Institutional report - Pulmonary

Prediction of hypoxemia after lung resection surgery

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Abstract

Pulmonary resection under general anesthesia induces various degrees of hypoxemia that adversely impacts on postoperative recovery. Consecutive of 53 patients undergoing anatomical pulmonary resection were enrolled in this study to accurately define predictors of postoperative hypoxemia. Preoperative variables studied included spirometric variables, blood gases, and extent of low attenuation area (below −910 Hounsfield units) on a three-dimensional computed tomography lung model. Arterial oxygen saturation was calculated from arterial partial pressure of oxygen measured 1 day before and 1 day after surgery with patients at rest breathing room air. Postoperatively, the patients were managed according to a standardized regimen. According to stepwise multiple regression analysis, preoperative oxygen saturation and the extent of low attenuation area were selected as the best predictors of postoperative oxygen saturation. Regression equation was generated with these two variables. The predicted postoperative oxygen saturation was significantly dependent on the length of management (P<0.01). Using a radiographic parameter, we established a novel means of predicting postoperative hypoxemia that impacted on postoperative recovery. Because this radiographic parameter was superior to conventional spirometric variables for prediction of postoperative hypoxemia, further confirmation of its usefulness in predicting risk after pulmonary resection is warranted.

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Keywords: Quantitative CT; Pulmonary resection; Low attenuation area; Postoperative hypoxemia; Pulmonary function; Spirometry

1. Introduction

Pulmonary resection is frequently followed by a decrease in arterial oxygen that persists for many days postoperatively. This impaired gas exchange is called postoperative hypoxemia and adversely impacts on perioperative outcomes. However, little is known about factors predictive of hypoxemia after pulmonary resection. Filaire and colleagues showed that predicted postoperative forced expiratory volume in 1 s (expressed as a percentage, %FEV1ppo) was the best predictor of hypoxemia among various spirometric variables in patients undergoing major lung resection [1]. FEV1ppo is a well-known indicator of increased risk after lung resection that is determined by the baseline ventilatory capacity and the extent of lung resection, and is impaired in accordance with the progression of emphysema [2].

Emphysema is defined pathologically as an increase in size of the air-spaces distal to the terminal bronchiole, accompanied by destruction of the alveolar walls [3]. Therefore, the preoperative diagnosis of emphysema, without lung tissue biopsy, is always indirect. Pulmonary function studies rely on detecting an increase in airway resistance and a decrease in the surface area of the alveolar-capillary membrane [4,5]. These tests are relatively insensitive and nonspecific for the cause of airway obstruction. In contrast, quantitative computed tomography (CT) is recognized as an objective diagnostic technique that uses computer software to distinguish voxels with abnormally low attenuation, representing emphysema, from those of normal lung parenchyma [6,7]. According to the previous studies, this computer-assisted quantification of lung morphology more directly reflects the actual extent of emphysema than is reflected by conventional visual grading technique [6] and is more effective than pulmonary function tests in detecting early-stage emphysema [8].

In this study, we aimed to accurately predict postoperative hypoxemia and to evaluate the effect of predicted postoperative hypoxemia on postoperative recovery. Prediction of postoperative hypoxemia may help to clarify the mechanism of postoperative hypoxemia and thus to shorten hospitalization after pulmonary resection.

2. Patients and methods

During the period August 2001 to September 2003, consecutive of 53 patients that underwent anatomical pulmonary resection for diagnosed or suspected localized lung malignancy at our institution were enrolled in this study. This clinical study was approved by our institutional review board. Operability was determined according to the existing guidelines for pulmonary resection [9]. Pulmonary assess-
ment included complete history, physical examination, and pulmonary function tests. We especially regarded a PaCO₂ ≤ 50 mmHg, mean pulmonary arterial pressure < 30 mmHg, and a calculated FEV1ppo of 500 ml as requirements before resection. Patient characteristics assessed prior to surgery included age, sex, smoking habits, breathlessness, Eastern Cooperative Oncology Group-performance status, body mass index, spirometric variables, FEV1ppo, extent of low attenuation area, and preoperative arterial blood gases. In addition, we quantified the extent of low attenuation area by means of quantitative CT (described later). The study group comprised 33 men and 20 women with a mean age of 67 ± 9.5 years (range, 29 to 86 years), mean body mass index of 22 ± 2.9 kg/m² (range, 14.7 to 27.6 kg/m²), mean smoking index of 40 ± 40 pack-years (range, 0 to 180 pack years), and mean total of 3.7 resected segments (range, 1 to 7 segments).

2.1. Assessment of hypoxemia

Arterial blood gases were also studied within the first 24 h after surgery, 20 min after supplementary oxygen had been stopped. Additional oxygen was provided under prescription with a face mask during the first postoperative night. A decrease in PaO₂ is observed in a large majority of patients in the first postoperative days, so we defined hypoxemia on the basis of the patient’s PaO₂ status within the first 24 postoperative hours. In linear regression analysis of postoperative hypoxemia, PaO₂ was converted arterial oxygen saturation (SaO₂) by means of Keltan’s formula [10] because SaO₂ is linearly dependent upon arterial oxygen consumption.

2.2. CT technique and the extent of low attenuation area

CT examinations were performed with a commercially available scanner (Siemens Volume Zoom; Siemens-Asahi Medical, Tokyo, Japan) in the helical mode without intravascular contrast material. With the patient in the supine position, scans were obtained during full inspiration with the following parameters: 120–140 kVp, 280–320 mA, 10-mm collimation, and 1.5 pitch. The DICOM data were electronically transferred to the teleradiologic workstation, and the volume-rendering three-dimensional (3D) models of the lungs were reconstructed using the imaging software (M900 QUADRA, Zio Soft K.K., Osaka, Japan) (Fig. 1). Threshold limits of –600 to –1024 HU were applied to segment the lung parenchyma and to exclude soft tissues surrounding the lung and large vessels within the lung. The total number of voxels with any selected specific attenuation numbers (in HUs) in the lung model could be automatically counted by the computer. The extent of low attenuation area (%LAA) was defined as the percentage of the number of the voxels with attenuation values below –910 HU against the total voxel number of the whole lung because the low attenuation thresholds that have been used most widely to identify emphysema on conventional 10-mm-thick CT sections are –900 or –910 HU [6,11–13].

2.3. Postoperative management

All patients were managed postoperatively as follows:

1. Remove the chest tube day after surgery if no air leak is detected, regardless of pleural drainage.
2. Discontinue oxygen support on the morning after surgery; reintroduce support only if the patient complains of dyspnea and his or her saturation level is less than 95%.
3. Discontinue intravenous antibiotic (Cefazolin) administration on the morning after surgery.
4. Start meal intake on the day after surgery.
5. Start ambulation on the day after surgery.
6. Discontinue urinary catheterization and epidural analgesia when the patient is able to walk without assistance.
7. Discontinue intravenous infusion when the patient is able to take meals.

We previously confirmed that this regimen could be used as a critical pathway for patients undergoing pulmonary resection and that postoperative recovery was achieved when all 7 steps were completed [14].

2.4. Statistical analysis

Simple regression analysis was used to determine whether any preoperative variables were associated with preoperative SaO₂ (SaO₂pre), postoperative SaO₂ (SaO₂post), and %LAA. Stepwise multiple regression analysis was used to define the best predictors of SaO₂post, and to generate regression equation for predicted SaO₂post (SaO₂ppo). In addition, simple regression analysis was used to determine whether SaO₂ppo impacted on the postoperative recovery. Differences in SaO₂ or %LAA between the groups were analyzed by unpaired t test. A probability less than 0.05 was accepted as statistically significant.

3. Results

Postoperatively, all patients were extubated in the operating room, and thereafter, none required reintubation for
Table 1
Patient characteristics and values of SaO\textsubscript{pre}, SaO\textsubscript{post}, and %LAA

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>SaO\textsubscript{pre} (%)</th>
<th>P</th>
<th>SaO\textsubscript{post} (%)</th>
<th>P</th>
<th>%LAA (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>33</td>
<td>95.8 ± 1.2</td>
<td>0.864</td>
<td>91.7 ± 4.3</td>
<td>0.572</td>
<td>10.2 ± 9.5</td>
<td>0.007</td>
</tr>
<tr>
<td>Female</td>
<td>20</td>
<td>95.7 ± 1.4</td>
<td></td>
<td>92.4 ± 4.2</td>
<td></td>
<td>3.7 ± 5.2</td>
<td></td>
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<tr>
<td>Breathlessness</td>
<td>37</td>
<td>95.2 ± 1.8</td>
<td>0.041</td>
<td>91.1 ± 4.1</td>
<td>0.346</td>
<td>9.9 ± 11.9</td>
<td>0.240</td>
</tr>
<tr>
<td>No</td>
<td>16</td>
<td>96.0 ± 0.9</td>
<td></td>
<td>92.3 ± 4.3</td>
<td></td>
<td>6.8 ± 6.8</td>
<td></td>
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<tr>
<td>ECOG-PS</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>0</td>
<td>41</td>
<td>95.9 ± 1.1</td>
<td>0.125</td>
<td>92.4 ± 3.9</td>
<td>0.142</td>
<td>7.2 ± 8.3</td>
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<tr>
<td>1</td>
<td>12</td>
<td>95.2 ± 1.8</td>
<td></td>
<td>90.3 ± 5.0</td>
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<td>9.5 ± 10</td>
<td></td>
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<td>Smoking history</td>
<td>33</td>
<td>95.7 ± 1.4</td>
<td>0.622</td>
<td>91.5 ± 4.2</td>
<td>0.327</td>
<td>10.3 ± 9.5</td>
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<tr>
<td>No</td>
<td>20</td>
<td>95.9 ± 1.2</td>
<td></td>
<td>95.9 ± 1.2</td>
<td></td>
<td>3.6 ± 5.0</td>
<td></td>
</tr>
</tbody>
</table>

SaO\textsubscript{pre} = preoperative saturation of arterial oxygen; SaO\textsubscript{post} = postoperative SaO\textsubscript{s}; Breathlessness = inability to keep up with normal individuals of equivalent age on hills or stairs; ECOG-PS = European Cancer Organization group-performance status; %LAA = percentage of low attenuation area determined by three-dimensional computed tomography lung model.

Table 2
Correlations between preoperative variables and SaO\textsubscript{pre}, SaO\textsubscript{post}, and %LAA

<table>
<thead>
<tr>
<th>Mean ± S.D.</th>
<th>SaO\textsubscript{pre}</th>
<th>SAO\textsubscript{post}</th>
<th>%LAA</th>
</tr>
</thead>
<tbody>
<tr>
<td>r</td>
<td>P</td>
<td>r</td>
<td>P</td>
</tr>
<tr>
<td>Age</td>
<td>67 ± 9.5</td>
<td>-0.093</td>
<td>0.508</td>
</tr>
<tr>
<td>Pack year</td>
<td>40 ± 40</td>
<td>-0.132</td>
<td>0.345</td>
</tr>
<tr>
<td>Body mass index</td>
<td>22 ± 2.9</td>
<td>-0.284</td>
<td>0.039</td>
</tr>
<tr>
<td>SaO\textsubscript{pre}</td>
<td>96 ± 1.3</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>%VC (%)</td>
<td>102 ± 17</td>
<td>0.001</td>
<td>0.966</td>
</tr>
<tr>
<td>%FEV\textsubscript{1} (%)</td>
<td>76 ± 12</td>
<td>0.173</td>
<td>0.214</td>
</tr>
<tr>
<td>%FEV\textsubscript{1}ppo (%)</td>
<td>60.2 ± 11</td>
<td>0.118</td>
<td>0.402</td>
</tr>
<tr>
<td>%LAA</td>
<td>7.73 ± 8.7</td>
<td>0.068</td>
<td>0.629</td>
</tr>
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</table>

SaO\textsubscript{s} = saturation of arterial oxygen; SaO\textsubscript{pre} = preoperative SaO\textsubscript{s}; SaO\textsubscript{post} = postoperative SaO\textsubscript{s}; %LAA = percentage of low attenuation area determined by three-dimensional computed tomography lung model.

Mechanical ventilation. There was no cardiogenic lung edema or low output syndrome that might have caused hypoxemia. Three patients suffered from postoperative cardiopulmonary complications: lobar atelectasis in one case and atrial fibrillation in the other 2 cases. Two patients required additional intervention for postoperative complications; reoperation due to prolonged air leak in one case and chest tube drainage due to chylothorax in the other. No other medical treatment was required after the standardized postoperative management regimen was completed. The mean duration of oxygen supplementation was 2.7 ± 2 days (range, 0 to 8 days), that of chest tube drainage was 3.1 days (range, 1 to 17 days), and that of postoperative management was 3.8 days (range, 1 to 17 days).

Patient characteristics are shown in Table 1. Preoperative variables including age, body mass index, smoking index, percentage of predicted vital capacity (%VC), percentage of predicted forced expiratory volume in 1 s (%FEV\textsubscript{1}), %FEV\textsubscript{1}ppo, and %LAA are shown on Table 2. Sex and smoking status were significant predictors of %LAA (Table 1). Age, smoking index, body mass index, %FEV\textsubscript{1}, and %FEV\textsubscript{1}ppo were linearly dependent upon %LAA (Table 2). Some of these preoperative variables were also linearly dependent upon SaO\textsubscript{pre} and SaO\textsubscript{post} (Table 2). SaO\textsubscript{pre} and %LAA were significant predictors of SaO\textsubscript{post} (Table 2 and Fig. 2).

2). Among all preoperative variables, SaO\textsubscript{pre} and %LAA were identified as the best predictors of SaO\textsubscript{post} by stepwise multiple regression analysis (r = 0.61; regression equation: SaO\textsubscript{ppo} = -50 + 1.5 SaO\textsubscript{pre} - 0.21 %LAA) (Fig. 3).

The SaO\textsubscript{ppo} was significantly dependent upon the duration of postoperative management (P < 0.01) (Fig. 4).

4. Discussion
Postoperative hypoxemia is often attributed to general anesthesia, which temporarily decreases functional residual
volume by reducing the muscle tone of the chest wall, impairs bronchomotor and vascular tone due to reflex effects of tracheal intubation, limits immune function, and depresses secretion mobilization [15]. In patients with underlying lung diseases, these impairments result in intrapulmonary shunting or reduction of ventilation/perfusion ratio by closure of small airways. Therefore, postoperative hypoxemia can result predominantly from atelectasis in the dependent part of the lung. In the present study, %LAA was related to the postoperative reduction in arterial oxygen. Low attenuation area, correspondent to over-inflated lung, might enhance to reduce functional lung volume induced by general anesthesia, because such disease lung remains inflated even postoperatively due to air trapping.

Postoperative hypoxemia also derives from the surgical procedure [1]. Three surgical factors are known to cause postoperative hypoxemia: abnormal gas exchange induced by excessive pulmonary resection, reduced chest wall compliance induced by wide thoracotomy, and reduced diffusing capacity induced by lung edema resulting from surgical stress. In our series, the extent of lung resection was not associated with postoperative hypoxemia because of the preservation of pulmonary functional reserve (FEV1ppo ≥ 500 ml). In addition, we found that none of the operative variables such as operation time (minutes) \( r = -0.02, P = 0.94 \) or intraoperative hemorrhage (g) \( r = -0.05, P = 0.58 \) was related to postoperative hypoxemia. Our series also did not include extended thoracotomy or chest wall resection that might have reduced chest wall compliance. Therefore, surgical factors might have played a minimal roll in initiating postoperative hypoxemia in our series.

When analysis was restricted to 33 consecutive patients having smoking history, %LAA and SaO2,pre were also significantly dependent upon SaO2,post \( r = -0.55 \) for %LAA, \( r = 0.53 \) for SaO2,pre), whereas %FEV1ppo showed no significant relevance to SaO2,post \( r = 0.12, P = 0.51 \) by means of simple regression analysis. Thus, %LAA was found to be more reflective of postoperative hypoxemia than spirometric variables especially for patients with smoking history. This finding is compatible with another report of the advantage of chest CT over function tests in detecting early-stage emphysema [8]. However, further analysis should be carried out to determine whether %LAA is useful for predicting postoperative pulmonary complications.

Regardless of existing definitions for postoperative pulmonary complications [1], it is not easy to accurately detect the complications induced by lung resection surgery because some respiratory abnormality is likely to be overlooked in patients with preserved pulmonary function, whereas minimal impairment can be exacerbated in patients with limited pulmonary function reserve. In our series, only one patient suffered a definitive postoperative pulmonary complication, although some might have experienced subclinical pulmonary complications that resulted in impaired gas exchange. To clarify the peroperative outcomes of these patients, we measured the duration of postoperative management, which we defined as the time required for completion of the standardized postoperative management regimen. As we showed previously [14], the duration of postoperative recovery is a more accurate reflection of the patient’s perioperative physical status, in comparison to postoperative hospital stay, because, in Japan, patients elect to stay in the hospital long after recovery from surgery. We found, as expected, that SaO2,post was closely dependent upon the duration of postoperative management. Therefore, predicting SaO2,post may be clinically useful for taking additional measures to prevent prolonged hospitalization and reduce medical expenditure, and for counseling preoperatively those patients at increased risk of prolonged hospitalization.

In conclusion, using the CT-determined extent of low attenuation area, we established a novel method of predicting postoperative hypoxemia that impacted on postoperative recovery. Because this radiographic index was superior to conventional spirometric variables for predicting postoperative hypoxemia, further confirmation of its usefulness as a preoperative assessment of patients undergoing pulmonary resection is warranted.
References


