Relevance of pleural adhesions for short- and long-term outcomes after lung volume reduction surgery

Claudio Caviezel, MD, Medea Rodriguez, Pavel Sirotkin, Ulrike Held, PhD, Isabelle Opitz, MD, Didier Schneiter, MD

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How do adhesions influence the outcome of LVRS?

3-6 months after LVRS

△ FEV₁ unilateral 27% p<0.0001
△ FEV₁ total 28% p<0.0001

PLA ➔ Prolonged air leak

OR 2.83, 95% CI from 1.36 to 5.89; p = 0.006

PLA ➔ FEV₁ estimate -1.52; 95% CI from -5.67 to 2.63; p = 0.47

PLA ➔ Exacerbations

OR 1.11, 95% CI from 0.5 to 2.45; p = 0.79

While PLA correlates with prolonged air leak, there was no evidence of correlation between PLA and lung functional outcome or infections. Unilateral and bilateral LVRS both showed significant improvements in lung function.

187 patients after LVRS
94 unilateral (50.3%), 93 bilateral
46 with PLA (24.6%)
61 with prolonged air leak (> 7 days, 31.6%)
7.84 days mean chest tube time

LVRS = lung volume reduction surgery; PLA = severe pleural adhesions; FEV₁ = forced expiratory volume in the first second; OR = odds ratio
Relevance of pleural adhesions for short- and long-term outcomes after lung volume reduction surgery

Claudio Caviezel¹, MD; Medea Rodriguez¹; Pavel Sirotkin²; Ulrike Held², PhD; Isabelle Opitz¹, MD; Didier Schneiter¹, MD

¹Department of Thoracic Surgery, University Hospital Zürich, Zürich, Switzerland
²Epidemiology, Biostatistics and Prevention Institute, University Zürich, Zürich, Switzerland

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Corresponding author:
Claudio Caviezel, MD
Department of Thoracic Surgery, University Hospital Zürich, Rämistrasse 100, 8091 Zürich, Switzerland; e-mail: claudio.caviezel@usz.ch; phone: +41 43 253 88 77

Word count: 2,935
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Central message

Pleural adhesions might prolong hospitalization after LVRS, but do not seem to affect pulmonary function outcome.

Central picture: Thoracoscopic adhesiolysis of severe pleural adhesions

Perspective Statement

LVRS patients are fragile and it is important to know whether adhesiolysis of severe pleural adhesions, which leads to potential prolongation of hospitalization and subsequent risk of complications, has an impact on outcomes. This study confirms prolonged chest tube time after LVRS with severe adhesions, but finds no correlation between adhesiolysis and pulmonary function outcome.
Graphical abstract

How do adhesions influence the outcome of LVRS?

3-6 months after LVRS

- $\Delta FEV_{1_{unilateral}}$: 27% $p=0.0006$
- $\Delta FEV_{1_{bilateral}}$: 28% $p<0.0001$

PLA
- Prolonged air leak
  - OR 2.83, 95% CI from 1.36 to 5.69; $p=0.006$
- FEV1
  - Estimate: -1.52; 95% CI from -5.67 to 2.63; $p=0.47$

PLA
- Exacerbations
  - OR 1.11, 95% CI from 0.5 to 2.45; $p=0.79$

While PLA correlates with prolonged air leak, there was no evidence of correlation between PLA and lung functional outcome or infections. Unilateral and bilateral LVRS both showed significant improvements in lung function.

Unilateral LVRS with PLA: proceed

Bilateral LVRS with PLA: consider unilateral surgery

187 patients after LVRS
94 unilateral (50.3%), 93 bilateral
46 with PLA (24.6%)
61 with prolonged air leak (>7 days, 31.6%)
7.84 days mean chest tube time

LVRS = lung volume reduction surgery; PLA = severe pleural adhesions; FEV1 = forced expiratory volume in the first second; OR = odds ratio
Abstract

Objective: Pleural adhesions (PLA) have been shown to be a possible risk factor for air leak after lung volume reduction surgery (LVRS), but the relevance of PLA for lung functional outcome (LFO) remains unclear. We analyzed our LVRS cohort for the impact of PLA on short-term [prolonged air leak (PAL)] and long-term (LFO) outcomes.

Methods: Retrospective observational cohort study with 187 consecutive patients who underwent LVRS from January 2016 to December 2019. PLA were defined as relevant if they were distributed extensively at the dorsal pleura; were present in at least at two areas, including the dorsal pleura; or present extensively at the mediastinal pleura. In patients with bilateral emphysema, bilateral LVRS was performed preferentially.

The objectives were to quantify the association of PLA and rate of PAL (chest tube >7 days), and the association of PLA with postoperative exacerbations (PE) and with forced expiratory volume in 1 s (FEV1) 3 months postoperatively. The associations were quantified with odds ratios (OR) for binary outcomes, and with between-group differences for continuous outcomes. To account for missing observations, 100-fold multiple imputation was used.

Results: PLA were found in 46 of 187 patients (24.6%). There was a 32.6% rate of PAL (n = 61), chest tube time was a mean of 7.84 days. A total of 94 (50.3%) LVRS were unilateral and 93 were bilateral. There was evidence for an association between PLA and the rate of PAL (OR 2.83; 95% confidence interval (CI), 1.36–5.89; p = 0.006). There was no evidence for an association between PLA and PE (OR 1.11; 95% CI, 0.5–2.45; p = 0.79). There was no evidence for an association between PLA and FEV1 (estimate -1.52; 95% CI –
5.67 to 2.63; \( p = 0.47 \)). Both unilateral and bilateral LVRS showed significant postoperative improvements in FEV1 by 27\% (8.43 units; 95\% CI, 3.66–13.12; \( p = 0.0006 \)) and by 28\% (7.87 units; 95\% CI, 4.68–11.06; \( p < 0.0001 \)) and a reduction in residual volume of 15\% (–33.9 units; 95\% CI, –56.37 to –11.42; \( p = 0.003 \)) and 15\% (–34.9 units; 95\% CI, –52.57 to –17.22; \( p = 0.0001 \)), respectively.

**Conclusions**: Patients should be aware of potential prolongation of hospitalization due to PLA. However, there might be no relevant influence of PLA on LFO.

**Key words**: LVRS, emphysema, pleura, adhesions
**Introduction**

Lung volume reduction surgery (LVRS) has been shown to improve lung function, exercise capacity and even survival in highly selected patients with severe emphysema (1,2). The only available randomized evidence deals with a lot of open surgery cases, in a study conducted during the late 1990s and early 2000s (3). With the advent of video-assisted thoracic surgery (VATS), the surgical approach has become much less harmful, thus reducing operative morbidity, especially by allowing earlier recovery at lower cost (3,4). Nevertheless, candidates eligible for LVRS still represent one of the most vulnerable patient groups within the thoracic surgery community (5). Short operation times and short length of hospital stays are preferable to decrease the risk of postoperative complications such as delirium and hospital-acquired pneumonia (6). In most thoracic surgery procedures, and especially in LVRS, by far the most frequent postoperative complications are prolonged air leak (PAL) and the need for chest tube drainage (7). Data from the randomized National Emphysema Treatment Trial (NETT) were analyzed regarding postoperative air leaks and their associated risk factors. In these 552 patients, 90% developed an air leak, with a mean duration of 7 days. Not surprisingly, severe pleural adhesions (PLA) were a risk factor, as were low diffusion capacity (DLCO), low values of forced expiratory volume in 1 second (FEV1), and patients using inhaled steroids. Regarding PLA, there is no standardized definition to grade severity. However, PLA seem to prolong the operation itself, increase the risk of PAL postoperatively, and thus keep the patient in hospital for a longer time. Whether PLA also alter the outcome of LVRS in the long term has not yet been investigated. Long-term outcomes of LVRS might be measured by monitoring increase in lung function performance, as this is the main goal of the
procedure. Our group has long wondered whether longer hospital stays due to PAL, sometimes even accompanied by revision surgery, influence the targeted outcome of emphysema surgery 3 months postoperatively. If this were the case, a surgeon may decide to abort surgery after spotting severe PLA. Especially in bilateral LVRS, after one side has already been operated, PLA might be a reason to halt the procedure if explorative thoracoscopy discovered PLA on the second side. We hypothesize poorer lung functional outcome (LFO) 3 months postoperatively after LVRS accompanied by adhesiolysis of severe PLA.

Methods
A retrospective observational cohort study was conducted, with 187 consecutive patients who underwent LVRS at our institution from January 2016 to December 2019. The time frame was chosen due to the availability of standardized information on PLA from 2016 onwards and the initiation of a Masters thesis (by MR) during 2020.

Patient Selection
Inclusion criteria for LVRS are listed in Table 1. All patients who were potential candidates for LVRS were discussed by our interdisciplinary emphysema board.

Operation
LVRS was preferentially performed bilaterally. The decision to perform a bilateral or unilateral operation depends primarily on the predominance of disease distribution. Additionally, besides their emphysema morphology, patients with borderline inclusion criteria, such as DLCO <20% or mild-to-moderate pulmonary hypertension, endobronchial
valves in situ (on the nonoperated side), suspicious nodule/proven lung cancer planned for
concomitant resection, and patients who had already had a thoracic operation (LVRS,
pleurodesis, anatomical resection) on the other side, were operated unilaterally.

Target areas on computed tomography (CT) scans, combined with perfusion scintigraphy
scans, were resected with standard staplers (Endo GIA Ultra Universal; Medtronic, Dublin,
Ireland). In the case of macroscopically extremely fragile-looking tissue, we buttress the
stapling lines. This practice is at the surgeon’s discretion.

PLA were completely freed in order to mobilize the whole lung. In case of severe adhesions,
a Ligasure Maryland tool (Medtronic, Dublin, Ireland) is sometimes used, as well as a
monopolar cautery hook. However, if possible, we try not to use energy-requiring devices, as
the closer they come to lung tissue, the more the heat they generate, potentially creating
predetermined breaking points. We therefore usually use scissors only as much as possible. In
case of severe air leak at the end of the procedure, we might staple the lesion, and add
Tachosil (Takeda, Tokyo, Japan) and/or Progel (Becton, Dickinson and Company, Franklin
Lakes, USA). Other measures, for example, pleural tents or pleurodesis, are never used.

Definition of PLA
In 2016, a standardized definition of PLA was introduced and applied prospectively by
noting it in the operation report. Severe PLA were defined as relevant if they were distributed
extensively at the dorsal pleura; in at least at two areas, including the dorsal pleura; or
extensively at the mediastinal pleura (Figure 2 shows non-relevant/non-severe PLA, Figure 3
shows relevant severe PLA). Please refer to the video for an example of severe PLA in
LVRS.

Follow-Up and Outcome Measures
All pulmonary function tests (PFTs) were performed using a standard body plethysmograph and DLCO. At our institution, most patients are monitored for only 3 months after LVRS.

Patients from other institutions were sent back for follow-up and their referring physicians were asked to perform the PFTs. As PAL (chest tube >7 days) and, in our setting, prolonged hospitalization (patients are not dismissed until tube-free) are the main and almost sole postoperative complications—even in borderline patients with mild-to-moderate pulmonary hypertension and with very low DLSO—these were regarded as short-term outcomes (8,9).

Lung functional performance is an important and, in retrospective analyses, easily measurable parameter and was therefore regarded as a long-term outcome.

More frequent chronic obstructive pulmonary disease (COPD) exacerbations (pulmonary exacerbations, PE) were chosen as a documented parameter for another possible complication after hospitalization, as there was no documented cases of pneumonia or empyema in the patient group analyzed. As 70–80% of COPD exacerbations are due to respiratory infections (one- to two-thirds due to viruses, and one-third to one-half due to bacteria), some might be triggered by prolonged hospitalization (10).

**Objectives**

The primary hypothesis was poorer LFO 3 months postoperatively after LVRS accompanied by adhesiolysis of severe PLA. Therefore, we aimed to quantify the association of PLA with lung function (i.e. FEV1%) 3 months postoperatively.

Besides collecting patient demographics and perioperative data, further objectives were to quantify the:

- association of PLA and rate of PAL (chest tube >7 days);
- association of PAL with PE;
change in lung function 3 months postoperatively in uni- and bilateral surgery; and

association of PLA and length of stay in hospital (days).

Statistical Methods

Associations of the binary independent variables of interest were quantified with odds ratios (OR) for binary outcomes, and with between-group differences for continuous outcomes. In a first step, unadjusted associations were estimated and reported. In a second step, adjusted associations were estimated and reported. All estimates were reported with 95% confidence intervals (CI) and exploratory p-values. The confounding variables accounted for in this context were location, baseline FEV1, sex, and age. To account for missing observations, 100-fold multiple imputation was used. All analyses were performed with the programming language R (R core team), in combination with dynamic reporting using knitr.

Ethics

This study was approved by the Swiss local ethics committee with the number KEK #2016-00716, last updated by the committee on November 24, 2020. Beginning in 2016, written consent is standardized for publication of patient data and is available for all patients.

Results

Within the study time period, 187 consecutive patients underwent LVRS at our institution. Table 2 shows baseline demographics of age, sex, lung function values, and whether bilateral or unilateral LVRS was performed. The graphical abstract presents a summary of the study (Figure 1).
269  **Perioperative Outcomes**

A subset of 14 patients underwent thoracotomy; all others (173, 92.5%) were operated on using VATS. A total of 94 patients (50.3%) were operated unilaterally: 37 (39.7%) due to disease distribution, 15 (15.9%) due to history of contralateral operation, 12 (12.8%) due to endobronchial valves in situ, 11 (11.7%) due to concomitant nodule/cancer resection, and 7 (7.4%) because of borderline inclusion criteria. Twelve patients (12.8%) were planned as bilateral LVRS, but the operation was terminated after the first side due to PLA with severe air leak.

Regarding morphology, 142 (75.9%) patients showed heterogeneous and 45 (24%) non-heterogeneous emphysema. Mean chest tube time for all patients was 7.8 days (SD 7.2 days).

The rates of PLA and PE were 24.6% (46 patients) and 27.4% (51 patients), respectively.

281  **Association of PLA with PAL**

There was strong evidence for an association between PLA and PAL; the unadjusted OR was 2.71 (95% CI, 1.36 to 5.41; p = 0.005). The adjusted OR of adhesions was 2.83 (95% CI, 1.36 to 5.89; p = 0.006).

285  **Association of PAL with PE**

There was no evidence for an association between PAL with PE (OR = 1.65; 95% CI, 0.84–3.32; p = 0.15). This result remained unchanged after adjusting for confounders.
Lung Function

Spirometric and bodyplethysmographic lung function values are displayed in Table 3.

Both unilateral and bilateral LVRS showed significant postoperative improvements in FEV1 by 27% (+8.43 units; 95% CI, 3.66–13.12; p = 0.0006) and 28% (7.87 units; 95% CI, 4.68–11.06; p < 0.0001) and a reduction in RV by 15% (–33.9 units; 95% CI, –56.37 to –13.12; p = 0.003) and 15% (34.9, 95% CI, –52.57 to –17.22; p = 0.0001), respectively.

Results from the 6-minute walking distance (6-MWD) test were available pre-operatively in 161 patients (86.1%) and postoperatively in 130 (69.5%). Pre-operative mean distance was 300 m (SD 110), postoperative mean distance was 375 m (SD 106), p < 0.001.

Association of PLA with Lung Function

There was no evidence for an association between PLA and FEV1 at 3 month follow-up when adjusting for baseline FEV1 (estimate 2.34; 95% CI, –3.08 to 7.77; p = 0.39). The results remained unchanged when adjusting for confounders.

Association of PLA and Length of Stay in Hospital

There was evidence for an association between length of stay in hospital (days) and the presence of adhesions (estimate 3.83; 95% CI, 1.4–6.25; p = 0.002).

Discussion

This retrospective observational cohort study found evidence of a correlation between PLA and PAL but no evidence of a correlation between PLA and functional outcome of LVRS; patients with PLA showed the same improvement in FEV1 3 months post-operation as
patients without PLA. Neither was there evidence of correlation between PLA and postoperative COPD exacerbations. As this study again confirmed the known correlation between PLA and PAL with subsequent prolongation of hospitalization, our group always feared that there might be a lesser functional benefit in the long term (7). Reasons for this included the possible increased risk of infectious complications and/or missed, or at least postponed, initiation of efficient mobilization and rehabilitation. Regarding length of hospital stay versus PAL as outcome measurements, there are differing views. In our practice, patients have to stay in hospital for a direct transfer to inpatient postoperative rehabilitation. Nowadays, a lot of patients still go to rehabilitation, but a growing number are discharged directly home (accompanied by an outpatient rehabilitation program). The latter patients usually leave the day after the chest tube has been removed, but others might wait much longer due to, among others, health insurance reasons. Therefore, we consider days with chest tube (or PAL) a better real-life indicator of postoperative course than length of hospital stay. There was evidence for an association between length of stay in hospital and the presence of adhesions (estimate 3.83; 95% CI, 1.4–6.25; p = 0.002). However, the distribution of outcomes was not Gaussian and therefore the results need to be interpreted with caution. We always considered terminating surgery in cases of severe adhesions to prevent prolonged length of hospital stay with no benefit, although we are not always confident that this is advantageous for the patient. However, based on the results of the present study, we will continue with unilateral surgery regardless of the type of PLA encountered. We usually perform bilateral surgery in patients with bilateral disease distribution; however, we now consider terminating the operation after the first side is completed if either severe PLA on the
first side led to intraoperative air leak, or if severe PLA are discovered when exploring the second side. Notably, this practice arises from our experience and common sense and cannot be derived from the results of this study. Here, we show only that there is no correlation between PLA and postoperative improvement in FEV1%.

As lung functional improvement after unilateral LVRS is as effective as after bilateral LVRS, the latter patients might profit from the avoidance of PAL in terms of length of hospitalization. There is some debate in the literature on unilateral versus bilateral emphysema surgery, generally voting for a bilateral approach (11,12). Kotloff et al. compared 119 bilateral with 32 unilateral LVRS. Functional follow-up in 86 and 23 patients, respectively, showed a significant, but rather small, difference in FEV1 of 90 ml between the two groups, favoring the bilateral approach. The difference in 6-WMD was 195 feet (bilateral LVRS) compared with 147 feet (unilateral LVRS). However, of the 32 unilateral LVRS patients, 24 were part of a planned staged bilateral approach but only 10 received their contralateral operation; 10 were satisfied enough after the first side, 3 patients had a poor outcome with subsequent listing for transplantation, and 1 patient had intercurrent abdominal surgery (11).

Argenziano et al. report significantly better improvements in spirometrics (FEV1 difference of 70% versus 28%) in bilateral surgery, but equal improvements in 6-WMD and dyspnoea score in both procedures (12). This might reflect the difficulties of comparing often very heterogeneous groups of unilateral cases versus bilateral operated patients in an non-prospective, randomized setting. A tendency towards better results after bilateral LVRS is usually reported in patients with upper lobe-predominant heterogeneous emphysema—a group in which we also usually favor the bilateral approach. In contrast, the group of David Waller always vote for an unilateral approach (13, 14). Implying enough benefit after one side, the second side might be spared treatment until lung function declines further.
Nevertheless, many patients might get lost inbetween, as COPD worsens and/or other comorbidities take their toll.

The results of this study do not show relevant outcome differences between uni- and bilateral operations, although almost all the unilateral operations were indicated unilaterally due to contraindications on the other side. Either there was unilateral disease, borderline inclusion criteria, a history of pleurodesis, or concomitant nodule/cancer resection. Only 12 patients actually had bilateral emphysema and were planned as bilateral LVRS, but were finally operated on only one side due to adhesions or a massive air leak. Although this study was not intended to solve this issue, good results were confirmed in both unilateral and bilateral surgery. The interesting subgroup in which surgery was terminated prematurely, cannot be assessed due to low numbers.

We chose COPD exacerbations as an outcome parameter as we saw no cases of postoperative pneumonia or empyema. Theoretically, PLA and prolonged length of hospital stay might predispose the vulnerable emphysema lung to exacerbations. This study shows a relatively high rate of postoperative COPD exacerbations (27.5%), but there was no evidence for a correlation of these PE with PLA.

The NETT trial reported a postoperative pneumonia rate of 18% (1). So far, there is no standardized approach for perioperative antibiotic prophylaxis in LVRS patients. We prefer broad-spectrum antibiotics as long as the chest tube is in situ—this might be questioned but might also explain our zero rate of pneumonia or empyema in these patients (15).

This study has some limitations. Its retrospective nature makes it prone to selection bias. Nevertheless, it was a consecutive observational cohort of all our LVRS patients over 4 years. PLA cannot be assessed definitively prior to surgery and therefore cannot be used as selection criteria (so far). A large limitation is the missing detailed information on the course of patients with PE. This potential complication after LVRS with PLA was more a guess than
a known postoperative sequela but, lacking other infections, we consider it meaningful to
check our patients for PE.

We have information only on spirometry, bodyplethysmography, and 6-MWD, and some
postoperative values are missing. However, FEV1 seems to correlate well with both general
condition and improvement (16–18). Nevertheless, more precise data including
questionnaires about quality of life and patient-reported outcome measures would be useful
(19).

Last, but not least, there is no standardized definition about the severity of PLA. Their impact
on air leak—also in LVRS—has been demonstrated in the NETT data and now in this study
as well (7). Regarding the surgical population in the NETT study, De Camp et al. reported
none or minimal, moderate, or marked adhesions, with the latter two being found in 23% and
18% of cases, respectively. This might reflect our 24.6% rate of severe adhesions. Our
definition of severe adhesion is as follows: severe dorsal adhesions potentially located also at
the base of the upper lobe and at the lower lobe, therefore complicating easy resection or
fistula closure after classical LVRS in an upper-lobe predominant emphysema (Figure 3).
Apical adhesions (e.g., potential parenchyma lesions) would be included in the LVRS
specimen. The same might be true for severe mediastinal adhesions, as these can be found at
the lingula or anterior part of the right upper lobe; neither should be resected in the majority
of LVRS procedures.

For our own practice, we consider complete adhesiolysis in patients scheduled for unilateral
surgery, as LVRS still has potential for lung functional improvement despite PLA. In
scheduled bilateral cases, we consider terminating the operation after successful LVRS on the
first side if PLA are detected on the second side.

In conclusion, PLA might not influence the LFO of LVRS, although they can prolong chest
tube time and, therefore, hospitalization time.
References


Table 1: Inclusion and exclusion criteria for LVRS (CT = computer tomography, 6-MWD = 6-minute walking distance)

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<tr>
<th>Patient</th>
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<td>nicotine abstention</td>
<td>nicotine abstention &gt;4 months</td>
<td>daily steroid intake &gt;20 mg</td>
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<td>CT morphology</td>
<td>lung emphysema</td>
<td>significant bronchiectasis</td>
</tr>
<tr>
<td>lung function</td>
<td>FEV1 &lt;45% TLC &gt;100% RV &gt;150%</td>
<td>FEV1 &lt;20% and DLCO &lt;20% in homogeneous emphysema</td>
</tr>
<tr>
<td>6-MWD</td>
<td>&lt; 450 m</td>
<td>paCO2 &gt;6.7 Pa paO2 &lt;6.0 Pa in homogeneous emphysema</td>
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Table 2: Patient demographics (PLA = severe pleural adhesions, SMD = standardized mean difference)

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<tr>
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<th>Overall</th>
<th>No adhesions</th>
<th>PLA</th>
<th>SMD</th>
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<td>Patients</td>
<td>187</td>
<td>141</td>
<td>46</td>
<td></td>
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<tr>
<td>Age (mean (SD))</td>
<td>65.24 (8.45)</td>
<td>65.23 (8.49)</td>
<td>65.26 (8.43)</td>
<td>0.004</td>
<td>0</td>
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<td>Female (%)</td>
<td>78 (41.7)</td>
<td>64 (45.4)</td>
<td>14 (30.4)</td>
<td>0.312</td>
<td>0</td>
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<td>FEV1% predicted (mean (SD))</td>
<td>29.71 (10.28)</td>
<td>29.06 (8.64)</td>
<td>31.80 (14.25)</td>
<td>0.232</td>
<td>1.1</td>
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<td>TLC% predicted (mean (SD))</td>
<td>129.06 (24.50)</td>
<td>128.38 (25.19)</td>
<td>131.30 (22.19)</td>
<td>0.123</td>
<td>3.2</td>
</tr>
<tr>
<td>RV% predicted (mean (SD))</td>
<td>226.61 (65.24)</td>
<td>225.59 (67.09)</td>
<td>229.99 (59.32)</td>
<td>0.069</td>
<td>3.2</td>
</tr>
<tr>
<td>RV/TLC % (mean (SD))</td>
<td>65.88 (10.47)</td>
<td>66.00 (10.19)</td>
<td>65.47 (11.50)</td>
<td>0.048</td>
<td>3.7</td>
</tr>
<tr>
<td>DLCO% predicted (mean (SD))</td>
<td>32.33 (11.53)</td>
<td>32.01 (10.88)</td>
<td>33.35 (13.47)</td>
<td>0.109</td>
<td>4.3</td>
</tr>
<tr>
<td>Bilateral LVRS (%)</td>
<td>93 (49.7)</td>
<td>80 (56.7)</td>
<td>13 (28.3)</td>
<td>0.602</td>
<td>0</td>
</tr>
<tr>
<td>Unilateral LVRS (%)</td>
<td>94 (50.3)</td>
<td>61 (43.3)</td>
<td>33 (71.7)</td>
<td>0.602</td>
<td>0</td>
</tr>
</tbody>
</table>
Table 3: Spirometric and body plethysmographic outcomes (SMD = standardized mean difference)

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Bilateral</th>
<th>Unilateral</th>
<th>SMD</th>
<th>Missing (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>187</td>
<td>93</td>
<td>94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1 before surgery</td>
<td>29.71 (10.28)</td>
<td>27.92 (7.79)</td>
<td>31.52 (12.07)</td>
<td>0.354</td>
<td>1.1</td>
</tr>
<tr>
<td>FEV1 after 3 months</td>
<td>37.89 (15.06)</td>
<td>35.79 (11.81)</td>
<td>39.95 (17.53)</td>
<td>0.278</td>
<td>22.5</td>
</tr>
<tr>
<td>TLC before surgery</td>
<td>129.06 (24.50)</td>
<td>130.85 (21.03)</td>
<td>127.25 (27.57)</td>
<td>0.147</td>
<td>3.2</td>
</tr>
<tr>
<td>TLC after 3 months</td>
<td>123.04 (19.36)</td>
<td>124.77 (19.61)</td>
<td>121.27 (19.09)</td>
<td>0.181</td>
<td>28.3</td>
</tr>
<tr>
<td>RV before surgery</td>
<td>226.61 (65.24)</td>
<td>231.29 (53.44)</td>
<td>221.89 (75.33)</td>
<td>0.144</td>
<td>3.2</td>
</tr>
<tr>
<td>RV after 3 months</td>
<td>192.25 (61.81)</td>
<td>196.39 (57.46)</td>
<td>187.99 (66.17)</td>
<td>0.136</td>
<td>28.3</td>
</tr>
<tr>
<td>RV/TLC before surgery</td>
<td>65.88 (10.47)</td>
<td>67.05 (7.35)</td>
<td>64.70 (12.80)</td>
<td>0.225</td>
<td>3.7</td>
</tr>
<tr>
<td>RV/TLC after 3 months</td>
<td>60.03 (17.10)</td>
<td>58.41 (9.37)</td>
<td>61.69 (22.41)</td>
<td>0.191</td>
<td>28.3</td>
</tr>
<tr>
<td>DLCO before surgery</td>
<td>32.33 (11.53)</td>
<td>32.69 (9.90)</td>
<td>31.97 (13.05)</td>
<td>0.062</td>
<td>4.3</td>
</tr>
<tr>
<td>DLCO after 3 months</td>
<td>37.21 (12.43)</td>
<td>37.24 (11.43)</td>
<td>37.18 (13.40)</td>
<td>0.005</td>
<td>27.8</td>
</tr>
</tbody>
</table>

FEV1, TLC, RV and DLCO as % predicted. Contains mean values, standard deviation in brackets.
Legends

Figure 1 (Graphical abstract): Summary of the study.

Figure 2: Non-severe pleural adhesions. Top: Red circle indicates a singular adhesion between the apex of the right lung and the upper mediastinum. Bottom: Several non-severe pleural adhesions between the right lower lobe and the diaphragm. Both pictures were taken during an LVRS procedure.

Figure 3: Severe pleural adhesions. Top left: Scar at the apical dorsal pleura (red circle), indicating expleural adhesiolysis—the adhesions included the basal upper lobe (asterisk = lung, cross = chest tube). Top right: Severe adhesions between sternum and right upper lobe (asterisk = lung). Bottom left: Adhesions between lingula and paracardial fatty tissue (red circle). Bottom right. Complete adhesive right pleural cavity (asterisk = lung); this operation was terminated without LVRS on this side after successful LVRS on the contralateral side.

Video Legend: Case report of unilateral LVRS in a patient with severe pleural adhesions.
How do adhesions influence the outcome of LVRS?

3-6 months after LVRS

- FEV₁ unilateral: 27% p=0.0006
- FEV₁ total: 28% p<0.0001

PLA → Prolonged air leak
PLA estimate: -1.52; 95% CI from -5.67 to 2.83; p = 0.47

PLA → Exacerbations
PLA estimate: -1.11; 95% CI from 0.5 to 2.45; p = 0.79

While PLA correlates with prolonged air leak, there was no evidence of correlation between PLA and lung functional outcome or infections. Unilateral and bilateral LVRS both showed significant improvements in lung function.

187 patients after LVRS
94 unilateral (50.3%), 93 bilateral
46 with PLA (24.6%)
61 with prolonged air leak (>7 days, 31.6%)
7.84 days mean chest tube time

LVRS = lung volume reduction surgery, PLA = severe pleural adhesions, FEV₁ = forced expiratory volume in the first second, OR = odds ratio

Unilateral LVRS with PLA: proceed
Bilateral LVRS with PLA: consider unilateral surgery
The Relevance of Pleural Adhesions for the Short- and Long-term Outcome of Lung Volume Reduction Surgery

C Caviezel, M Rodriguez, P Sirotkin, U Held, I Opitz, D Schneiter

Claudio Caviezel, MD
Deputy Head of Department
Department of Thoracic Surgery
University Hospital Zurich