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ORIGINAL ARTICLE

Physical function and health-related quality of life in patients undergoing surgical treatment for malignant pleural mesothelioma

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Abstract

Introduction Malignant pleural mesothelioma (MPM) is a rare cancer that affects the thin cell wall lining of internal organs and structures. Studies have shown that patients with lung cancer have decreased pulmonary function and exercise capacity after pneumonectomy. However, to date, physical function and health-related quality of life (HRQOL) in surgically treated MPM patients have not been evaluated in detail. The aim of this study was to assess physical function and HRQOL of MPM patients following pleurectomy/decortication (P/D).

Methods The subjects were 22 MPM patients (20 men and 2 women) who completed P/D between December 2013 and March 2015. Physical function was assessed using handgrip strength and knee extensor strength tests, the 6-min walk distance (6MWD), and pulmonary function tests, including forced expiratory vital capacity (FVC) and forced expiratory volume in 1 s (FEV1). HRQOL was assessed using the Medical Outcome Study 36-item Short Form Health Survey (SF-36).

Results The handgrip strength ($P < 0.05$), 6MWD, FVC, and FEV1 values following P/D decreased significantly compared to baseline ($P < 0.001$ for each comparison). Additionally, scores of three of the eight SF-36 domains were significantly lower following P/D: physical functioning ($P < 0.001$), body pain ($P = 0.002$), and vitality ($P = 0.005$). 6MWD correlated role physical ($P < 0.05$) and vitality ($P < 0.01$). Significant correlations were also observed between FEV1 and physical functioning ($P < 0.05$) and social functioning ($P < 0.05$).

Conclusion Patients with MPM who completed P/D have decreased physical function and HRQOL. Following surgery, exercise capacity and pulmonary function decreased more than limb muscle strength. Physicians, nurses, and rehabilitation staff should note these findings, which may provide insight into the development of customized rehabilitation strategies for patients with MPM who completed P/D.

Keywords Malignant pleural mesothelioma · Physical function · Health-related quality of life · Rehabilitation

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Introduction

Malignant pleural mesothelioma (MPM) is an aggressive tumor arising from the mesothelial cells lining the pleura. MPM is a rare malignancy that is difficult to treat and is usually associated with asbestos exposure [1]. Treatment focuses on surgery combined with radiation and/or chemotherapy in a multimodality approach [2–4]. The goal of surgery in the multimodal treatment of MPM is to achieve maximum cytoreduction. Two surgical methods have evolved: extrapleural pneumonectomy (EPP) and pleurectomy/decortication (P/D) [2, 4, 5]. EPP involves en bloc resection of the lung, pleura, pericardium, and diaphragm. P/D is a lung-sparing surgery that removes only the parietal/visceral pleura [2]. Compared with EPP, P/D is theoretically less radical but is associated with less perioperative mortality/morbidity and less postoperative deterioration of cardiopulmonary function [2].

A previous study of the physical activity of lung cancer patients showed that individuals with non-small cell lung cancer were less physically active than healthy individuals [6]. In another previous study, at 5 days after lung resection, a significant deterioration in quadriceps strength was observed in a control group, while the strength was maintained in an intervention group that underwent a training program following the procedure [7]. On the other hand, after lung resection, a significant worsening of the effort tolerance and symptomatic status occurred [8]. Other studies showed worsened pulmonary function after lung resection for cancer [9–12]. For example, after lung resection, a significant loss of forced expiratory volume in 1 s (FEV1) and forced expiratory vital capacity (FVC) have been observed [9, 10]. Regarding quality of life (QOL) after lung resection, an average medium decline was observed in the physical domains [11, 12]. Thus, physical function, pulmonary function, and QOL decrease after lung resection for cancer. Likewise, after MPM, there is a possibility that the physical function, pulmonary function, and QOL decrease.

There have only been a few reports concerning pulmonary function and QOL after EPP or P/D [13–16]. However, there have not been any reports concerning physical function after EPP or P/D. Furthermore, there are no reports regarding physical function, pulmonary function, or QOL in the acute phase after EPP or P/D. Therefore, to understand the characteristics of the change in physical function and QOL in the acute phase after an operation seems useful for rehabilitation program planning during this same period.

The aims of this study were to assess the physical function and health-related QOL (HRQOL) before and after MPM surgery in patients undergoing P/D and to assess how the physical function and HRQOL are affected by the response to surgery in the acute phase.

Subjects and methods

Design

This was a prospective, observational study to compare the preoperative and postoperative physical function of MPM patients undergoing P/D. The study was approved by the Hyogo College of Medicine Institutional Committee on Human Research. Written informed consent to participate was obtained from all participants.

Demographic, clinical, and diagnostic data

The following data were extracted from the medical records of each patient: age, sex, disease stage at surgery, affected side, duration of disease (from initial diagnosis to hospitalization), previous P/D, and cycles of chemotherapy received prior to P/D. Anthropometric, muscle strength, and submaximal exercise capacity data were measured during physical examination before and after the procedure. All other data were collected during physical examination before and after the procedure.

Participants

Twenty-two MPM patients who underwent P/D between December 2013 and March 2015 were recruited from the Hyogo College of Medicine Hospital, Nishinomiya, Hyogo, Japan. Before the operation, the patients were assessed for handgrip and knee-extensor strength, submaximal exercise capacity using the 6-min walk distance (6MWD), forced expiratory vital capacity (FVC), FEV1, and HRQOL using the Medical Outcome Study 36-item Short Form Health Survey (SF-36).

Physiotherapy

Physiotherapy was begun promptly the day after the surgery. We instituted early rehabilitation with mobilization (such as sitting, standing, and walking) in the intensive care unit (ICU) or high care unit five to six times a week.

Measurements

Anthropometric measurements

Height (in centimeters) and weight (in kilograms) were measured with a wall-mounted stadiometer and a body composition analyzer (BC-118D; Tanita Co., Ltd., Tokyo, Japan), respectively. Body mass index (BMI) was calculated by dividing the body weight (in kilograms) by the height (in meters) squared.

Handgrip strength

A standard adjustable-handle dynamometer (T.K.K. 5101; TAKEI Scientific instruments Co. Ltd., Niigata, Japan) was used to measure handgrip strength as the index of upper-limb muscle strength and was set at the second grip position for all subjects. Grip strength was measured with the same handgrip dynamometer, and the examination was performed by the same physical therapist. Attention was paid to a possible Valsalva effect, and grip strength of both hands was measured. Measured data were used as the index of handgrip strength (kilogram-force [kgf]).

Knee extensor muscle strength

Hand-held dynamometers ([HHD]; μ-tas MT1; ANIMA Co., Tokyo, Japan) were used to measure knee extensor muscle strength as an index of lower-limb muscle strength. In all sessions, we used an HHD equipped with a stabilizing belt that functioned as an aid for the tester to hold when applying resistance. The HHD was used in the manual mode with kgf units. A previous study showed that the intraclass correlation coefficients (ICCs) were 0.98 with a belt and 0.04 without a belt [17]. In a reliability test–retest of the belt-restrained HHD, ICCs were 0.94 to 0.96 [18]. Knee extension force was tested in a sitting position with the knee flexed at approximately 90°. The dynamometer was applied just proximal to the malleoli. The maximum force during 10 s of effort was recorded in kgf. The HHD was reset to kgf at the start of each measurement. Two measurements were carried out with each leg, and the higher value of the two measurements was selected for analysis.

Submaximal exercise capacity

Submaximal exercise capacity was assessed using the 6MWD measured in accordance with the American Thoracic Society guidelines [19]. Patients walked up and down a 20-m corridor for 6 min at their own pace. They were encouraged to cover as much distance as possible, but were permitted to rest and continue walking as soon as they felt able, or to stop if they showed symptoms of dyspnea or leg pain [20]. The following data were collected and analyzed: distance after 6 min (in meters), duration (in minutes), and heart rate at initiation and at 6 min [21].

Pulmonary function

Pulmonary function was assessed with spirometry (Minato Autospiro AS-302; Minato Medical Science Co., Ltd., Osaka, Japan) measured in accordance with the American Thoracic Society guidelines [22]. FVC and FEV1 were expressed in liters.

Health-related quality of life

HRQOL was assessed with the SF-36 by direct questioning of the subjects, thus excluding those who were too confused or dysphasic to answer. This self-administered questionnaire has been widely used and validated in the Japanese general population [23–25] and in patients after P/D. The SF-36 assesses physical and mental health components in eight domains: physical functioning (PF), physical role functioning (RP), bodily pain (BP), general health perceptions, vitality (VT), social role functioning (SF), emotional role functioning, and mental health. The SF-36 measures the multidimensional properties of HRQOL on a scale of 0 to 100, with higher scores indicating better HRQOL.

Statistical analysis

Data are summarized as mean ± standard deviation or median with interquartile range. A two-tailed t test was used to compare paired continuous data (BMI, handgrip, knee extensor muscle strength, 6MWD, FVC, FEV1, and preoperative and postoperative scores of eight SF-36 domains). The correlation between physical function (body weight, handgrip and knee extensor muscle strength, and 6MWD) and lung function (FVC and FEV1) were analyzed using Pearson's correlation coefficient. The correlation between eight SF-36 domains and physical-lung function (body weight, handgrip and knee extensor muscle strength, 6MWD, FVC, and FEV1) was analyzed using Pearson's correlation coefficient. Statistical analysis was performed with SPSS 17.0J statistical software (SPSS Japan, Inc., Tokyo, Japan). P values <0.05 were considered statistically significant.

Results

The demographic and diagnostic data for the cohort are summarized in Table 1. In total, 22 MPM patients (20 men and 2 women) underwent P/D between December 2013 and March 2015. The disease stage at surgery was I in 12 patients (55%), II in eight patients (36%), and III in two patients (9%). The median duration of disease was 5 months (range 3–8). The median number of chemotherapy cycles received before P/D was three (range 2–5).

Physiological variables

Patient body weight, muscle strength, and submaximal exercise capacity data are summarized in Table 2. Postoperative body weight was 4.7% lower compared to preoperative values ($P < 0.001$). Postoperative and preoperative handgrip strength values differed significantly ($P < 0.05$), but knee extensor strength values did not (handgrip: −5.5%; knee extension:

Table 1 Patient baseline data (n = 22)

Characteristics	
Age (years)	64 (54–77)
Weight (kg)	64.4 (11.8)
Height (m)	1.64 (0.09)
Body mass index (kg/m^2)	23.8 (2.7)
Sex	
Men	20 (91%)
Women	2 (9%)
Disease stage at surgery	
I	12 (55%)
II	8 (36%)
III	2 (9%)
Affected side	
Right	12 (55%)
Left	10 (45%)
Duration of disease(month)	5 (3–8)
Number of chemotherapy cycles	3 (2–5)

Data are given as mean (SD), median (range), or n (percent)

−3.8%). Postoperative submaximal exercise capacity was also significantly lower compared to preoperative values ($P < 0.001$).

Pulmonary function

Pulmonary function data are summarized in Table 2. Postoperative FVC was 41.5% lower compared to preoperative values ($P < 0.001$). Postoperative FEV1 was 33.2% lower compared to preoperative values ($P < 0.001$).

Health-related quality of life

HRQOL data are summarized in Table 3. After surgery, PF, BP, vitality, and physical component summary scores decreased significantly, while changes in scores in other domains were not statistically significant.

Correlations between physical function, lung function, and health-related quality of life

Correlations between physical function, lung function, and HRQOL, representing the difference before and after P/D, are presented in Tables 4 and 5. There was a significant correlation between FVC and knee extensor strength values and 6MWD. There was a significant correlation between body weight and VT. There was a significant correlation between 6MWD and RP and VT. There was a significant correlation between FVC and SF and physical component summary scores. There was a significant correlation between FEV1 and PF and SF.

Discussion

Our results showed that patients who underwent P/D surgery had significantly lower postoperative exercise capacity compared to preoperative values. In addition, we found that these patients had significantly lower postoperative body weight, lung function, and QOL compared to preoperative values. We also found correlations between physical function, lung function, and HRQOL, representing the difference before and after P/D.

A previous study of MPM patients undergoing EPP reported that physical and respiratory function changed during the convalescent phase [26]. Another study reported a deterioration of global QOL, in particular when focusing on disease-related pain and physical role functioning at 3 months after surgery; the results worsened after 12 months [27]. This is one of the few studies that have evaluated physical function and QOL before and after surgery of MPM patients who underwent P/D and that have assessed how both physical function and QOL are affected by the acute phase response to surgery.

We used the 6MWD as an easily obtainable measure of submaximal exercise capacity. The 6MWD results may reflect patient ability to perform activities of daily living [19, 28]. The

Table 2 Body weight, strength, submaximal exercise capacity, and lung function

Physiological variables	Before P/D (n = 22)	After P/D (n = 22)	P
Body weight (kg)	64.4 (11.8)	61.4 (11.1)	<0.001
Hand grip (kgf)	34.5 (6.8)	32.6 (7.8)	<0.05
Knee extension (kgf)	38.5 (11.1)	37.2 (10.6)	0.256
6MWD (m)	470.6 (83.8)	399.7 (69.9)	<0.001
FVC (L)	3.28 (0.85)	1.92 (0.40)	<0.001
FEV1 (L)	2.35 (0.59)	1.57 (0.37)	<0.001

Data are given as mean (standard deviation)

P/D pleurectomy/decortication, *6MWD* 6-min walk distance, *FVC* forced vital capacity, *FEV1* forced expiratory volume in 1 s

Table 3 Health-related quality of life

SF-36 domain	Before P/D (n = 22)	After P/D (n = 22)	P
Physical functioning	83.6 (11.3)	66.1 (19.4)	<0.001
Role-physical	66.8 (25.7)	49.0 (27.7)	0.073
Bodily pain	67.2 (28.8)	45.1 (25.0)	0.002
General health	53.5 (15.7)	52.6 (14.0)	0.769
Vitality	62.0 (25.1)	47.2 (21.0)	0.005
Social functioning	65.9 (29.7)	56.8 (24.6)	0.084
Role-emotional	71.4 (26.2)	56.8 (28.9)	0.051
Mental health	62.5 (23.9)	56.8 (20.8)	0.121
Physical component summary	43.2 (8.8)	29.0 (15.0)	<0.001
Mental component summary	48.1 (12.8)	46.0 (10.9)	0.171

Data are given as mean (SD)

Higher scores indicate better quality of life; domain scores range from 0 to 100

SF-36 short form 36, *P/D* pleurectomy/decortications

6MWD 1 week after lung surgery should be a total assessment of postoperative pulmonary dysfunction, chest pain, muscle weakness, and nutritional status [29]. Pulmonary function decline was particularly considered a reason for 6MWD decline. A previous study reported that significant improvement in 6MWD correlated with improvement of ventilator function after lung resection [8]. Therefore, reduced values of the 6MWD after surgery should be a good indicator of the risk for postoperative pulmonary complications [29]. Maruyama et al. found that 6MWD was decreased by 23.4% compared to preoperative values [30]. Arbane et al. reported that 6MWD was decreased by 27.8% compared to preoperative values [7]. Our findings are similar in that they showed that the postoperative submaximal exercise capacity was decreased by 15% compared to preoperative values (Table 2). In our study, 6MWD values were associated with FVC values (Table 4). Thus, it was considered that invasion of the lung with an operation had an influence on the submaximal exercise capacity after the operation.

On the other hand, we found no postoperative and preoperative differences in skeletal muscle power in the current study. This may be due to the effect of early rehabilitation with mobilization (such as sitting and standing) in the ICU. These results were similar to those of Arbane et al., who reported that changes in quadriceps strength from baseline were not significant after lung resection [7]. Concerning physical function, our findings suggest that P/D has a greater effect on the submaximal exercise capacity compared to skeletal muscle strength.

Table 4 Correlations between physical function and lung function

	Δ Body weight	Δ Hand grip	Δ Knee ext	Δ 6MWD
Δ FVC			0.472*	0.449*
Δ FEV1				

FVC forced vital capacity, *FEV1* forced expiratory volume in 1 s, *Knee ext.* knee extension, *6MWD* 6-min walk distance, *Δ* delta, represents the difference before and after pleurectomy/decortications

Statistical analysis using Pearson's correlation coefficient**$P < 0.01$, *$P < 0.05$

Only significant correlation coefficients are presented

In this study, in patients who underwent P/D, postoperative pulmonary function test results were significantly lower compared to preoperative values (Table 2), which is consistent with previous lung lobectomy reports [29, 31–34]. On the other hand, Ploenes et al. showed that, in patients who had undergone P/D, pulmonary function was not significantly reduced after 150 days postoperatively [13]. We hypothesize that the reduction in pulmonary function immediately after surgery may be caused by a phrenic nerve being cut off during the procedure and/or by a lack of compliance in the tissue in the acute phase postoperative due to surgical stress. Lima et al. found that FVC and FEV1 were decreased by 10.1 and 23.9% compared to preoperative values [9]. Patients undergoing pneumonectomy generally lose a substantial amount of their lung parenchyma and are at risk for various respiratory complications, primarily lung edema and infection of the remaining lung, especially during the initial postoperative phase [34]. It could be hypothesized that similar complications may also affect postoperative pulmonary function in patients who undergo P/D.

An important aspect to be considered is the QOL during and after treatment, but unfortunately, there are few results in the acute phase after P/D concerning this problem [1]. In a previous study, nearly all SF-36 domains showed a significant deterioration at 3 months following surgery in patients undergoing EPP [27]. Salati et al. reported that no differences were found in any of the eight domains, nor in the composite scores after major lung resection for lung cancer [35]. In our study, postoperative scores in some HRQOL domains were significantly lower in patients undergoing P/D compared to

Table 5 Correlations between health-related QOL and physical function

	Δ Physical functioning	Δ Role-physical	Δ Bodily pain	Δ General health	Δ Vitality	Δ Social functioning	Δ Role-emotional	Δ Mental health	Δ PCS	Δ MCS
Δ Body weight					0.491*					
Δ Hand grip										
Δ Knee ext										
Δ 6MWD		0.458*			0.564**					
Δ FVC						0.448*			0.428*	
Δ FEV1	0.445*					0.463*				

QOL quality of life, Δ delta, represents the difference before and after pleurectomy/decortications, *PCS* physical component summary, *MCS* mental component summary, *Knee ext.* knee extension, *6MWD* 6-min walk distance, *FVC* forced vital capacity, *FEV1* forced expiratory volume in 1 s

Statistical analysis using Pearson's correlation coefficient $^{**}P < 0.01$, $^{*}P < 0.05$

Only significant correlation coefficients are presented

preoperative values. Our results are similar to those of previously reported MPM studies [14, 16]. We found that HRQOL was significantly associated with exercise capacity and lung function. Concerning the HRQOL, our findings suggest that P/D has a greater effect on physical rather than mental components.

This study has a few limitations. First, we recruited a small sample, which could affect the external validity of this study. In subsequent studies, it is necessary to recruit a larger number of patients and perform multivariate analyses of the data. Second, this was not an interventional study; therefore, we could not estimate the causal effects of rehabilitation on the outcomes measured in the current study. Third, we did not investigate air leakage after P/D. Persistent air leak after P/D is an ongoing problem in MPM patients. We would like to examine the air leak problem in a future study. Finally, we did not evaluate the amount of daytime physical activity and activities of daily living. Therefore, the influence of the amount of physical activity after the operation on the outcomes measured in the current study is unclear.

In summary, the present study showed the following: (1) reduced postoperative exercise tolerance and pulmonary function in patients undergoing P/D compared to preoperative values and (2) a decrease in the HRQOL, in particular in the physical components. Our findings indicate that, for patients undergoing P/D, it may be important to perform an exercise tolerance test at an early phase. Physicians, nurses, and rehabilitation staff should note these findings, which may provide insight into the development of customized rehabilitation strategies for patients with MPM who undergo P/D.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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