Physiological rehabilitation after video-assisted lung lobectomy for cancer: a prospective study of measuring daily exercise and oxygenation capacity

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Abstract

Objective: Video-assisted thoracic surgery followed by fast-track rehabilitation has been claimed to accelerate physiological recovery after lung lobectomy for cancer; however, we are still uncertain when the exercise and oxygenation capacity recover and how to determine the rehabilitation time required by each patient. The aim of this study was to evaluate the rehabilitation time after this type of surgery and determine the best predictors of rehabilitation time. Methods: We measured exercise and oxygenation capacity daily during the perioperative period on a prospective series of 40 patients who had scheduled to undergo video-assisted lung lobectomy for cancer. Postoperative rehabilitation was confirmed when patients had regained more than 80% of their baseline exercise capacity and more than 98% of their baseline oxygenation capacity without the use of routine tubes for oxygen supplementation, fluid transfusion, bladder catheterization, chest drainage, and epidural catheterization. The hypoxemia index, which we found to have correlated with early-postoperative oxygenation capacity, was calculated preoperatively using baseline arterial oxygen saturations and the severity of emphysema on computed tomography.

Results: The median rehabilitation time was 3 days. Stepwise Cox regression analysis revealed that the postoperative predicted forced expiratory volume in 1 s (relative ratio 1.043, \( p < 0.01 \)) and the hypoxemia index (relative ratio 1.343, \( p = 0.02 \)) were the best independent determinants of the postoperative rehabilitation time.

Conclusions: By conducting daily physiological assessments, we identified the rehabilitation time and its determinants in patients who underwent video-assisted lung lobectomy for cancer. Our results are valuable for planning patient-specific fast-track surgery in the hospital setting.

Keywords: Pulmonary resection; Lung cancer; Recovery; Rehabilitation; Fast-track surgery

1. Introduction

For patients with clinical stage I lung cancer, video-assisted lung lobectomy followed by fast-track rehabilitation has become one of a standard therapeutic strategy [1—3]. Although some patients recover quickly and are discharged from hospital within a couple of days [2], the length of stay after this type of surgery varies individually and depends largely on how long normalization of lung function takes; including ventilation, gas exchange, and exercise capacity. It remains uncertain when these capacities recover and what factors determine the corresponding rehabilitation time because until now, postoperative functional assessment has only been done on a fixed postoperative day [3—5].

To resolve this issue, we performed a prospective study of the perioperative daily assessment of gas exchange capacity and exercise capacity in patients undergoing video-assisted lung lobectomy for clinical stage I lung cancer. Our findings may contribute to the establishment of selection criteria for fast-track surgery in patients with resectable lung cancer, and to the counselling of patients at increased risk of prolonged hospitalization.

2. Materials and methods

2.1. Patients

The subjects of this study were 40 consecutive patients scheduled to undergo video-assisted lung lobectomy for clinical stage I lung cancer at our hospital between October...
2003 and October 2004. This study was approved by the institutional review board of the Yamaguchi University School of Medicine. Operability was determined according to the existing guidelines for pulmonary resection [6]. Criteria for resection included a partial pressure of arterial carbon dioxide (PaCO₂) ≤ 50 mmHg, a mean pulmonary arterial pressure < 30 mmHg, and a calculated predicted postoperative forced expiratory volume in 1 s in percentage of the predicted value > 30%. Patient data evaluated preoperatively included age, sex, smoking habits, spirometric variables, arterial blood gas values, 6-min walking distance, and the proportion of low-attenuation areas (%LAA) on computed tomography (CT). Smoking data included pack years smoked (smoking index; average number of packages of cigarettes smoked per day multiplied by the number of years smoked). The %LAA was determined by measuring the low-attenuation areas and the total lung area on a CT scan, as described below. Our previous study showed that early-postoperative oxygenation capacity after pulmonary resection can be predicted by the baseline oxygenation capacity and the %LAA [7]. Based on these results, we defined a new parameter, the hypoxemia index, which is directly proportional to the early-postoperative oxygenation capacity; calculated as: hypoxemia index = saturation of arterial oxygen (SaO₂) – 0.14 × %LAA.

The patients’ characteristics are summarized in Table 1. The mean smoking index was 39 ± 38 pack years (range, 0–180 pack years), and the mean number of resected segments was 4.1 ± 1.2. Twenty patients complained of slight breathlessness preoperatively, defined by the inability to keep up on hills or stairs with healthy persons of equivalent age [8], and 17 patients were restricted by physically strenuous activity (Eastern Cooperative Oncology Group-performance status grade 1 [9]).

### 2.2. Preoperative pulmonary assessment

Spirometric variables were obtained within the preoperative month and included vital capacity (VC) and forced expiratory volume in 1 s (FEV₁). Arterial blood gases (PaO₂, PaCO₂) were measured within 5 min after sampling in patients resting and breathing room air. Predicted postoperative FEV₁ was calculated using Nakahara’s formula [10]; namely, FEV₁ppo = FEV₁[1 – (b – n)/(42 – n)], where n is the number of obstructed subsegments, and b is the total number of removed subsegments. The total number of pulmonary subsegments is 42, with 10 each in the left upper lobe and the left lower lobe, 6 in the right upper lobe, 4 in the right middle lobe, and 12 in the right lower lobe. The n-value was calculated from the findings of preoperative bronchoscoppy or CT. The VC, FEV₁, and FEV₁ppo are expressed as percentages of the predicted values for age, gender, and height.

#### 2.3. Operation

After establishing single-lung ventilation, the patient was flexed in the lateral decubitus position. We inserted a thoracoscope through the seventh or eighth intercostal space in the midaxillary line. We made an anterolateral minithoracotomy, 6–8 cm long, in the fifth intercostal space. Rib spreading was done only when the intercostal space was not wide enough for the resected specimen to fit through. One or two additional 5- to 10-mm incisions were made in the posterior axillary line to allow the insertion of instruments. During anatomic resection, we used an endoscopic stapler (Ethicon, Tokyo, Japan) to divide the lung parenchyma and incomplete fissures, and excise the bronchi. The pulmonary arteries or veins were also divided by endoscopic stapler if the diameter of the vessels was greater than 3 mm. After anatomic resection and mediastinal lymphadenectomy, we performed a water-seal test to ensure pneumostasis. Suture lines were not buttressed, but evident pulmonary fistulae were closed with sutures and sealed with fibrin glue. A 20F chest tube was placed in the hemithorax, and the wounds were closed.

#### 2.4. Assessment of oxygenation capacity

Arterial blood gases were analyzed within the first 24 h after surgery, 20 min after supplementary oxygen was discontinued. Additional oxygen was given via a face mask during the first postoperative night. Arterial oxygen saturation (SaO₂) was calculated by the Kelman’s formula [11]. Daily arterial blood gas analysis continued until the SaO₂ had recovered to more than 98% of the baseline value.

#### 2.5. Assessment of exercise capacity

The 6-min walking distance was measured using a standardized protocol [12] and the 6-min walking capacity was evaluated daily until it had recovered to more than 80% of the baseline value.

#### 2.6. CT technique and measurement of %low-attenuation area

CT scans were done using a four detector-row CT scanner (Siemens Volume Zoom, Siemens-Asahi Medical Ltd., Tokyo, Japan). With the patient in the supine position, high resolution

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**Table 1**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number of patients or mean ± SD (median)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66.9 ± 12 (69.5)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>24/16</td>
</tr>
<tr>
<td>Breathlessness (yes/no)</td>
<td>7/33</td>
</tr>
<tr>
<td>ECOG-PS (0/1)</td>
<td>31/9</td>
</tr>
<tr>
<td>Smoking history (yes/no)</td>
<td>24/16</td>
</tr>
<tr>
<td>Resected subsegments</td>
<td>7.4 ± 4.1 (7)</td>
</tr>
<tr>
<td>Six-minute walking distance (m)</td>
<td>354 ± 84 (360)</td>
</tr>
<tr>
<td>PaO₂ (mmHg)</td>
<td>79.7 ± 7 (79.0)</td>
</tr>
<tr>
<td>PaCO₂ (mmHg)</td>
<td>41 ± 2.1 (41)</td>
</tr>
<tr>
<td>VC (%)</td>
<td>107 ± 16 (107)</td>
</tr>
<tr>
<td>FEV₁ (%)</td>
<td>72.6 ± 11 (71.5)</td>
</tr>
<tr>
<td>FEV₁ppo (%)</td>
<td>60.1 ± 13 (58.5)</td>
</tr>
<tr>
<td>%LAA (%)</td>
<td>6.57 ± 7.6 (3.1)</td>
</tr>
<tr>
<td>Hypoxemia index</td>
<td>94.5 ± 1.7 (94.7)</td>
</tr>
</tbody>
</table>

Breathlessness, inability to keep up on hills or stairs; ECOG-PS, European Cancer Organization Group-performance status; VC, vital capacity; FEV₁, forced expiratory volume in 1 s; FEV₁ppo, predicted postoperative FEV₁; %LAA, extent of low-attenuation areas (below –910 HU) on computed tomography; hypoxemia index = saturation of arterial oxygen – 0.14 × %LAA.
CT images covering the entire lungs were obtained in 512 \times 512 matrix during deep inspiratory breath-hold, using 10-mm collimation, with a scan time of 1.5 s, at 120—140 kVp, 280—320 mA. Transaxial CT images were reconstructed with the lung algorithm. To evaluate the distribution of emphysematous areas in each patient, we created volume-rendering three-dimensional density-masked images, which highlighted the lung areas with attenuation values lower than −910 HU, representative of emphysematous lung areas, using the imaging software M900 QUADRA (Zio Soft K.K., Osaka, Japan). Threshold limits of −600 to −1024 hounsfield units (HU) were applied to segment the entire lungs and to exclude soft tissues surrounding the lung and large vessels within the lung. The proportion of voxels with attenuation values lower than −910 HU within the total voxels in the entire lung was taken as the percentage of the low-attenuation area (\%LAA). The low-attenuation thresholds that have been used most often to identify emphysema on conventional 10-mm-thick CT sections are −900 or −910 HU [13—16].

2.7. Fast-track rehabilitation protocol

All patients were managed postoperatively in the following way [17]: chest tubes were removed on postoperative day (POD) 1 if no air leak was detected, regardless of pleural drainage. Oxygen support was discontinued on the morning after surgery and reintroduced only if the patient complained of dyspnea and the SaO2 was lower than 95%. Intravenous infusions were discontinued on POD1 if the patient was able to tolerate food. Urinary catheterization and epidural analgesia were discontinued on POD 1 if the patient was able to walk without assistance.

2.8. Statistical analysis

Univariate and multivariate proportional hazards analyses were used to determine the influence of preoperative variables on postoperative rehabilitation. Stepwise variable selection was used in the multivariate analyses. \( p < 0.05 \) was considered significant.

3. Results

The cumulative postoperative recovery rates, in relation to oxygenation capacity, exercise capacity, dependence on routine tubes, and all the references are shown in Fig. 1. The median times to recovery of oxygenation capacity, exercise capacity, dependence on routine tubes, and all the references were 2, 3, 2, and 3 days, respectively. Postoperative rehabilitation was defined as recovery of both oxygenation capacity and exercise capacity without dependence on routine tubes.

By univariate proportional hazards analysis, smoking index, VC, FEV1, FEV1ppo, %LAA, preSaO2, and hypoxemia index were identified as significant predictors of the rehabilitation time (\( p < 0.05 \) for all; Table 2). By multivariate analysis, FEV1ppo (odds ratio = 1.043, 95% CI 1.012—1.074, \( p = 0.0439 \)) and the hypoxemia index (odds ratio = 1.343, 95% CI 1.046—1.723, \( p = 0.0097 \)) were identified as the best independent determinants of postoperative rehabilitation time. The correlation between FEV1ppo and the hypoxemia index is shown in Fig. 2 (\( y = 0.46x + 91.8, r = 0.351, \rho = 0.026 \)). Based on the relative probabilities of rehabilitation for FEV1ppo and the hypoxemia index, the patients were divided into the following three groups according to a 1.043 FEV1ppo + 1.343 hypoxemia index: those with values higher than 200 (good, \( n = 12 \)), those with values between 180 and 200 (medial, \( n = 17 \)), and those with values lower than 180 (poor, \( n = 11 \)). The cumulative recovery rates for patients with good, medial, and poor pulmonary function are shown in Fig. 2. The median times to recovery for patients with good, medial, and poor pulmonary function were 2, 3, and 7 days, respectively (log-rank test, \( p < 0.0001 \)).

Postoperative cardiopulmonary complications developed in seven patients: as lobar atelectasis in three, prolonged (more than 7 days) air leak in two, pneumonia in one, and atrial fibrillation in one. These complications occurred most frequently in patients with poor pulmonary function (\( \chi^2 \)-test, \( p < 0.0001; \) Fig. 2).

### Table 2

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds ratio</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.967</td>
<td>0.0334</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>3.416</td>
<td>0.0018</td>
</tr>
<tr>
<td>Smoking history (yes)</td>
<td>4.525</td>
<td>0.0008</td>
</tr>
<tr>
<td>Breathlessness (yes)</td>
<td>2.067</td>
<td>0.1359</td>
</tr>
<tr>
<td>ECOG-PS (1)</td>
<td>0.978</td>
<td>0.9548</td>
</tr>
<tr>
<td>Six-minute walking distance (m)</td>
<td>0.999</td>
<td>0.7369</td>
</tr>
<tr>
<td>preSaO2 (%)</td>
<td>1.322</td>
<td>0.0567</td>
</tr>
<tr>
<td>Resected subsegments</td>
<td>0.907</td>
<td>0.0352</td>
</tr>
<tr>
<td>VC (%)</td>
<td>1.010</td>
<td>0.3194</td>
</tr>
<tr>
<td>FEV1 (%)</td>
<td>1.057</td>
<td>0.0011</td>
</tr>
<tr>
<td>FEV1ppo (%)</td>
<td>1.058</td>
<td>0.0002</td>
</tr>
<tr>
<td>%LAA (%)</td>
<td>0.925</td>
<td>0.0099</td>
</tr>
<tr>
<td>Hypoxemia index</td>
<td>1.449</td>
<td>0.0012</td>
</tr>
</tbody>
</table>

preSaO2, preoperative saturation of arterial oxygen; VC, vital capacity; FEV1, forced expiratory volume in 1 s; FEV1ppo, predicted postoperative FEV1; %LAA, extent of low-attenuation areas (below −910 HU) on computed tomography; hypoxemia index = saturation of arterial oxygen − 0.14 %LAA.
assess the outcome of fast-track surgery [18], but this does not always reflect the actual rehabilitation time: some patients require additional recuperation time or readmission for treatment of late complications, whereas others might stay in hospital long after complete rehabilitation. Thus, in the present study, we assessed the postoperative rehabilitation time objectively by measuring the oxygenation and exercise capacity of each patient daily. After the establishment of physiological rehabilitation, none of our patients experienced subsequent complications, with the exception of one, who required chest tube reinsertion for a pneumothorax. Therefore, our results may contribute to establishing a case-specific hospital setting, and to counsel patients at risk of prolonged hospitalization, by dividing patients undergoing lung cancer surgery into specific subgroups according to their pulmonary function test results; namely, FEV1ppo and the hypoxemia index. Patients with good pulmonary functional reserve may require a postoperative hospital stay of only 2–3 days, whereas those with poor functional reserve would require at least 5 postoperative days to recover (Fig. 2). In addition, the risk of postoperative cardiopulmonary complication could be predicted with a sensitivity rate of 66.6% and a specificity rate of 91.2%, with a cut-off value of 50% for FEV1ppo and 94% for hypoxemia index.

Apart from the time needed for normalization of lung function, the duration of air leak may be the most critical factor for postoperative rehabilitation. In our institute, patients are easily mobilized postoperatively by using a chargeable suction device fixed on the assistant car. In fact, two of our patients recovered their exercise capacity before chest tube removal, suggesting that it may even be possible to send these patients home with their chest tube connected to a Heimlich valve. Previously, we reported that the %LAA was superior to the FEV1 for predicting air leak time, especially in patients with a smoking history [19]. Therefore, the control of an air leak in patients with a high %LAA may lead to successful fast-track surgery.

Emphysema is a pathological disease, which can be graded objectively by measuring the low-attenuation areas on a CT scan, using computer software [13–16]. This computer-assisted quantification of emphysema reflects accurately the lung pathology and the clinical features of chronic obstructive pulmonary disease [13,15,20]. Although thoracic surgeons have shown that emphysema has the most adverse effect on the early outcome of pulmonary resection, they based this conclusion on spirometric variables alone, rather than the %LAA, to grade emphysema. We previously found that the %LAA, but not FEV1, was a predictor of postoperative hypoxemia in patients undergoing lobectomy for cancer [7]. The SaO2 can be calculated on POD 1, using the following regression equation:

\[
\text{SaO}_2 \text{ on postoperative day 1} = -50 \div 1.5 \text{hypoxemia index.}
\]

\[
\text{hypoxemia index} = \frac{\text{preoperative } \text{SaO}_2 - 0.14 \% \text{LAA}}{1}
\]

In the present validation series, the hypoxemia index was dependent on the SaO2 measured on POD 1 \( (r = 0.744, p < 0.001) \). Furthermore, we found that the hypoxemia index, together with the FEV1ppo, was a significant predictor of postoperative cardiopulmonary complications (Fig. 2).
Since the hypoxemia index is calculated from routine preoperative examinations, without significant costs or labor, determining the hypoxemia index preoperatively may be indispensable for predicting the early-postoperative outcome after lung cancer surgery.

In conclusion, based on perioperative daily physiological assessment, we identified the rehabilitation time and its determinants in patients undergoing video-assisted lung lobectomy for cancer. Our results will prove valuable in planning patient-specific fast-track surgery in the hospital setting.

References