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Evaluation of predictive factors related to the presence or absence of supplemental oxygen therapy and comparison of physical functions after video-assisted thoracic surgery

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ABSTRACT

We performed a retrospective study of 102 individuals to evaluate predictive factors for needing supplemental oxygen therapy following video-assisted thoracic surgery (VATS) and to compare patients' physical functions before and after surgery. Prior to surgery, we evaluated quadriceps torque, 6-minute walk distance (6MWD), timed up and go test, and grip strength. During the 6MWD, patients' oxygen saturation was recorded every minute. Quadriceps torque and 6MWD were evaluated again following surgery. The indication for supplemental oxygen therapy was determined based on desaturation (<85%) during the 6MWD in room air. A total of 14 patients needed oxygen therapy at discharge (group A), while 88 patients did not need oxygen therapy (group B). In group A, the postoperative 6MWD was repeated with supplemental oxygen. Compared with the same parameters in group B, in group A the percentage diffusing capacity for carbon monoxide was significantly lower (p=0.011), while a history of smoking (p=0.016), exercise-induced hypoxemia (EIH, p<0.001), chronic obstructive pulmonary disease (p<0.001), and interstitial pneumonia (p=0.008) were significantly higher. Logistic regression analysis showed that EIH was an independent risk factor for requiring supplemental oxygen therapy following surgery (odds ratio: 46.2, 95% CI: 9–237.1; p<0.001). In group A, patients' minimum oxygen saturation was significantly improved by oxygen administration (83.4±3.4 vs. 87.7±3.3, p=0.002), but there was no difference in walking distance (359.5±64.2 vs. 353.6±41.6, p=0.482). Our data indicate that patients should be preoperatively evaluated to predict postoperative hypoxemia and that this evaluation could complement the prediction of postoperative need for oxygen therapy.

Keywords: VATS, supplemental oxygen therapy, physical function, rehabilitation

Abbreviations:
VATS: video-assisted thoracic surgery
6MWD: 6-minute walk distance
EIH: exercise-induced hypoxemia
ANOVA: analysis of variance

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INTRODUCTION

Although the advances made in lung cancer diagnosis and treatment techniques have been impressive, lung cancer remains a leading cause of cancer-related death.[1] Lung resection is the most effective treatment for early-stage lung cancer and is commonly performed via minimally invasive video-assisted thoracic surgery (VATS) lobectomy.[2,3] VATS is superior to thoracotomy in terms of perioperative morbidity and a reduced length of hospital stay.[4,5] Many patients with lung cancer are elderly, have a history of smoking, and often have chronic respiratory disease; the increased use of VATS has enabled curative therapy for such patients, ie, those who are elderly or have poor lung function.[6,7] However, in some cases, postoperative hypoxemia occurs following lung resection, and supplemental oxygen therapy might be necessary. For this reason, it is useful to predict, prior to surgery, the characteristics of patients who may need postoperative supplemental oxygen therapy. In general, the range of resected lung is predictive of the postoperative decline in lung function.[8] However, predicting the need for postoperative oxygen therapy based on preoperative physical function has not been evaluated. Furthermore, the difference in postoperative physical function with or without supplemental oxygen therapy has not been sufficiently studied.

The aim of this study was to observe the postoperative course of patients who underwent VATS and for whom a preoperative evaluation was performed, to identify predictive factors related to the presence or absence of supplemental oxygen therapy, and to compare patients' physical functions before and after surgery.

MATERIALS AND METHODS

This retrospective study was conducted between April 2015 and December 2017 in patients who underwent VATS at Shiga University of Medical Science Hospital, Otsu, Japan. Although 207 patients were initially enrolled except for 3 who were transferred, data in the hospital database were incomplete for 80 patients, and 25 patients had no preoperative prescription. Therefore, a total of 102 patients were eventually recruited. All patients lived independently and none of the patients had received supplemental oxygen therapy prior to undergoing VATS.

According to our protocol, on the day prior to their surgery, all participants were informed about the role and contents of a structured, postoperative pulmonary rehabilitation program, which was to be performed by physical therapists. For the preoperative evaluation of participants, the timed up and go test (TUG) and grip strength were measured, in addition to their quadriceps torque and 6-minute walk distance (6MWD). The 6MWD was performed according to the standardized procedure of the American Thoracic Society (ATS).[9] During the 6MWD, participants' oxygen saturation value was recorded every minute (PALSOX-300, KONICA MINOLTA Co., Tokyo, Japan), and their exercise-induced hypoxemia (EIH) was determined when their oxygen saturation reached 90% or less.[10] Isometric quadriceps torque was measured using an isometric dynamometer (Isoforce GT-360, OG Wellness Co., Okayama, Japan). The quadriceps torque was divided by the length of the lower limb (Nm). TUG was measured from an initial position seated on a 40 cm-high armrest chair; the patient rose at a signal, walked around a pole 3-m away, and returned to their seat.[11] Grip strength was measured using a digital grip force meter manufactured by Takei Instrumentation Industry (Tokyo, Japan). Patients' basic information at hospital admission, including preoperative lung function and comorbidities, was collected from their medical records (Table 1).

All patients underwent scheduled surgeries. As soon as the participants were clinically stable and adequate pain control was confirmed, early postoperative rehabilitation in the ward was started on postoperative day 1. From postoperative day 2, participants with no complications were started on postoperative aerobic exercise training and quadriceps resistance training in the rehabilitation room. This training continued until the time they were discharged from hospital. Patients' postoperative evaluation (quadriceps torque and 6MWD) was performed one or two days before their scheduled discharge. Quadriceps torque and the 6MWD were selected for postoperative revaluation, which were useful and effective evaluation methods for VATS cases.[12] When hypoxemia was exacerbated following surgery, we discussed indications for oxygen therapy. The criterion for oxygen supplementation used by our hospital is an oxygen saturation of less than 85% during the 6MWD in room air, which is based on the Japanese standards.[13] An oxygen saturation of between 85% and 90% during the 6MWD test was comprehensively determined based on a patient's background and their degree of comorbidities. Participants were divided into two groups: 14 patients who received supplemental oxygen therapy (group A) and 88 patients who did not receive supplemental oxygen therapy (group B) at discharge. Patients in group A were considered to need supplemental oxygen therapy, so their 6MWD the next day was performed with the amount of oxygen prescribed by the doctor (oxygen flow rate 2.2±0.9 L). The physical therapist performed evaluation by oxygen saturation to ensure their safety and the 6MWD was discontinued when a patient demonstrated exacerbation of clinical symptoms.

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki, as reflected in a priori approval by the clinical research ethical committee of our hospital (approval number: 29-286). Participants' informed consent was obtained in the form of opt-out.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics 22 (IBM, New York, NY, USA). Results were considered statistically significant if the two-tailed P-value was less than 0.05. Data are shown as means ± standard deviation (SD), except for non-normally distributed variables, which are shown as medians. Based on whether supplemental oxygen therapy was provided, baseline comparisons between patient information, comorbidities, lung function (vital capacity and forced expiratory volume in 1 second using predicted values to adjust for disproportionate physique), and physical function were performed using the Mann–Whitney U test or the chi-square test after examining normally distributed variables using the Shapiro–Wilk test. Range of resection and surgical procedures were performed chi-square test after cross-tabulation. The oxygen saturation values recorded every minute during the 6MWD were examined by repeated one-way analysis of variance (ANOVA) and the Bonferroni test. Following adjustments for the range of resection and surgical procedures, a logistic regression analysis using independent variables with significant differences (percentage diffusing capacity for carbon monoxide, %DLCO; EIH; history of smoking; chronic obstructive pulmonary disease, COPD; and interstitial pneumonia, IP) was taken as a comparison between groups involved in supplemental oxygen therapy and to estimate odds ratios and their 95% confidence intervals. Preoperative and postoperative changes in 6MWD and isometric quadriceps torque were determined using a two-way ANOVA to determine the main effects and interactions (period, before and after surgery; group, presence or absence of supplemental oxygen therapy). Finally, we performed 6MWD using supplemental oxygen therapy for patients who were decided to introduce supplemental oxygen therapy and compared their minimum oxygen saturation and walking distance using a paired t-test.

Table 1 Baseline characteristics of the patients at the time of hospitalization

	All patients (n=102)
Age (years)	72.4 ± 8.4
Sex (Men, %)	73 (71.6)
Height (cm)	161.8 ± 8.5
Weight (kg)	58.9 ± 10.4
Body mass index (kg/m^2)	22.5 ± 3.4
Pulmonary function	
VC (L)	3.2 ± 0.7
%VC (%)	99.4± 15.1
FEV1 (L)	2.2 ± 0.6
%FEV1 (%)	88.1 ± 19.7
FEV1/FVC (%)	70.5 ± 12.1
%DLCO (%)	95.5 ±30.2
Physical function	
6MWD (m)	463.4 ± 81.0
Quadriceps torque (Nm)	94.9 ± 34.1
Grip strength (kg)	29.4 ± 7.5
TUG (seconds)	7.6 ± 2.1
Comorbidities	
Diabetes (n, %)	30 (29.4)
Hypertension (n, %)	46 (45.1)
COPD (n, %)	16 (15.7)
IP (n, %)	6 (5.9)

Characteristics of participants are shown as mean ± SD for parametric data.
FVC: forced vital capacity
VC: vital capacity
FEV: forced expiratory volume
DLCO: diffusing capacity for carbon monoxide
6MWD: 6-minutes walk distance
TUG: timed up and go test
COPD: chronic obstructive pulmonary disease
IP: interstitial pneumonia

RESULTS

Surgical and oncological data, postoperative complications, surgery time, and postoperative hospital stay are shown in Table 2. There was no exacerbation of clinical symptoms during the 6MWD for any patients. For the trend of oxygen saturation during the 6MWD, patients in both groups A and B showed a significant decrease in oxygen saturation during the 6MWD at every 1-minute interval compared with when they were at rest. However, it was noteworthy during the 6MWD of the preoperative evaluation, the group that received supplemental oxygen therapy showed a significant decrease in oxygen saturation within 2 minutes of the start of the test, and this tendency became even more marked following surgery (Fig. 1).

The %DLCO was significantly lower in group A than in group B ($p=0.011$). EIH ($p<0.001$), a history of smoking ($p=0.016$), COPD ($p<0.001$), and IP ($p=0.008$) were significantly higher in group A than in group B (Table 3). Logistic regression analysis showed that EIH was an independent risk factor for requiring supplemental oxygen therapy following surgery (odds ratio 46.2, 95% CI: 9–237.1; $p<0.001$). Based on the two-way ANOVA, 6MWD showed a main effect, but interaction did not show. Quadriceps torque did not show either a main effect or any interactions (Table 4). Following surgery, 6MWD was performed with or without oxygen therapy in patients in group A, and their minimum oxygen saturation was significantly improved following oxygen administration (83.4±3.4 vs. 87.7±3.3, $p=0.002$); however, there was no difference in their walking distance (359.5±64.2 vs. 353.6±41.6, $p=0.482$, Fig. 2).

Table 2 Characteristics of video-assisted thoracic surgery (VATS) and post-surgery information for patients with lung cancer

	All patients (n=102)
Stage of lung cancer (n)	
IA/IB/IIA/IIB/IIIA/IIIB	65/16/9/5/6/1
surgical procedures (n, %)	
RUL	36 (35.3)
RML	7 (6.9)
RLL	16 (15.7)
LUL	26 (25.5)
LLL	17 (16.7)
Range of resection (n, %)	
Wedge resection	18 (17.6)
Segmentectomy	10 (9.8)
Lobectomy	74 (72.5)
Surgery time (minutes)	271.5 ± 120.1
Postoperative complications	
Paf (n, %)	15 (14.7)
Pneumonia (n, %)	4 (3.9)
Postoperative hospital stay (day)	
Median (IQR)	8.0 (6.0–10.0)

Characteristics of the participants are shown as mean ± SD for parametric data, and median for non-parametric data.
RUL: right upper lobectomy
RML: right middle lobectomy
RLL: right lower lobectomy
LUL: left upper lobectomy
LLL: left lower lobectomy
Paf: paroxysmal atrial fibrillation
IQR: interquartile range

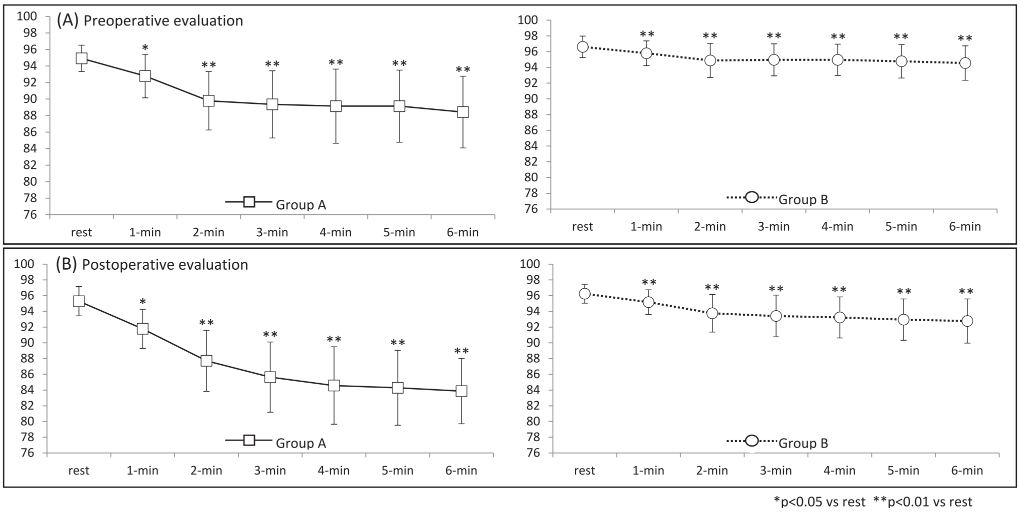

Fig. 1 Changes in oxygen saturation during 6-minute walk distance in patients with or without supplemental oxygen therapy

The left vertical axis represents oxygen saturation (%) accordingly. The left figure; patients with supplemental oxygen therapy (group A, n=14). The right figure; patients without supplemental oxygen therapy (group B, n=88).

Table 3 Comparison of preoperative characteristics in patients with or without supplemental oxygen therapy

Total (n=102)	Group A (n=14)	Group B (n=88)	p Value
Age (years)	74.0±4.6 (73.5)	72.2±8.8 (73.0)	0.367
Height (cm)	164.0±5.8 (162.9)	161.5±8.9 (161.5)	0.583
Weight (kg)	58.1±7.8 (59.6)	59.0±10.7 (65.8)	0.512
%VC (%)	107.0±13.4 (105.0)	98.3±15.1 (98.6)	0.054
%FEV1 (%)	87.4±18.9 (91.0)	88.2±19.9 (91.3)	0.931
FEV1/FVC (%)	65.1±12.9 (66.4)	71.4±11.8 (73.6)	0.172
%DLCO (%)	63.5±26.1 (58.5)	100.6±27.6 (102.1)	0.011
RUL (n, %)	4 (28.6)	32 (36.4)	
RML (n, %)	0 (0)	7 (8.0)	
RLL (n, %)	4 (28.6)	13 (14.8)	0.466
LUL (n, %)	3 (21.4)	23 (26.1)	
LLL (n, %)	3 (21.4)	13 (14.8)	
Wedge resection (n, %)	2 (14.3)	16 (18.2)	
Segmentectomy (n, %)	2 (14.3)	8 (9.1)	0.908
Lobectomy (n, %)	10 (71.4)	64 (72.7)	
EIH (n,%)	8 (57.1)	4 (4.5)	<0.001
6MWD (m)	441.7±77.7 (445.0)	466.8±81.4 (470.0)	0.123
Quadriceps torque (Nm)	98.6±28.2 (100.5)	94.3±35.0 (90.0)	0.673
Grip strength (kg)	29.2±6.3 (31.2)	29.4±7.7 (29.6)	0.501

TUG (second)	7.5±2.1 (7.7)	8.0±2.1 (6.7)	0.721
History of smoking (n, %)	14 (100)	61 (69.3)	0.016
Diabetes (n, %)	4 (28.6)	26 (29.5)	0.941
Hypertension (n, %)	5 (35.7)	40 (45.5)	0.447
COPD (n, %)	9 (64.3)	7 (8.0)	<0.001
IP (n, %)	3 (21.4)	3 (3.4)	0.008

Characteristics of participants are shown as mean ± SD and median.
FVC: forced vital capacity
VC: vital capacity
FEV: forced expiratory volume
DLCO: diffusing capacity for carbon monoxide
RUL: right upper lobectomy
RML: right middle lobectomy
RLL: right lower lobectomy
LUL: left upper lobectomy
LLL: left lower lobectomy
EIH: exercise-induced hypoxemia
6MWD: 6-minutes walk distance
TUG: timed up and go test
COPD: chronic obstructive pulmonary disease
IP: interstitial pneumonia

Table 4 Results of two-way analysis of variance

Group	Group A (n=14)		Group B (n=88)		Main effect		Interaction
period	before surgery	after surgery	before surgery	after surgery	Period (p value)	Group (p value)	Period × group (p value)
6MWD (m)	441.7 ± 77.7	359.5 ± 64.2	466.8 ± 81.4	421.9 ± 76.1	p<0.001	0.006	0.241
Quadriceps torque (Nm)	98.6 ± 28.2	98.3 ± 28.5	94.3 ± 35.0	91.1 ± 35.6	0.802	0.414	0.841

Group A: patients with supplemental oxygen therapy (n=14).
Group B: patients without supplemental oxygen therapy (n=88).
6MWD: 6-minutes walk distance

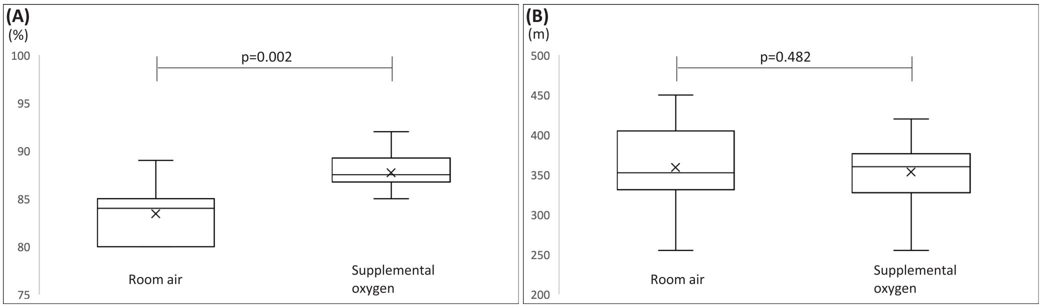

Fig. 2 Minimum oxygen saturation and walk distance during 6-minute walk distance after surgery in patients with supplemental oxygen therapy
Fig. 2A: Minimum oxygen saturation
Fig. 2B: Walk distance
(Group A, n=14)

DISCUSSION

In our study, supplemental oxygen therapy at discharge was introduced in 14 out of 102 patients (group A, 13.7%). Nicastri et al[14] suggested an oxygen therapy induction rate of 15.3%, which is supported by the results of the present study. The comorbidity rates of history of smoking, COPD, and IP were significantly higher, and %DLCO was significantly lower, in patients in group A. In addition, the EIH expression rate during the 6MWD prior to surgery was significantly higher in patients in group A. In other words, in patients with poor pulmonary function who experience hypoxemia during exertion prior to undergoing surgery, their lung function and oxygenation capacity are further reduced by resection of their lungs, and it is assumed that there is no choice but to introduce supplemental oxygen therapy. It should be noted that when EIH was observed in patients prior to surgery, the introduction of supplemental oxygen therapy was 46.2-times higher following surgery. A characteristic of oxygen saturation observed during the 6MWD prior to surgery was that oxygen saturation tended to significantly decrease in the first 2 minutes. Following surgery, the tendency of oxygen saturation to decrease became worse still. Ueda et al[15] demonstrated the importance of preoperative evaluation of hypoxemia in predicting early postoperative prognosis, and their findings are supported by the present study.

As Irie et al suggested,[12] the evaluation of quadriceps torque and 6MWD before and after lobectomy is important, so we also measured these values in our study. The results of the two-way ANOVA with two factors showed no major effects or interactions for quadriceps torque, but 6MWD had a major effect, although no interactions were observed. Surgical invasion and reduced lung function due to resected lungs are thought to be the cause of reduced exercise capacity. In a previous report[16] it was suggested that exercise capacity improves more rapidly following VATS, and the reduction rate was just 10% in patients in group B in this study. This suggests that pulmonary rehabilitation contributes to the prevention of low exercise capacity. Although no interactions were observed, the reduction rate was about 19% in patients in group A; it is speculated that it was more difficult to recover postoperative exercise capacity in patients who received supplemental oxygen therapy. At the very least, it is clear that the exacerbation of postoperative hypoxemia is involved.

Following surgery, 6MWD was performed without oxygen inhalation. The next day, 6MWD was performed again using a quantity of oxygen as determined by the doctor for patients in group A, and a comparison was made between the walking distance and the minimum oxygen saturation. As a result, the minimum oxygen saturation was seen to be significantly improved, but there was no significant difference in walking distance. Walking distance and pulmonary function during 6MWD were strictly related,[17] and oxygen therapy is considered not to supplement poor lung function. For that reason, there was no significant difference in walking distance. However, oxygen therapy is known to be a technique for supplementing oxygen deficiency, and the improvement in the minimum oxygen saturation showed that it obtained the desired effect. Therefore, when hypoxemia is exacerbated after surgery, supplemental oxygen therapy to supplement oxygen deficiency should be actively introduced. In addition, estimating the predicted lung function commensurate with the extent of lung resection is helpful in predicting postoperative oxygen therapy.[8] As in the present study, preoperative evaluation to predict postoperative hypoxemia could complement the prediction of postoperative oxygen therapy.

There are some limitations associated with the present study. First, it was performed at a single center, many cases were excluded, and open thoracotomy cases were not included. Second, differences such as complication rates and length of hospital stay were not examined. Additionally, the oxygen partial pressure in arterial blood could not be measured following the introduction of supplemental oxygen therapy. The oxygen partial pressure could be estimated from the oxygen saturation level, but the evaluation of arterial blood oxygen partial pressure could be more accurate when determining whether to introduce supplemental oxygen therapy. Third, follow-up studies were not conducted with patients in whom supplemental oxygen therapy was introduced at the time of discharge but later withdrew from supplemental oxygen therapy.

CONCLUSION

The present study evaluated factors that could be predictive of the need for induction of oxygen therapy and compared physical functions before and after surgery. EIH prior to surgery was an independent risk factor for the need to introduce oxygen therapy following surgery. Furthermore, when 6MWD was performed using oxygen inhalation, the minimum oxygen saturation was significantly improved. Therefore, when hypoxemia is exacerbated after surgery, oxygen therapy should be introduced. Our results demonstrate that preoperative evaluation of patients prior to them undergoing VATS is important and could complement the prediction of postoperative need for oxygen therapy.

CONFLICT OF INTEREST

None of the authors have any conflicts of interest to disclose.

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