0.163	0.533	-0.243	0.365	-0.006	0.981	0.001	0.997
FEV <sub>1</sub> , % predicted	0.135	0.593	0.104	0.690	-0.053	0.846	0.032	0.900	-0.348	0.157
DL <sub>CO</sub> , % predicted	0.470	0.049*	0.429	0.085	-0.329	0.213	0.505	0.033*	-0.296	0.232
Postoperative day of extubation	-0.223	0.374	-0.495	0.044*	-0.124	0.648	-0.171	0.498	0.080	0.752
Postoperative day of first walking with support	0.046	0.857	-0.312	0.224	0.034	0.901	-0.235	0.347	0.170	0.500
Hospital stay after surgery	0.032	0.900	-0.273	0.290	-0.461	0.072	-0.188	0.455	0.067	0.791

Notes: Values (ρ) are Spearman's rank correlation coefficients.  
 \*Significant correlation (p < 0.05).

**Table 5. Comparison of clinical and pulmonary function data with and without major complications defined by Clavien-Dindo grade system**

Variable	With major complication (n = 6)	Without (n = 12)	p-value
Age, years	66.7 ± 4.3	65.3 ± 7.3	0.687
Body mass index, kg/m <sup>2</sup>	22.1 ± 2.6	24.0 ± 3.4	0.241
Clinical stage I	N = 3 (50.0%)	N = 4 (33.3%)	0.428
Induction chemotherapy	N = 5 (83.3%)	N = 6 (50.0%)	0.316
Hand grip strength, kgf	31.3 ± 7.2	36.4 ± 4.6	0.109
6MWD, m	493.0 ± 120.6	452.4 ± 85.0	0.418
Minimum SpO <sub>2</sub> during 6MWT	94 (91–95)	95 (86–97)	0.661
CONUT score	1 (0–3)	1 (0–4)	1.000
Hemoglobin, g/dL	11.0 ± 1.1	12.4 ± 1.9	0.122
VC, % predicted	80.8 ± 6.3	86.0 ± 19.8	0.542
FEV <sub>1</sub> , % predicted	77.9 ± 12.4	79.1 ± 21.8	0.899
DLco, % predicted	89.2 ± 23.7	95.5 ± 21.7	0.583
Extrapleural pneumonectomy	N = 4 (66.7%)	N = 3 (25.0%)	0.141
Right side surgery	N = 4 (66.7%)	N = 6 (50.0%)	0.437
Operation time, min	533.6 ± 153.2	422.5 ± 154.6	0.169
Blood loss during surgery, g	2906 ± 1808	1719 ± 1471	0.154
Red blood cell transfusion	N = 5 (83.3%)	N = 6 (50.0%)	0.316
Postoperative days of first walking with support	4.5 (3–10)	3 (1–4)	0.033*
ICU stay after surgery, days	3.5 (1–6)	1 (0–3)	0.036*
Hospital stay after surgery, days	51.5 (22–102)	12.5 (8–19)	0.001*

Note: Data are given as mean ± SD, median (range), or number (%).

\*Significantly difference ( $p < 0.05$ ) between groups compared by Mann-Whitney test.

#### 4. Discussion

The main findings of the present study are that in patients with MPM who underwent surgery, (1) the preoperative 6MWD significantly correlated with inspiratory capacity and % of predicted value of DL<sub>CO</sub>, (2) the minimum SpO<sub>2</sub> during the 6MWT significantly correlated with % of predicted values of VC and TLC and longer postoperative intubation, and (3) the incidence of major postoperative complications led to delayed ambulation and longer ICU and hospital stays after surgery. In contrast, preoperative physical fitness or pulmonary function test parameters were not associated with postoperative major complications. To our knowledge, this is the first study to characterize the preoperative 6MWT results, 6MWD, and minimum SpO<sub>2</sub> and relate them to pulmonary functions and postoperative outcomes in patients with resectable MPM.

We used the 6MWT as a simple method to evaluate submaximal exercise capacity. In our cohort, there was a positive correlation between preoperative 6MWD and pulmonary function test results (Table 4), consistent with findings in COPD (Cote, Pinto-Plata, Kasprzyk, Dordelly, & Celli, 2007) and esophageal cancer (Inoue et al., 2016). We further investigated how SpO<sub>2</sub> declines during the 6MWT and found significant associations between minimum SpO<sub>2</sub> and pulmonary function parameters and longer duration of postoperative intubation (Table 4). Exercise hypoxia and desaturation have been recognized predictors of poor prognosis and pulmonary hypertension in patients with respiratory diseases, specifically COPD (Casanova et al., 2008; Nakahara et al., 2017). Ninan et al. demonstrated that preoperative exercise desaturation was associated with major complications and longer ICU stays after pneumonectomy in patients with lung cancer (Ninan et al., 1997). Nakagawa et al. demonstrated that desaturation during the 6MWT as well as 6MWD significantly correlated with

maximum oxygen consumption ( $VO_{2max}$ ) as assessed by a cardiopulmonary exercise test in patients with lung cancer before surgery (Nakagawa, Chiba, Saito, Sakaguchi, & Ishikawa, 2014). Our results suggest that measurements of 6MWD and minimum  $SpO_2$  are convenient and useful to assess preoperative exercise capacity in patients undergoing invasive surgery for MPM.

In the present study, six patients (33.3%) experienced a total of 14 major complications after surgery without 30-day or in-hospital mortality (Table 3). Importantly, the incidence of major postoperative complications led to longer ICU and hospital stays after surgery (Table 5). Moreover, the postoperative days of first walking with support were significantly longer in patients with major complications than in those without (Table 5). It has been reported that induction chemotherapy, right-side tumors, prolonged operation time, and necessity of transfusion of red blood cells are risk factors for complications after EPP (de Perrot et al., 2007; Stewart, Martinucar, Edwards, West, & Waller, 2005). In our results, however, either preoperative or intraoperative parameters including the above known risk factors were not significantly associated with development of major postoperative complications (Table 5). For example, hand grip strength was less, the ratio of EPP and blood loss during surgery were more, and operation time and postoperative days of first walking with support were longer in patients with major complications than those without, but the differences did not reach statistically significant levels. EPP is more invasive than P/D. Indeed, postoperative hospital stays were longer in patients who underwent EPP than those with P/D (supplemental Table S1). The ratio of EPP was higher in cases with major complications (66.7%) than those without (25.0%). However, the difference was not statistically significant. One possible reason is the small size of our cohort. Future studies with large numbers are required to elucidate predictive risk factors for postoperative complications and survival in patients with resectable MPM.

Perioperative rehabilitation has been expected to promote early mobilization and reduce postoperative complications in patients who undergo thoracic surgery (Brunelli et al., 2009). Moreover, the implementation of a preoperative exercise-based intervention called “prehabilitation” could optimize the functional status of patients before surgery and improve postoperative outcomes after lung resection in patients with lung cancer (Sebio García, Yáñez Brage, Giménez Moolhuyzen, Granger, & Denehy, 2016; Varela, Ballesteros, Jiménez, Novoa, & Aranda, 2006). In the present study, preoperative physical therapy was not provided to patients. Thus, it is unknown whether improvement of physical levels by preoperative prehabilitation reduces the mortality and risk of postoperative complications in patients with MPM.

This study has several limitations. The data were collected retrospectively from patients with different stages, pathological diagnoses, and surgical invasiveness. We did not perform multiple regression analysis in order to control cofounders due to the small sample size. Additionally, we did not aim to examine long-term outcomes because the shortest observation period after surgery was less than two years. Future studies are warranted to elucidate the relationship between preoperative physical fitness and long-term survival.

In conclusion, preoperative assessment of 6MWD and minimum  $SpO_2$  during the 6MWT combined with pulmonary function tests may be useful for evaluating preoperative exercise capacity in patients with MPM undergoing surgery resection.

#### Supplementary material

Supplementary material for this article can be accessed here <https://doi.org/10.1080/2331205X.2017.1421007>

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#### Competing Interests

The authors declare no competing interest.

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