



Physical function and health-related quality of life in the convalescent phase in surgically treated patients with malignant pleural mesothelioma

Takashi Tanaka¹ · Shinichiro Morishita^{2,3} · Masaki Hashimoto⁴ · Toru Nakamichi⁴ · Yuki Uchiyama³ · Seiki Hasegawa⁴ · Kazuhisa Domen³

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Abstract

Purpose According to reports, patients with lung cancer have decreased pulmonary function and exercise capacity after surgery. However, to date, physical function and health-related quality of life (HRQOL) after surgery for malignant pleural mesothelioma (MPM) have not been evaluated in detail in the convalescent phase. This study aimed to assess physical function and HRQOL of MPM patients following pleurectomy/decortication (P/D) in the convalescent phase.

Methods The study included 16 male MPM patients who underwent P/D between September 2014 and August 2016. Physical function was assessed based on handgrip and knee extensor strengths, the six-minute walk distance (6MWD), and pulmonary function, including forced vital capacity (FVC) and forced expiratory volume in one second (FEV1). HRQOL was assessed using the Medical Outcome Study 36-item Short Form Health Survey (SF-36). The assessment was performed preoperatively, postoperatively, and 1-year after surgery.

Results The 6MWD, FVC, and FEV1 values 1-year postoperatively improved significantly compared with baseline ($P < 0.05$ all). Additionally, the scores of six of the eight SF-36 domains were significantly improved 1 year after P/D: physical functioning, body pain, general health, vitality, social functioning, and mental health (all $P < 0.05$). 6MWD, FVC, and FEV1 were correlated with vitality, mental health, and physical functioning ($P < 0.05$ all).

Conclusions Patients with MPM who underwent P/D showed improved physical function and HRQOL compared with postoperative values in the convalescent phase. Physicians, nurses, and rehabilitation staff should note these findings, which may provide insight into the development of customized rehabilitation strategies in the convalescent phase for such patients.

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

✉ Takashi Tanaka
pt-tana@hyo-med.ac.jp

Shinichiro Morishita
morishita@nuhw.ac.jp

Masaki Hashimoto
masaki-h@hyo-med.ac.jp

Toru Nakamichi
trnkmc@hyo-med.ac.jp

Yuki Uchiyama
yutti@hyo-med.ac.jp

Seiki Hasegawa
hasegawa@hyo-med.ac.jp

Kazuhisa Domen
kdomen@mac.com

¹ Department of Rehabilitation Medicine, Hyogo College of Medicine Hospital, 1-1 Mukogawa-cho, Nishinomiya, Hyogo 663-8501, Japan

² Institute for Human Movement and Medical Sciences, Niigata University of Health and Welfare, Niigata, Japan

³ Department of Rehabilitation Medicine, Hyogo College of Medicine, Nishinomiya, Japan

⁴ Department of Thoracic Surgery, Hyogo College of Medicine, Nishinomiya, Japan

Introduction

Malignant pleural mesothelioma (MPM) is an aggressive tumor arising from the mesothelial cells lining the pleura [1]. More than 80% of MPM cases are associated with occupational exposure to asbestos [2]. Treatment focuses on surgery combined with radiation and/or chemotherapy in a multimodal approach [3–5]. There are two surgical procedures for the treatment of MPM according to the IASLC classification: (i) extrapleural pneumonectomy (EPP) which is defined as the complete, en bloc, removal of the whole lung, including the parietal and visceral pleura, diaphragm, and pericardium and (ii) extended pleurectomy/decortication (P/D) which is similar to EPP but spares the lung in order to obtain a macroscopic resection of the tumor (pulmonary-sparing surgery with removal of the parietal and visceral pleura) [3, 5, 6]. P/D is theoretically less radical than EPP and is associated with less perioperative mortality/morbidity and less postoperative deterioration of cardiopulmonary function [3].

Previously, we reported that in patients undergoing P/D, postoperative exercise tolerance and pulmonary function were significantly lower than preoperative values in the acute phase [7]. Moreover, our previous study showed a decrease in the health-related quality of life (HRQOL), particularly in the physical components, after P/D. A previous study demonstrated that the six-minute walking distance (6MWD) improved from 2 weeks postoperatively and was comparable with preoperative values after 6 months. However, pulmonary function remained significantly decreased postoperatively [8].

In another previous study, at 12 months after EPP, a significant deterioration was noted in pulmonary function, exercise tolerance, and HRQOL. For HRQOL, this deterioration was predominant in the physical components [9].

Although there are a few reports concerning pulmonary function and the HRQOL after EPP or P/D [10–12], to our knowledge, there are no reports concerning physical function after EPP or P/D. Furthermore, no study has investigated physical function, pulmonary function, or QOL 1 year after P/D. Clarifying the characteristics of the change in physical function and QOL in the maintenance phase after a surgery seems useful for rehabilitation program planning during this period.

Thus, this study aimed to assess the physical function and HRQOL before, after, and 1 year after MPM surgery in patients undergoing P/D, and to assess how physical function and HRQOL are affected by the response to surgery.

Subjects and methods

Design

This was a prospective observational study. The study was approved by the Hyogo College of Medicine Institutional

Committee on Human Research. Written informed consent 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

Sixteen MPM patients who underwent P/D between September 2014 and August 2016 were recruited from the Hyogo College of Medicine Hospital, Nishinomiya, Hyogo, Japan. Before the surgery, the patients were assessed for handgrip and knee-extensor strength, submaximal exercise capacity based on 6MWD, forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and HRQOL using the Medical Outcome Study 36-item Short Form Health Survey (SF-36).

Physiotherapy

Physiotherapy was promptly commenced 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. This intervention is standard of care for mesothelioma patients after pleurectomy in Japan. After leaving the hospital, there was no rehabilitation intervention.

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 the grip strength of both hands were measured. The 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 the tester held when applying resistance. The HHD was used in the manual mode using kgf units. A previous study showed that the intraclass correlation coefficients (ICC) were 0.98 with a belt and 0.04 without a belt [13]. In a reliability test-retest of the belt-restrained HHD, ICCs ranged from 0.94 to 0.96 [14]. 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 conducted for 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 [15]. 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 experienced symptoms of dyspnea or leg pain [16]. 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 [17].

Pulmonary function

Pulmonary function was assessed with spirometry (Minato Autospiro AS-302; Minato Medical Science Co., Ltd., Osaka, Japan) and was measured in accordance with the American Thoracic Society guidelines [18]. FVC and FEV1 were expressed in liters.

Health-related quality of life

HRQOL was assessed with the SF-36 by the direct questioning of the subjects. Thus, those who were too confused or too dysphasic to answer were excluded. This self-administered questionnaire has been widely used and validated in the Japanese general population [19, 20] 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 (RE), and mental health (MH). 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 \pm standard deviation or median with interquartile range. Repeated-measure analysis of variance was used to compare continuous data (BMI, handgrip, knee extensor muscle strength, 6MWD, FVC, FEV1, preoperative, postoperative, and 1-year postoperative scores of the 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), and the correlation between the eight SF-36 domains and physical-lung function (body weight, handgrip and knee extensor muscle strength, 6MWD, FVC, and FEV1) were analyzed using Pearson's correlation coefficient. Statistical analysis was performed with SPSS 17.0J (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. Sixteen patients with MPM (16 men) underwent P/D between September 2014 and August 2016. The disease stage at surgery was I in 12 patients (75%), II in 3 patients (19%), and III in 1 patient (6%). The median duration of disease was 4 (range, 3–6) months. The number of chemotherapy cycles received before P/D was 3 in all patients.

Physiological variables

The body weight, muscle strength, and submaximal exercise capacity data of the patients are summarized in Table 2. The postoperative body weight was significantly lower compared with preoperative values ($P = 0.008$). The body weight 1-year postoperatively was higher than postoperative values and lower than preoperative values; however, these differences were non-significant. For muscle strength values (handgrip and knee extension), postoperative values after surgery were lower compared with preoperative values, while values 1 year after surgery were higher than the postoperative values and lower than the preoperative values; however, all the noted differences were non-significant. The postoperative submaximal exercise capacity was significantly lower compared with the preoperative ($P < 0.001$) and 1-year postoperative ($P < 0.001$) values. No significant difference was noted

Table 1 Patient baseline data ($n = 16$)

Characteristics	
Age(years)	63 (51–77)
Weight(kg)	69.2 (11.7)
Height(m)	1.67 (0.07)
Body mass index(kg/m ²)	24.6 (2.9)
Sex	
Men	16(100%)
Disease stage at surgery	
I	12 (75%)
II	3 (19%)
III	1 (6%)
Affected side	
Right	8 (50%)
Left	8 (50%)
Duration of disease(month)	4 (3–6)
Number of chemotherapy cycles	3 (3–3)

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

between 1-year postoperative and preoperative submaximal exercise capacity ($P = 0.441$).

Pulmonary function

The pulmonary function data are summarized in Table 2. Postoperative FVC and FEV1 were significantly lower compared with preoperative values ($P < 0.001$ both). FVC and FEV1 1-year postoperatively were significantly higher than preoperative values ($P < 0.001$ both). FVC and FEV1 1-year postoperatively were significantly lower compared with the preoperative values ($P < 0.001$ and $P = 0.02$, respectively).

Health-related quality of life

HRQOL data are summarized in Table 3. Compared with preoperative values, postoperative RP, BP, GH, VT, RE, and

physical component summary scores decreased significantly, while changes in scores in other domains were not statistically significant. Compared with the postoperative period, significant increases were noted 1-year postoperatively in the PF, BP, GH, VT, SF, physical component summary scores, and mental component summary scores, while changes in the scores in other domains were not statistically significant. There was no significant difference in domain scores between the preoperative and 1-year postoperative period.

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

The correlations between physical function, lung function, and HRQOL, with respect to the differences between these values in the preoperative, postoperative, and 1-year postoperative periods are presented in Table 4.

Regarding the difference between the preoperative and postoperative values, knee extension was correlated with GH. Considering the difference between the preoperative and 1-year postoperative values, knee extension was correlated with GH, VT, MH, and mental component summary scores, FVC was correlated with VT, SF, and MH, while FEV1 was correlated with VT, MH, and mental component summary scores.

Discussion

Our results showed that patients who underwent P/D surgery had a significantly lower postoperative exercise capacity compared with preoperative values. However, 1 year later, their exercise capacity markedly improved compared with postoperative values. In addition, we found that these patients had a significantly lower postoperative body weight, lung function, and HRQOL compared with preoperative values. Moreover, 1 year later, their lung function showed marked improvement compared with postoperative values. We also found correlations between physical function,

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

Physiological variables	Before P/D ($n = 16$)	After P/D ($n = 16$)	1 year after P/D ($n = 16$)	P (Before vs after)	P (After vs 1 year after)	P (Before vs 1 year after)
Body weight (kg)	69.2 (11.7)	66.2 (11.5)	68.5 (12.7)	0.008	0.061	0.680
Hand grip (kgf)	35.2 (7.1)	33.4 (7.7)	34.9 (8.5)	0.290	0.439	0.954
Knee extension (kgf)	41.9 (14.3)	37.3 (13.0)	39.1 (11.3)	0.710	0.636	0.360
6MWD (m)	457.1 (70.7)	356.8 (78.0)	475.4 (59.5)	< 0.001	< 0.001	0.441
FVC (L)	3.53 (0.91)	1.93 (0.40)	2.51 (0.65)	< 0.001	< 0.001	< 0.001
FEV1 (L)	2.65 (0.65)	1.59 (0.29)	2.00 (0.44)	< 0.001	0.002	< 0.001

Data are given as mean (standard deviation). P/D, pleurectomy/decortication; 6MWD, six-minute walk distance; FVC, forced vital capacity, FEV1, forced expiratory volume in one second

Table 3 Health-related quality of life

SF-36 domain	Before P/D (n = 16)	After P/D (n = 16)	1 year after P/D (n = 16)	P (Before vs after)	P (After vs 1 year after)	P (Before vs 1 year after)
Physical functioning	84.4 (12.8)	61.6 (21.3)	80.6 (10.5)	< 0.001	0.001	0.727
Role-physical	65.6 (22.4)	46.5 (26.7)	59.0 (23.3)	0.035	0.218	0.637
Bodily pain	67.8 (25.5)	36.9 (23.7)	62.3 (15.8)	0.001	0.004	0.732
General health	55.4 (11.8)	43.8 (12.5)	52.8 (15.2)	0.002	0.015	0.657
Vitality	56.3 (16.6)	43.4 (13.0)	57.0 (17.7)	0.025	0.017	0.986
Social functioning	66.4 (24.5)	51.6 (23.7)	70.3 (27.0)	0.073	0.019	0.820
Role-emotional	69.3 (26.1)	50.5 (24.8)	65.6 (24.1)	0.034	0.102	0.866
Mental health	63.1 (17.0)	52.8 (14.5)	70.9 (15.2)	0.083	0.001	0.227
Physical component summary	43.7 (9.3)	25.0 (14.3)	39.6 (7.4)	< 0.001	0.001	0.505
Mental component summary	47.5 (7.9)	43.8 (5.9)	50.7 (10.1)	0.337	0.030	0.431

Data are given as mean (SD). *SF-36*, short form 36; *P/D*, pleurectomy/decortications. Higher scores indicate better quality of life; domain scores range from 0 to 100

lung function, and HRQOL, considering the differences between the preoperative, postoperative, and 1-year postoperative values.

A previous study of patients with MPM undergoing EPP reported that physical and respiratory function changed during the convalescent phase [9]. Another study reported a

deterioration of global QOL, particularly when focusing on disease-related pain and physical role functioning at 3 months after surgery; the results worsened after 12 months [21]. However, our results are not consistent with those of previous studies. Reasons for this may be that P/D preserves the lung

Table 4 Correlations between health-related QOL and physical function

		General health			Vitality			Social functioning			Mental health			MCS		
		Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ
		pre- post	post- 1 year	pre- 1 year	pre- post	post- 1 year	pre- 1 year	pre- post	post- 1 year	pre- 1 year	pre- post	post- 1 year	pre- 1 year	pre- post	post- 1 year	pre- 1 year
Body weight	Δ pre-post Δ post-1 year Δ pre-1 year															
Hand grip	Δ pre-post Δ post-1 year Δ pre-1 year															
Knee ext	Δ pre-post Δ post-1 year Δ pre-1 year	.647**														
6MWD	Δ pre-post Δ post-1 year Δ pre-1 year		.511*													
FVC	Δ pre-post Δ post-1 year Δ pre-1 year						-.618*						-.604*			-.501*
FEV1	Δ pre-post Δ post-1 year Δ pre-1 year						.527*			.58- 8*			.531*			.587*
							.570*						.587*			.512*

QOL, quality of life; Δ, delta, represents the difference preoperation, postoperation, and 1 year after operation; PCS, physical component summary; MCS, mental component summary; *Knee ext*, knee extension; *6MWD*, six-minute walk distance; *FVC*, forced vital capacity; *FEV1*, forced expiratory volume in one second

Statistical analysis using Pearson’s correlation coefficient

Only significant correlation coefficients are presented. “Physical functioning,” “role-physical,” “bodily pain,” “role-emotional,” and “PCS” were not statistically significant correlations. These columns were removed from the table

parenchyma and does not markedly disrupt the patient's daily activities. Many patients continue MPM management while working, so their levels of daily activities are maintained.

This, to our knowledge, is one of the few studies to evaluate physical function and QOL before, after, and 1 year after the surgery of MPM patients who underwent P/D, and which assessed how physical function and QOL are affected by response to surgery in the acute and convalescent phases.

We used the 6MWD as an easily obtainable measure of submaximal exercise capacity. The 6MWD results may reflect the patient's ability to perform activities of daily living [15, 22]. An increase in pulmonary function could be a reason for an increase in 6MWD. A previous study reported that a significant improvement in 6MWD was correlated with the improvement of ventilatory function after lung resection [23]. Therefore, reduced 6MWD values after surgery should be a good indicator of the risk for postoperative pulmonary complications [24]. Timmerman et al. [25] found that 6MWD was increased by 3.1% compared with preoperative values at 6 months after resection. Our findings are similar in that the postoperative submaximal exercise capacity was increased by 3.9% compared with preoperative values (Table 2). In our previous study, 6MWD values were associated with FVC values [7]. Thus, it was considered that surgical invasion of the lung had an influence on the postoperative submaximal exercise capacity.

However, we found no differences in skeletal muscle power between the preoperative, postoperative, and 1-year postoperative values 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. [26], who reported that changes in quadriceps strength from baseline were not significant after lung resection. Concerning physical function, our findings suggest that P/D has a greater effect on the submaximal exercise capacity than on skeletal muscle strength.

In this study of patients who underwent P/D, the postoperative pulmonary function test results were significantly lower compared with preoperative values. Moreover, the 1-year postoperative values were significantly higher than the postoperative values, consistent with previous lung lobectomy reports [27–29]. In addition, Nunes et al. [30] found that FVC and FEV1 were decreased by 10.1% and 23.9%, respectively, compared with preoperative values. 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 [31]. It could be hypothesized that similar complications may also affect postoperative pulmonary function in patients who undergo P/D.

An important consideration is the QOL during and after treatment; however, there are few reports on this problem in the acute phase after P/D [1]. In this study, all SF-36 domains showed a deterioration after P/D. However, 1 year after surgery,

all SF-36 domains improved to preoperative levels. In particular, mental components tended to improve compared with physical components. In a previous study, the physical components tended to improve compared with mental components at 12 months following surgery in patients undergoing EPP [21]. We found that HRQOL was significantly associated with lung function 1 year after P/D. Concerning HRQOL, our findings suggest that P/D has a greater effect on the mental component than on the physical components in the convalescent phase.

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 will be necessary to recruit a larger number of patients and perform a multivariate analysis of the data. Second, this was not an interventional study; therefore, we could not estimate causality regarding the effects of rehabilitation interventions (such as prehabilitation) on the outcomes measured in the current study. Third, we did not investigate the factors of poor pulmonary function of patients pre and post-operatively. Persistent poor pulmonary function after P/D is an ongoing problem in MPM patients. In order to explain the factors of poor pulmonary function, we would like to perform a multivariate analysis in a future study. Fourth, we did not investigate the effects of the type and staging of lung cancer on the recovery of physical functions and HRQOL after P/D. Moreover, it was difficult to explain their cause-and-effect relationship using the small sample size used in this study. Finally, we did not evaluate the amount of daytime physical activity and activities of daily living. Therefore, the influence of the amount of postoperative physical activity on the outcomes measured in the current study is unclear.

In conclusion, patients with MPM who underwent P/D demonstrated improved physical function and HRQOL compared with postoperative values in the convalescent phase. Physicians, nurses, and rehabilitation staff should note these findings, which may provide insight into the development of customized rehabilitation strategies in the convalescent phase for patients with MPM who undergo P/D.

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Compliance with ethical standards

The study was approved by the Hyogo College of Medicine Institutional Committee on Human Research. Written informed consent was obtained from all participants.

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

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