Comparative results of non-resectional lung volume reduction performed by awake or non-awake anesthesia

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Received 6 September 2010; received in revised form 17 November 2010; accepted 29 November 2010

Abstract

Objective: In a prospective non-randomized study, we compared results and costs of non-resectional lung volume reduction surgery (LVRS) performed through awake or non-awake anesthesia that was freely chosen by recruited patients. Method: Non-resectional LVRS was performed by epidural anesthesia in 41 patients (awake group) and by general anesthesia in 19 patients (non-awake group). Perioperative outcome included analysis of oxygenation ($PaO_2/FiO_2$) at fixed time points and global time spent in the operating room (anesthesia plus surgery plus weaning plus recovery times). Costs were evaluated at discharge. Forced expiratory volume in 1 s (FEV$_1$), plethysmographic residual volume (RV$_{pleth}$) and maximal incremental treadmill test (MITT) score were assessed preoperatively and every 6 months, postoperatively. Results: Perioperative outcome was better in the awake group with better oxygenation 1 h after the operation ($P = 0.004$) and shorter global in-operating room stay ($P < 0.0001$). There was no operative mortality. In the awake group, median hospital stay was shorter (6 days vs 7 days, $P = 0.006$), whereas median hospital charges were lower than in the non-awake group (7800 euros vs 8600 euros, $P = 0.006$). At 6 months, there was no difference (awake vs non-awake) in median $\Delta$FEV$_1$ (0.33 l vs 0.28 l, $P = 0.09$), $\Delta$RV ($-0.99$ l vs $-0.98$ l, $P = 0.95$), and $\Delta$MITT score (1.0 vs 0.75, $P = 0.31$). Conclusion: In our study, awake non-resectional LVRS was preferred by the majority of patients. It resulted in better perioperative outcome, shorter hospital stay, and lower costs than equivalent procedures performed by non-awake anesthesia. Six months’ clinical results were comparable, showing that the awake approach had no impact on late clinical benefit.

Keywords: Lung volume reduction surgery; Emphysema; VATS; Awake thoracic surgery; Thoracic epidural anesthesia

1. Introduction

Lung volume reduction surgery (LVRS) is an established, palliative surgical treatment that can considerably improve pulmonary function, exercise capacity, quality of life and survival in select patients with severe emphysema and impaired exercise tolerance [1—4].

Typically, the operation entails staple non-anatomical resection of most emphysematous lung tissue carried out through general anesthesia and single-lung ventilation. Unfortunately, following resectional LVRS, expected mortality and major morbidity are 5.5% and 30%, respectively [5], whereas up to 90% of patients can develop an air leak [6]. As a result, time spent for postoperative recovery is often prolonged, causing the cost-effectiveness of LVRS to be still in question [7].

For these reasons, new surgical [8] and non-surgical [9,10] lung volume reduction methods are being actively investigated in an attempt to reduce the typical shortcomings of the resectional procedure.

To minimize both anesthesiological and surgical traumas, we have developed an original awake non-resectional LVRS method, which respects the basic concepts of the resectional procedure, but adds some theoretical advantages and can be performed under sole thoracic epidural anesthesia [8,11].

Previous studies from our group [8,12] comparing results of awake LVRS with those of the standard resectional technique have suggested an advantage of the awake approach in terms of air-leak occurrence and duration of hospital stay with comparable clinical improvements.

However, it is unclear whether these better results could be attributed to the avoidance of general anesthesia and one-lung ventilation or rather to the use of a non-resectional LVRS method. Yet, questions have been raised as to the liberal acceptance and tolerability of an awake surgical procedure in functionally fragile patients.

In this study, we sought to comparatively analyze comprehensive results and procedure-related costs of...
non-resectional LVRS performed by awake or non-awake anesthesia.

2. Material and methods

Sixty patients undergoing unilateral non-resectional LVRS at the Tor Vergata University School of Medicine between March 2007 and March 2010 were included in the study.

The study was designed as an observational, prospective clinical investigation aimed at assessing the comparative outcome of non-resectional LVRS carried through sole thoracic epidural (awake group) or general anesthesia (non-awake group), and was approved by the Tor Vergata Ethical committee. All patients gave written informed consent for the procedure and were free to choose the preferred type of anesthesia. For this purpose, together with the informed consent to be signed, each patient received a written explanation of the main characteristics and theoretical advantages and disadvantages of non-resectional LVRS performed either by sole epidural anesthesia or through general anesthesia and one-lung ventilation. In particular, the text advised that during an awake operation, surgical maneuvers might turn out to be somewhat more technically demanding and that the procedure might be less comfortably tolerated in some instances due to risks of hypercapnia and panic attacks, although the immediate postoperative course was expected to be smoother than after general anesthesia due to lack of weaning-related adverse effects. Conversely, general anesthesia might allow achievement of an immmobile operative field and avoids risks of panic attacks, although a longer stay in the recovery room and early postoperative respiratory discomfort were likely to be more common.

Eligibility criteria for LVRS have been already reported [13] and included the finding of severe emphysema with radiologic evidence of distinct heterogeneity of disease associated with severe disability despite maximized medical care, post-bronchodilator forced expiratory volume in 1 s (FEV1) less than 40% predicted, and plethysmographic residual volume (RVplet) more than 180% predicted.

Patients with radiologic evidence of extensive pleural adhesions with pleural scarring and calcifications and/or a contraindication for thoracic epidural anesthesia including patient’s refusal or non-compliance, unfavorable anatomy, previous surgery of the cervical or upper thoracic spine, compromised coagulation (thromboplastin time <80%, pro-thrombin time >40 s, or platelets <100 thousand /l), or bleeding disorder were excluded from this study.

Preoperative work-up was that typically employed in LVRS candidates and included spirometry with plethysmography and high-resolution computed tomography.

All patients were former smokers and had quit smoking at least 4 months before the operation; no patient was homozygous for α1-antitrypsin deficiency.

Results were assessed according to three different outcome domains: perioperative outcome, cost analysis and postoperative outcome. Perioperative outcome measures included the ratio of arterial oxygen tension to fraction of inspired oxygen (PaO2/FIO2), arterial carbon dioxide tension (PaCO2), mean arterial pressure and heart rate (HR), assessed at three fixed time points (T1 = preoperative in lateral decubitus; T2 = end-operative; and T3 = 1 h after the operation). In addition, patients’ satisfaction with the chosen type of anesthesia was assessed according to a four-grade ordinal scale ranging from 4 = excellent to 1 = unsatisfactory. Cost analysis included costs of devices, dressing materials, medications, surgical instrumentation and hospital stay, whereas costs of preoperative rehabilitation and diagnostic work-up were excluded. Postoperative clinical outcome included changes in FEV1, RVplet, exercise capacity assessed by both the maximal incremental treadmill test MITT and the 6-min walking test (SMWT); dyspnea according to the modified Medical Research Council; health-related quality of life measure of physical functioning according to the Short Form 36 Health Survey (SF-36) items score; these were assessed at 6 months and every 6 months thereafter. In the awake group, patients requiring conversion to general anesthesia were excluded from perioperative analysis, whereas, when dealing with clinical outcome, they were included in the general anesthesia group.

2.1. Anesthesia and surgical technique

2.1.1. Awake anesthesia

The technique for awake anesthesia has been already described in detail [11]. Briefly, objective of thoracic epidural anesthesia was to achieve somatosensory and motor block at the T1–T8 level while preserving diaphragmatic motion. The thoracic epidural catheter was inserted at T4 level. In the operating room, patients received a continuous infusion of ropivacaine 0.5% and sufentanil 1.66 μg ml⁻¹ into the epidural space. During the procedure, patients breathed O2 through a Venturi mask/face to keep oxygen saturation above 90%.

Permissive hypercapnia has been commonly accepted and did not require any correction, as it was satisfactorily tolerated during surgery. Anyway, we set up as a safety limit for correction of hypercapnia, pH < 7.2. During wound closure, the anesthetic regimen was changed to ropivacaine 0.16% and sufentanil 1 μg ml⁻¹ at 2–5 ml h⁻¹. In all patients, the epidural catheter was removed 48 h after surgery.

2.1.2. Non-awake anesthesia

In patients undergoing non-resectional LVRS through general anesthesia, this was induced by intravenous propofol (1.5–2 mg kg⁻¹), fentanyl (0.1 mg), and vecuronium (0.1 mg kg⁻¹) and subsequently maintained using a continuous infusion of propofol, fentanyl, and vecuronium. Intra-operative ventilatory management was carried out according to a protective ventilation strategy to assure adequate oxygenation by low tidal volume and maximized exhalation time. A left-sided double-lumen tube was used for single-lung ventilation.

2.1.3. Surgical technique

In all instances, the operation was carried out by video-assisted thoracoscopic surgery (VATS). The patient was placed in full lateral decubitus position. A Four-trocars access was employed for a 30° 10-mm camera and standard instrumentation. Whenever severe lung hyperinflation persisted despite creation of the surgical pneumothorax, an endopaddle lung retractor was employed to increase the operating space, whereas CO2 insufflation was never employed.
Table 1. Preoperative data.

<table>
<thead>
<tr>
<th></th>
<th>Awake group</th>
<th>Non-awake group</th>
<th>Intergroup P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>Quartile range</td>
<td>Median</td>
</tr>
<tr>
<td>BMI</td>
<td>22.5</td>
<td>22.25</td>
<td>23</td>
</tr>
<tr>
<td>FEV1 (l)</td>
<td>0.85</td>
<td>0.71—1.0</td>
<td>0.86</td>
</tr>
<tr>
<td>FEV1 (%)</td>
<td>28</td>
<td>24—34</td>
<td>30</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>2.48</td>
<td>2.11—2.7</td>
<td>2.69</td>
</tr>
<tr>
<td>FVC (%)</td>
<td>63</td>
<td>55—77</td>
<td>72</td>
</tr>
<tr>
<td>RV (l)</td>
<td>5.28</td>
<td>4.8—5.5</td>
<td>5.0</td>
</tr>
<tr>
<td>RV (%)</td>
<td>230</td>
<td>209—261</td>
<td>220</td>
</tr>
<tr>
<td>TLC (l)</td>
<td>9.0</td>
<td>8.2—9.6</td>
<td>8.75</td>
</tr>
<tr>
<td>TLC (%)</td>
<td>139</td>
<td>134—152</td>
<td>140</td>
</tr>
<tr>
<td>SMWT (m)</td>
<td>380</td>
<td>350—420</td>
<td>360</td>
</tr>
<tr>
<td>PO2 (mmHg)</td>
<td>69</td>
<td>65—74</td>
<td>67</td>
</tr>
<tr>
<td>PaCO2 (mmHg)</td>
<td>40</td>
<td>39—42</td>
<td>41</td>
</tr>
<tr>
<td>Dyspnea index (score)</td>
<td>3.0</td>
<td>3.0—4.0</td>
<td>3.0</td>
</tr>
<tr>
<td>PF (SF-36 score)</td>
<td>30</td>
<td>25—35</td>
<td>25</td>
</tr>
</tbody>
</table>

BMI: body mass index; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; RV: residual volume; SMWT: 6-min walking test; MITT: maximal incremental treadmill test; dyspnea index score: modified Medical Research Council dyspnea score; PaO2: arterial oxygen tension; PaCO2: arterial carbon dioxide tension; and PF: Short Form 36 items physical functioning domain score.

The most emphysematous target areas were visualized and introflexed with a cotton swab while redundant lung edges were grasped by two ring forceps. Subsequently, both lung edges were grasped together by a single ring forcep, and a 45-mm, ‘no knife’ endostapler was applied on the plicated lung region starting at the apex of the upper lung lobe and continuing applying two other cartridges ventrally and dorsally to perform a linear, interrupted suture line.

2.2. Statistical method

Group descriptive statistics are presented as median with quartile range (QR), unless differently indicated. Two-way analysis of variance (ANOVA) for repeated measures was employed to analyze repeated perioperative and post-operative outcome measures. Variables showing significant \( P < 0.05 \) between-group difference at the ANOVA were subsequently analyzed stepwise by means of the Mann—Whitney U test. The Wilcoxon matched pairs test or the Fisher exact test were used for paired data and frequencies, respectively.

Survival was assessed by the Kaplan—Meier method and intergroup difference was assessed by the Log-rank test. All reported \( P \) values are two-sided. Statistical analysis was performed by Statistica© software version 7.0.

3. Results

During the study period, out of 84 screened patients, 24 were excluded because of insufficient severity of emphysema in 16 patients, too homogeneous emphysematous lung destruction with no target areas or radiologic evidence of diffuse fibrous adhesions requiring a thoracotomy approach in three patients each, and diffusing capacity for carbon monoxide less than 20% in 2 patients.

Out of 60 patients recruited for the study, 41 (38 males and three females) underwent an awake LVR5 procedure (awake group) and 19 (18 males and one female), a non-awake operation (non-awake group).

Median age in the awake and non-awake groups was 66 years (QR: 66—70 years) and 63 years (QR: 60—69 years), respectively \( (P = 0.86) \). There was no difference between the study groups in main baseline data (Table 1).

3.1. Perioperative outcome and costs

Conversion to general anesthesia was necessary in two patients in the awake group due to occurrence of a panic attack, whereas no patient in either group required conversion to thoracotomy.

In the awake group, thoracic analgesia induced by epidural catheterization was effective in 39 patients, whereas in two patients, additional local injection of anesthetic was required during the operation.

Changes in physiologic variables throughout the procedure are illustrated in Fig. 1. Overall, oxygenation remained satisfactory although the type of anesthesia had a significant impact on its perioperative behavior. In particular, stepwise analysis showed that at T3, PaO2/FiO2 returned toward the preoperative value in the awake group (Wilcoxon, \( P = 0.46 \)), whereas it decreased significantly in the non-awake group (Wilcoxon, \( P = 0.01 \)). Conversely, PaCO2 increased at T2 in both study groups; thereafter, it returned to the baseline values at T3 in the awake group only (Wilcoxon, \( P = 0.26 \)), whereas it continued to increase in the non-awake group (Wilcoxon, \( P = 0.0002 \)).

Mean arterial pressure and HR also varied significantly in both study groups, although the type of anesthesia did not affect changes in HR; at T3, no between-groups difference in either arterial pressure or HR was detected.

As far as the impact of the type of anesthesia on operating room times is concerned, Table 2 shows that recovery room time and the resulting global in-operating room time were significantly shorter in the awake group, whereas satisfaction with the type of anesthesia was similar between the study groups.

There was no difference in awake versus non-awake groups median VAS at 24 h \( (2 \text{ vs } 2, \ P = 0.23) \) nor in need of
additional analgesia on the fourth postoperative day (four vs two patients, Fisher’s exact test, $P = 1.0$).

There was no operative mortality. The most frequent non-fatal complication was prolonged air leaks (>7 days), which occurred in five patients of each group (Fisher’s exact test, $P = 0.26$). Other less frequent complications included transient atrial fibrillation, which occurred in no patient in the awake group and in two patients in the control group. Two patients in the awake group had urinary retention requiring temporary catheterization, whereas one patient in the non-awake group had atelectasis requiring aspiration bronchoscopy. Hospital stay was significantly shorter in the awake group, and overall procedure-related costs were lower in the same group (Table 2).

### 3.2. Clinical and functional outcome

Median follow-up was 25 months (QR: 10–30 months) in the awake group and 30 months (QR: 17–32 months) in the control group with no patient lost. At 6 months, body mass index (BMI), FEV$_1$, forced vital capacity (FVC), RV$_{p,let}$, SMWT, MITT, Pa$_O2$, Pa$_CO2$, dyspnea index, and SF-36 physical

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**Table 2. Perioperative results.**

<table>
<thead>
<tr>
<th></th>
<th>Awake group</th>
<th>Non-awake group</th>
<th>Intergroup P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>Quartile range</td>
<td>Median</td>
</tr>
<tr>
<td>Anesthesia time (min)</td>
<td>35</td>
<td>33–40</td>
<td>35</td>
</tr>
<tr>
<td>Surgery time (min)</td>
<td>40</td>
<td>32–50</td>
<td>35</td>
</tr>
<tr>
<td>Weaning time (min)</td>
<td>—</td>
<td>—</td>
<td>45</td>
</tr>
<tr>
<td>Recovery room time (min)</td>
<td>60</td>
<td>40–60</td>
<td>120</td>
</tr>
<tr>
<td>Global in-operating room time (min)</td>
<td>127</td>
<td>120–141</td>
<td>297</td>
</tr>
<tr>
<td>Anesthesia satisfaction (score)</td>
<td>3</td>
<td>3–4</td>
<td>3</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>6.0</td>
<td>5.0–7.0</td>
<td>7</td>
</tr>
<tr>
<td>Global cost (euros)</td>
<td>7800</td>
<td>7000–8600</td>
<td>8600</td>
</tr>
</tbody>
</table>
functioning score improved significantly in both study groups with no between-groups differences (Table 3). Among acutely observed clinical improvements, those in BMI, FEV1, FVC, RVplet, SMWT, MITT, dyspnea index, and quality of life lasted for up to 24 months (Fig. 2); PaO2 remained improved for up to 12 months in the non-awake group (Wilcoxon, P = 0.01) and for up to 24 months in the awake group (Wilcoxon, P = 0.009).

Estimated 3-year survival was 82% in the awake group and 86% in the non-awake group with no between-groups difference (Fig. 3). Late mortality was due to respiratory failure in two patients, myocardial infarction in two patients, and lung cancer development in one patient.

4. Comment

In this study, non-resectional LVRS resulted in significant clinical improvements that lasted for more than 24 months and occurred independent of the type of anesthesia that was chosen. However, in the awake group, there was a better

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Table 3. Absolute postoperative changes in outcome measures at 6 months.

<table>
<thead>
<tr>
<th></th>
<th>Awake group</th>
<th>Quartile range</th>
<th>Non-awake group</th>
<th>Quartile range</th>
<th>Between groups P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔBMI (l)</td>
<td>0.66 **</td>
<td>0.0—0.96</td>
<td>0.34**</td>
<td>0.0—0.74</td>
<td>0.20</td>
</tr>
<tr>
<td>ΔFEV1 (l)</td>
<td>0.33 *</td>
<td>0.25—0.42</td>
<td>0.28**</td>
<td>0.20—0.34</td>
<td>0.09</td>
</tr>
<tr>
<td>ΔFVC (l)</td>
<td>0.40 **</td>
<td>0.30—0.54</td>
<td>0.32**</td>
<td>0.16—0.44</td>
<td>0.11</td>
</tr>
<tr>
<td>ΔRV (l)</td>
<td>0.99 *</td>
<td>1.2—0.8</td>
<td>0.98 **</td>
<td>1.19—0.70</td>
<td>0.95</td>
</tr>
<tr>
<td>ΔSMWT (M)</td>
<td>90 **</td>
<td>60—120</td>
<td>80*</td>
<td>60—90</td>
<td>0.40</td>
</tr>
<tr>
<td>ΔMITT (Bruce)</td>
<td>1 **</td>
<td>0.5—1.5</td>
<td>0.75 **</td>
<td>0.50—1.0</td>
<td>0.31</td>
</tr>
<tr>
<td>ΔDyspnea index (score)</td>
<td>1 **</td>
<td>2.0—1.0</td>
<td>1 **</td>
<td>2—1</td>
<td>0.95</td>
</tr>
<tr>
<td>ΔPF (SF-26 score)</td>
<td>25 **</td>
<td>20—40</td>
<td>25 **</td>
<td>20—35</td>
<td>0.35</td>
</tr>
<tr>
<td>ΔPaO2 (mmHg)</td>
<td>3 **</td>
<td>2—5</td>
<td>2 **</td>
<td>1—3</td>
<td>0.1</td>
</tr>
<tr>
<td>ΔPaCO2 (mmHg)</td>
<td>1 **</td>
<td>0—3</td>
<td>2 **</td>
<td>0—3</td>
<td>0.28</td>
</tr>
</tbody>
</table>

BMI: body mass index; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; RV: residual volume; SMWT: 6-min walking test; MITT: maximal incremental treadmill test; dyspnea index: modified Medical Research Council dyspnea score; PF: Short Form 36 items physical functioning domain score; PaO2: arterial oxygen tension; and PaCO2: arterial carbon dioxide tension. Within group: *P < 0.0001; **P < 0.01.

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Fig. 2. Postoperative behavior of body mass index (BMI), forced expiratory volume in 1 s (FEV1), plethysmographic residual volume (RVplet), maximal incremental treadmill test; 6-min walk test and Short Form 36 physical functioning domain score. ANOVA: R1 = overall effect; R1*Group = between-groups effect.
perioperative outcome and a shorter hospital stay that eventually reflected in reduced procedure-related costs.

Different lung plication methods for surgical treatment of emphysema resulting in satisfactory morbidity rates and optimal clinical results have been reported in the past [14-16]. Each proposed method has peculiar characteristics and they differ from the introflexive lung plication method that we have developed.

Our non-resectional method respects the basic concepts advocated by Cooper et al. [17] including a reduction of 20-30% of the lung volume, suturing performed along a single ideal line, and use of stapling devices. Yet, it adds some conceptual differences that include peripheral suturing to minimize interruption of segmental anatomic structures and an interrupted suture line. Furthermore, we expect to produce a fourfold pleural buttress of the suture line as well as an inlay buttress created by the plicated bullous tissue itself.

4.1. Perioperative outcome

A recent analysis of the National Emphysema Treatment Trial (NETT) trial results [6] has shown that prolonged air leak occurs in nearly 30% of patients undergoing LVRS and is commonly associated with a complicated and protracted hospital course.

In this study, non-resectional LVRS resulted in a relatively low rate of prolonged air leaks, which occurred in the awake and non-awake groups in 12% and 26% of the patients, respectively. These data compare favorably with previously reported results [6,17] and suggest that independent of the type of anesthesia, the low occurrence of prolonged air leaks we have observed was mainly attributable to the type of non-resectional method per se.

General anesthesia and single-lung ventilation has been deemed inevitable for LVRS. However, several adverse effects can derive from this type of anesthesia, including risks of pneumonia, cardiovascular and neuromuscular problems, bronchospasm and airways injury, and a multifactorial injury related to mechanical ventilation [18].

Most of these adverse effects can be avoided by employing thoracic epidural anesthesia in awake patients.

Conversely, with awake anesthesia and spontaneous ventilation, surgical maneuvering can be complicated by maintenance of diaphragmatic motion and coughing reflexes, which can be elicited by lung hilum stretching and compression of cartilaginous bronchi. However, we have found that, by our lung plication method entailing peripheral suturing with reduced manipulation of the central part of the lung, risk of coughing reflexes is minimized.

Use of thoracic epidural anesthesia in respiratory compromised patients had raised concerns related to the fear that the motor blockade might lead to respiratory impairment and that sympathetic blockade could increase bronchial tone and airway reactivity [19].

It also survived Sauerbruch's belief [20] that an open pneumothorax could cause severe respiratory impairments due to mediastinal shift with kinking of mediastinal vessels and compression of the dependent lung. In addition, collapse of the non-dependent lung due to the presence of an intrapleural atmospheric pressure environment increases the inspiratory load and might also negatively affect respiration.

Our growing experience with awake non-resectional LVRS, as well as data reported by other investigators with awake cardiac surgery [21], indicates that most of the aforementioned concerns were unfounded. Indeed, in the current study, even in patients with baseline $PaO_2$ as low as 55 mmHg, simple administration of oxygen through a Venturi mask permitted to maintain oxygenation to satisfactory levels throughout the procedure.

To this respect, some recently reported data suggest that suprapontine compensatory mechanisms are active in defending ventilation in awake subjects challenged with an inspiratory load [22].

The perioperative behavior of $PaCO_2$ differed in the study groups. In the awake group, there was an end-operative rise in $PaCO_2$ and a rapid fall toward normal values 1 h after the operation; instead, in the non-awake group, $PaCO_2$ increased moderately during the operation but continued to increase 1 h after its completion.

In the immediate postoperative period, physiologic changes in patients operated by awake or non-awake anesthesia differ meaningfully. Following awake LVRS, the maintained diaphragmatic motion facilitates synchronized rib—cage—abdominal motion during ventilation, whereas rib—cage—abdominal paradoxical motion is commonly observed during weaning from general anesthesia with mechanical ventilation, an event that is attributed to inspiratory muscle loading. Indeed, weaning from general anesthesia and mechanical ventilation in emphysema patients can be complicated by several adverse events. Immediately after surgery, expiratory flow limitation hampers expiration and worsens gas trapping, leading to rapid shallow breathing that, in time, increases inspiratory workload, decreases respiratory muscle capacity, and hampers CO₂ elimination [23].

Other factors can contribute to cause incomplete expiration and thus increase gas trapping following thoracic surgery, including post-intubation airways' irritation and secretions' accumulation that increase expiratory resis-
tance; expiratory muscle recruitment; and occult small airway disease secondary to increased lung water [24]. In accordance with these findings, Buduhan et al. [25] have shown in an experimental study that immediately after non-awake LVRS, there is impairment in lung mechanical properties due to decreased respiratory compliance and increased gas trapping that may contribute to difficult weaning and other respiratory complications.

4.2. Cost analysis

Lung volume reduction is considered an expensive procedure for a highly prevalent disease, and, thus, its impact on health-care budgets is potentially relevant.

In a multicenter study, Miller et al. [4] reported that LVRS costs an additional C$28,119 compared with best medical care. Their conclusions were that cost of LVRS is high, but, in keeping with other treatment modalities currently available. In the cost-effectiveness analysis of NETT [7], the incremental cost-effectiveness ratio for LVRS compared with medical therapy was $190,000 at 3 years but decreased to $93,000 when projected at 10 years. Conclusions of this study were that LVRS may be cost effective if benefits are maintained over time as it occurred in patients with upper-lobe predominant emphysema and low exercise capacity, in whom the estimated cost per quality-adjusted life year gained was $21,000 only at 10 years.

We had previously reported that awake non-resectional LVRS could be as effective as the standard non-awake resectional procedure in terms of clinical outcome, but resulted in a reduced incidence of prolonged air leak, a significantly shorter hospital stay, and lower costs [8].

Results of the current analysis adds to these findings, showing that even when comparing awake versus non-awake anesthesia in patients undergoing the same type of non-resectional LVRS method, preference of awake anesthesia can account per se for a significant reduction in overall costs.

4.3. Postoperative outcome

In a recent update of the NETT results [3], patients with upper-lobe predominant emphysema and low exercise capacity demonstrated improved 3-year exercise capacity and 5-year relief of dyspnea, and better 5-year survival than medically treated patients.

In the current series, all patients had severe heterogeneous emphysema with impaired exercise capacity, estimated 3-year survival rate was higher than 80%, and significant clinical improvements, including respiratory function measures, maximal (MWT) and submaximal (SWMT) exercise capacity measures as well as perceived quality of life and subjective dyspnea scores, occurred for up to 24 months in both study groups with no between-groups difference. These results indicate that use of awake anesthesia did not jeopardize the possibility to achieve an effective non-resectional reduction in lung volume. They also confirm that satisfactory survival rate and long-lasting clinical improvements can be achieved with unilateral LVRS that we now routinely prefer to one-stage bilateral treatment. We have chosen this unconventional treatment strategy, as we believe that initial unilateral LVRS with unilateral treatment delayed until when benefit of the first operation is lost, can assure more stable and long-lasting improvements than a simultaneous bilateral operation.

It is worth noting that, in this observational study, most patients have liberally preferred the awake anesthesia. This finding supports our perceived feeling that patients with poor pulmonary function can be reluctant to accept LVRS mainly due to a fear of general anesthesia.

4.4. Limitations

Main limitations of our analysis include the non-randomized nature and discrepancies in patients’ samples that may have affected statistical analysis of between-group results, particularly regarding the lack of differences in clinical outcome measures. The particular study design adopted for this study allowed to provide insights into patients’ preferred type of anesthesia without the bias of the surgeon’s influence in the choice. Nonetheless, leaving patients to decide the anesthesia technique did not exclude other potential biases, including the occurrence of extra-surgical-staff environmental inference on the patient’s choice.

Finally, because of literature data suggesting beneficial effects of TEA on diaphragmatic function in patients undergoing upper abdominal surgery, a note of caution must be raised when interpreting data on the better perioperative outcome observed in the awake group with TEA, as this was not employed also in the control group.

4.5. Conclusion

Our study results have shown that following non-resectional LVRS, sustained clinical improvement lasting for up to 24 months occurred in both study groups, although better perioperative outcome, shorter hospital stay, and lower costs have been observed in the awake group. We now await results of a randomized study to confirm or contradict these findings.

References

Dr K. Athanassiadi (Athens, Greece): I have to comment that in reading your paper, I did not find big differences from the paper you published back in 2006. You also are very intelligent in pointing out in one of your last slides the limitations of your study. I think that you had a really good statistical analysis, although I found that if you could from the beginning put out the statistical power, you could find that even the 1-day difference for the hospitalization stay could have been statistically significant. You state that there was no influence from the surgeon on the patient, so there was no bias, but, on the other hand, there is a bias from the patient because he chose the anesthesia.

Dr Pompeo: Of course.

Dr Athanassiadi: I’m looking forward to seeing the 5-year survival because I think that’s more important.

Dr R. Cerfolio (Birmingham, USA): I still think the majority of us, at least in North America, are doing resections as opposed to non-resections, and what happens to your staple line? Does that staple line open? You’ve addressed those concerns before, but could you readdress that, the advantages not so much of awake versus not awake but of doing a resection as opposed to a non-resection type of LVRS?

Dr Pompeo: Actually, lung plication techniques were developed many years ago. One is from Crosa-Dorado. This has been applied by Swanson through thoracoscopic surgery. One was from Iwasaki. Even Brantigan employed lung plication to perform lung volume reduction surgery while also doing resectional lung volume reduction. Indeed we actually believe that through the non-resectional method there may be some advantage, probably along the suture line. This is in my opinion the main point, because with the introflexing ligation, bullous tissue is pulled down, then creating an infalt buttress over the suture line, then the suture line is interrupted. Although it’s performed along a single ideal line, as Cooper advocated for the resectional technique, we believe that the apex of the lung, the apical part of the lung is more flexible with an interrupted suture and then can fit the pleural cavity better. So these are the theoretical advantages we believe we can obtain with this technique, but a randomized study is needed, and I think comparing the standard resectional technique versus the non-resectional technique will give the final answer.

Dr Cerfolio: My second question would be about the art of doing this operation with the patient awake and your cooperation with anesthesia. Can every anesthesiologist in your department do these, or have you picked one or two that can do it? And tell us some tricks. In addition, if you’re using a local anesthetic, like lidocaine or Marcaine, do you calculate a toxic dose and then try to stay below it? What are the logistics of numbing the patient up and doing this awake?

Dr Pompeo: We have cooperation with the anesthesiologists in our group. Not all of them can face this kind of procedure. I must say that a well-done thoracic epidural anesthesia is the secret to having the patient quiet during the operation. It’s rarely necessary to increase anesthesia locally with lidocaine, although it sometimes can be necessary as well. An important point is the panic attacks. Not all patients can stay perfectly quiet and calm during the procedure despite a well-done thoracic epidural anesthesia. The patient does not feel pain, but the most important thing is the feeling of difficulty in breathing. This difficulty in breathing is due to the inspiratory load created by the surgical pneumothorax. You must reassure your patient that oxygenation can remain well despite this difficulty.

Dr C. Choong (Melbourne, Australia): Professor Pompeo, now that you have discovered these important findings, have you changed your practice? Are you persuading your patients more towards awake surgery?

Dr Pompeo: Yes, I must say that the possibilities of awake surgery are being actively investigated on several topics. And, as you probably know, we are searching to find advantages on other topics in thoracic surgery as well, yes.

Dr J. Mitchell (Denver, USA): I have a follow-up to Dr Cerfolio’s question regarding the technique. Is exposure ever a problem, that is, obtaining adequate visualization? Do you ever have issues thoracoscopically with people with severe upper-lobe predominant emphysema, and how do you deal with that when they are awake, breathing spontaneously?

Dr Pompeo: This is an important question. Sometimes exposure and visualization can be difficult due to lung hyperinflation, which remains even following the surgical pneumothorax. We usually use an endoscopic endopaddle and we press it moderately against the lung to have a nice view of the apex. Of course, division of adhesions can also be somewhat demanding in these patients, but we have seen that sometimes you can leave adhesions at the apex of the lung and go dorsally and anteriorly and then perform the lung plication without dividing the adhesions. This can also allow the lung to remain at the apex following the operation. There are several small tricks you can apply to perform this procedure, although with one-lung ventilation, of course the exposure is better.