Safety and Considerations of the Anaesthetic Management during Bronchoscopic Lung Volume Reduction Treatments

Roodenburg, Sharyn A.; Barends, Clemens R.M.; Krenz, Grita; Zeedijk, Eelco J.; Slebos, Dirk Jan

Published in:
Respiration

DOI:
10.1159/000528044

Respiration

Interventional Pulmonology

Respiration 2023;102:55–63
DOI: 10.1159/000528044

Received: February 21, 2022
Accepted: November 4, 2022
Published online: December 1, 2022

Safety and Considerations of the Anaesthetic Management during Bronchoscopic Lung Volume Reduction Treatments

Sharyn A. Roodenburg[a, b] Clemens R.M. Barends[c] Grita Krenz[c]
Eelco J. Zeedijk[c] Dirk-Jan Slebos[a, b]

[a]Department of Pulmonary Diseases, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; [b]Groningen Research Institute for Asthma and COPD, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; [c]Department of Anaesthesiology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Keywords
Anaesthesia · Bronchoscopy · Bronchoscopic lung volume reduction · Chronic obstructive pulmonary disease · Mechanical ventilation

Abstract
Background: Different bronchoscopic lung volume reduction approaches are available for a select group of patients with advanced COPD. General anaesthesia is the recommended method of sedation during these procedures. However, this patient population is at an increased risk of anaesthetic complications, and the best approach to general anaesthesia and mechanical ventilation is unknown. ***Objectives:*** The aims of this study were to describe the anaesthetic management techniques used during bronchoscopic lung volume reduction procedures and to investigate the number of anaesthesia-related events. ***Methods:*** Data were retrospectively collected from all endobronchial valve and lung volume reduction coil procedures performed between January 2018 and March 2020 in our hospital. Primary outcomes measures were anaesthetic technique including airway management; ventilation mode and settings; and the incidence of anaesthesia-related events, classified as catastrophic, severe, significant, or moderate. ***Results:*** 202 procedures were included. One procedure was performed under procedural sedation, 198 (98%) under general anaesthesia with endotracheal intubation, and 3 (1.5%) under general anaesthesia with laryngeal mask airway. Volume-controlled ventilation was used in 64% of the procedures and pressure-controlled in 36%. Patients were ventilated with a median respiration rate of 9.9 (IQR: 9.6–10.6) breaths per minute, mean tidal volume of 5.8 ± 1.4 mL/kg, and median inspiratory to expiratory (I:E) ratio of 1:2.8 (IQR: 1:2.1–1:3.2). No catastrophic anaesthesia-related events were observed. Hypotension was the most observed anaesthesia-related event. ***Conclusions:*** Despite the presence of advanced COPD, general anaesthesia and mechanical ventilation are well tolerated by patients undergoing endobronchial valve or lung volume reduction coil treatment. This is presumably strongly linked to the strict selection criteria. Other important considerations are using a low respiratory rate, low tidal volume, and high I:E ratio.

Karger@karger.com
www.karger.com/res

Correspondence to:
Sharyn A. Roodenburg, s.a.roodenburg@umcg.nl

Introduction

Bronchoscopic lung volume reduction (BLVR) provides an additional treatment option for a select group of patients with advanced chronic obstructive pulmonary disease (COPD). Several BLVR approaches have been developed, of which endobronchial valves (EBVs) and lung volume reduction coils (LVR-coils) are the most intensively studied and used in clinical practice [1–6]. EBVs are designed to occlude the bronchi of the most emphysematous lobe and allow for air to leave this lobe during expiration, leading to a decrease in volume [3]. LVR-coils are designed to compress the lung parenchyma, thereby re-tensioning the lung tissue which leads to reduced air trapping and hyperinflation [4].

Both EBV and LVR-coil procedures require an adequate level of sedation to provide optimal bronchoscopic conditions for device implantation, minimize movement, and ensure patient comfort. General anaesthesia is the preferred and recommended method of sedation for these procedures because it provides ease of airway and patient management and reduces procedure time [3, 4, 6, 7]. The anaesthetic management of patients eligible for EBV or LVR-coil treatment poses challenges. The intra- and post-operative complication risks are increased due to the presence of advanced COPD with severe airflow obstruction. In addition, the patients might also be of more advanced age and have a high likelihood of pre-existing diseases or comorbidities that further increase the risk of complications [8].

Despite an increasing number of patients undergoing a BLVR treatment worldwide, the literature on anaesthetic management, during these procedures, is still very limited [9]. Based on clinical experience and one small retrospective study, it is suggested that general anaesthesia with mechanical ventilation can be applied safely [6, 10]. However, the best approach to provide general anaesthesia and mechanical ventilation remains unknown. Therefore, we aimed to describe the anaesthetic management techniques used in our high-volume treatment centre and investigate the number of anaesthesia-related events.

Materials and Methods

Study Design and Participants

In this retrospective cohort study, data were collected from all EBV and LVR-coil procedures performed between January 1, 2018, and March 1, 2020, at the University Medical Centre Groningen (UMCG), The Netherlands. All EBV procedures were performed within our regular treatment program BREATHE-NL (NCT02815683). The LVR-coil procedures were performed within the ELEVATE trial (NCT03360396) [11] or as compassionate use within the BREATHE-NL treatment program. The ELEVATE trial received ethics approval by all participating site's Local Medical Ethics Committees. Due to the non-invasive nature of the BREATHE-NL Registry, formal ethics approval was waived by the Medical Ethics Committee of the UMCG. Due to the retrospective nature of the current study, it did not fall within the scope of the Dutch Medical Research Involving Human Subjects Act (WMO), and therefore, no formal ethics approval was needed. This study was conducted in accordance with the amended Declaration of Helsinki, and all included participants provided written informed consent for participation in the ELEVATE trial or for inclusion of their data in the BREATHE-NL registry.

Patient Selection and Preparation

The patient selection criteria for EBV and LVR-coil treatment are similar and have been described in previous publications [3, 4, 6]. Eligible patients suffer from advanced COPD of the emphysematous phenotype, have evident hyperinflation (residual volume >175% of predicted for EBVs and >200% of predicted for LVR-coils), and remain highly symptomatic (modified medical research council dyspnoea score ≥2) despite optimal medical treatment, which includes smoking cessation, guideline pharmacological treatment, and pulmonary rehabilitation and/or a structured physical therapy program. To be eligible for EBV treatment, the absence of collateral ventilation between the treated and ipsilateral lobe is essential, which is evaluated by visual inspection of a high-resolution computed tomography (HRCT) scan, qualitative analysis of the HRCT scan, and a collateral flow measurement using the Chartis System (Pulmonx Corp., CA, USA).

Patients are less or not at all eligible if one or multiple of the following are present: significant gas exchange abnormalities (diffusion capacity for carbon monoxide <20% of predicted, partial pressure of oxygen <6 kPa, or partial pressure of carbon dioxide >8 kPa), significant airway disease (asthma, unstable chronic bronchitis, clinical significant bronchiectasis), significant paraseptal emphysema, significant congestive heart failure (left ventricular ejection fraction <40%), unstable cardiovascular disease, pulmonary hypertension (right ventricular systolic pressure >55 mm Hg on echocardiogram), frequent infectious exacerbations, and nodules suspect for active infection or malignancy. In our hospital, patients are admitted 1 day before the procedure (for logistical reasons), continue their standard medication, and are prescribed a 5-day course of prophylactic prednisolone (30 mg daily, starting the day before the procedure) and antibiotics (azithromycin 250 mg daily, starting the day of the procedure).

Procedures and Anaesthesia Technique

The technical aspects of the treatments have been described elsewhere [3, 4, 6]. In brief, the implantation of EBVs (Pulmonx Corp., CA, USA) is preceded by a bronchoscopic collateral flow measurement using the Chartis System during the same procedure as the actual EBV placement. If the Chartis measurement confirms the absence of collateral ventilation, EBVs are implanted. Otherwise, the procedure is terminated. LVR-coils (PneumRx/BTG, CA, USA, and later Boston Scientific Corp., MA, USA) are implanted under fluoroscopic guidance. Preferably, LVR-coils are implanted bilaterally in two separate procedures 4–8 weeks apart.

In our hospital, patients are hospitalized for at least 3 days following EBV treatment and 1 day following LVR-coil treatment. A flexible fibre-optic bronchoscope (outer diameter: 6.2 mm, working channel: 2.8 mm) was used to perform all procedures. To reduce coughing after EBV implantation and thereby reduce the risk of a post-procedural pneumothorax or EBV dislocation, 50–100 mg lidocaine 1% was applied topically at the EBV treatment location.

The method of sedation and airway management was decided by the anaesthesiologist. However, general anaesthesia with endotracheal intubation was the preferred method. If intubated, a 9-mm flexible endotracheal tube (ETT) was used. Patient monitoring during anaesthesia consisted of a 3-lead electrocardiogram, peripheral blood oxygen saturation, end-tidal CO_2, non-invasive blood pressure monitoring, and electroencephalography-based depth of sedation monitoring using a bispectral index monitor. A Primus anaesthesia workstation (Dräger Medical, Lübeck, Germany) was used during all procedures. Five minutes before extubation, an intravenous bolus of opioids (fentanyl 50 μg/mL or morphine 1 mg/mL) was administered to suppress the cough reflex in the post-procedural period. Patients were extubated in the bronchoscopy suite and subsequently transferred to the post-anaesthesia care unit. After full recovery, patients were transferred to the general ward.

Outcome Measures and Data Collection

The primary outcome measures were (1) anaesthetic technique including airway management, (2) ventilation mode and settings, and (3) the incidence of anaesthesia-related events. Anaesthesia-related events were classified as catastrophic, severe, significant, or moderate based on a previous publication that used the official list of recognized anaesthetic complications of the Dutch Society for Anaesthesiology and existing literature [12–14]. Anaesthesia-related events included same-day death, cardiopulmonary resuscitation, unplanned intensive care unit (ICU) admission, re-intubation, hypotension requiring medication, desaturation, bradycardia, tachycardia, hypercapnia, aspiration, and allergic reaction. The secondary outcome was all post-procedural complications that occurred during hospitalization.

Pre-treatment patient characteristics, including age, gender, pulmonary function, and comorbidities, were extracted from the BREATHE-NL registry or the electronic patient record. Anaesthetic data, including mechanical ventilator settings, physiological data, and drug infusion information, were automatically recorded creating a complete digital record from which data were extracted.

The start of mechanical ventilation was defined as the moment where the ventilator mode was switched from manual/spontaneous to intermittent positive pressure ventilation (IPPV). The end was defined as the moment where the ventilation mode was switched back from IPPV to manual/spontaneous. If multiple ventilation modes were used within one procedure, the ventilation mode used for the longest duration was extracted as the main ventilation mode. Within the mechanical ventilation timeframe, all registered mechanical ventilation settings were extracted which included: inspiration to expiration (I:E ratio), inspiration time, respiration rate, tidal volume, minute volume, fraction of inspired oxygen (FiO_2), positive end-expiratory pressure (PEEP), peak pressure, and plateau pressure. Of all these variables, except I:E ratio and FiO_2, the mean setting during the procedure was calculated. For I:E ratio, the setting used for the longest duration was extracted, and for FiO_2 we calculated the median setting during the procedure, to exclude the FiO_2 of 100% used at the start of mechanical ventilation and just before extubation.

Statistical Analysis

Data are reported as mean ± SD, median (interquartile range [IQR]), or frequency (percentage), where appropriate. An independent sample *t* test, Mann-Whitney U test, or Fisher's exact test was used to compare groups. All tests were two-sided, and $p < 0.05$ was considered statistically significant. All statistical analyses were performed using R version 4.0.4 (2021-02-15) [15].

Results

Procedures and Patients

A total of 202 EBV/LVR-coil procedures, in 174 unique patients, were performed. These procedures consisted of 151 (75%) EBV procedures in 151 patients, and 51 (25%) LVR-coil procedures in 27 patients. In 23 (15%) of the EBV procedures, no valves were implanted due to: the presence of collateral ventilation ($n = 17$), severe bronchitis ($n = 4$), and significant desaturation during Chartis measurement ($n = 2$). Four patients with collateral ventilation were later treated with LVR-coils. Median procedure time was 18 (12–25) min and the duration of EBV procedures (15 [10–20] min) was shorter than LVR-coil procedures (28 [24–40] min, $p < 0.0001$).

Baseline characteristics are shown in Table 1. All patients were classified as ASA physical status III [16]. Patients had a median of 1 (0–1) comorbidity with hypertension being the most common ($n = 29$, 17%) (in online suppl. eTable 1; for all online suppl. material, see www.karger.com/doi/10.1159/000528044).

Anaesthesia and Mechanical Ventilation

Two hundred one (99.5%) procedures were performed under general anaesthesia with endotracheal intubation ($n = 198$, 99%) or laryngeal airway mask ($n = 3$, 1%). Procedural sedation was used in one procedure, but this procedure was terminated shortly after bronchoscope introduction due to local airway mucosal pathology, leading to ineligibility for EBV treatment. General anaesthesia was mainly induced and maintained by combined administration of propofol, rocuronium, and remifentanil ($n = 167$, 83%) (Fig. 1). The mean mechanical ventilation time was 41 ± 13 min. Mechanical ventilation time was longer for LVR-coil procedures compared to EBV procedures (45 ± 12 vs. 40 ± 13 min, $p = 0.01$).

Mechanical ventilation parameters are shown in Table 2. Volume-controlled mechanical ventilation was

Table 1. Baseline characteristics

	Overall (*n* = 174)	EBV (*n* = 151)	LVR-coil (*n* = 27)
Sex (male/female), *n* (%)	57 (33)/117 (67)	45 (30)/106 (70)	13 (48)/14 (52)
Age, years	62±8	62±8	62±7
BMI	23.9±3.9	23.8±3.9	24.3±3.7
Other comorbidities than COPD, *n*	1 (0–1)	1 (0–1)	1 (0–1)
Charlson Comorbidity Index (points)	3 (2–4)	3 (2–4)	3 (3–4)
LTOT (exercise/rest), *n* (%)	15 (9)/17 (10)	12 (8)/16 (11)	3 (11)/2 (7)
Smoking, packyears	40 (29–49)	40 (27–49)	46±26
FEV_1, % of predicted	26±7	27±8	24±6
RV, % of predicted	234±47	234±47	243±51
TLC, % of predicted	136±16	136±16	139±16
RV/TLC ratio	64±7	64±7	65±8
DLCO, % of predicted	34±9	34±9	32±7
pO_2, kPa	9.2±1.1	9.2±1.1	9.3±1.2
pCO_2, kPa	5.4±0.6	5.3±0.6	5.7±0.5

The "overall" column shows the characteristics of the unique patients. Four patients initially underwent an EBV procedure but were ineligible due to the presence of collateral ventilation. These patients subsequently underwent LVR-coil procedure(s). The results are displayed as mean ± SD, median (IQR), frequency (percentage), where appropriate. BMI, body mass index; COPD, chronic obstructive pulmonary disease; DLCO, diffusion capacity of the lung for carbon monoxide; EBV, endobronchial valve; FEV_1, forced expiratory volume in 1 s; IQR, interquartile range; LTOT, long-term oxygen treatment; LVR-coil, lung volume reduction coil; pCO_2, partial pressure of carbon dioxide; pO_2, partial pressure of oxygen; RV, residual volume; SD, standard deviation; TLC, total lung capacity.

Table 2. Mechanical ventilation settings

	Overall (*n* = 201)	Volume mode (*n* = 128)	Pressure mode (*n* = 73)	*p* value
Treatment (EBV/LVR-coil), *n* (%)	150 (75)/51 (25)	98 (77)/30 (23)	52 (71)/21 (29)	–
I:E (ratio)	1:2.8 (1:2.1–1:3.2)	1:2.9±0.8	1:2.5±0.6	<0.0001
Inspiration time, s	1.6 (1.3–2.0)	1.5±0.4	1.7±0.4	0.0001
Expiration time, s	4.5 (4.1–4.9)	4.6±0.6	4.3±0.8	0.0008
Respiration rate, breaths/min	9.9 (9.6–10.6)	9.9 (9.6–10.2)	10.2±1.5	0.09
Tidal volume, mL/kg	5.8±1.4	6.0±1.3	5.4±1.5	0.01
Minute volume, L/min	3.9±0.8	4.1±0.8	3.7±0.8	0.001
FiO2, %	51 (48–65)	49 (46–54)	59 (51–78)	<0.0001
PEEP, cm H_2O	3.9±1.4	4.0±1.2	3.9±1.7	0.68
Peak pressure, cm H_2O	20.2±5.5	22.4±5.2	16.4±3.5	<0.0001
Plateau pressure, cm H_2O	17.7 (14.7–22.1)	20.6±5.5	15.6±3.1	<0.0001

The results are displayed as mean ± SD, median (IQR), frequency (percentage), where appropriate. *p* values are calculated using an independent sample *t* test or Mann-Whitney U test in cases of a non-normal distribution. EBV, endobronchial valve; FiO2, fraction of inspired oxygen; LVR-coil, lung volume reduction coil; PEEP, positive end-expiratory pressure.

used in 128 (64%) procedures and pressure-controlled mechanical ventilation during 73 (36%) procedures. The median respiration rate was 9.9 (9.6–10.6) breaths/minute, and the median inspiration time was 1.6 (1.3–2.0) seconds, allowing for a median expiration time of 4.5 (4.1–4.9) seconds.

Anaesthesia-Related Events and Post-Procedural Complications

No catastrophic anaesthesia-related events, including same day death, cardiopulmonary resuscitation, unplanned ICU admission, and re-intubation, occurred. Hypotension was the most common anaesthesia-related

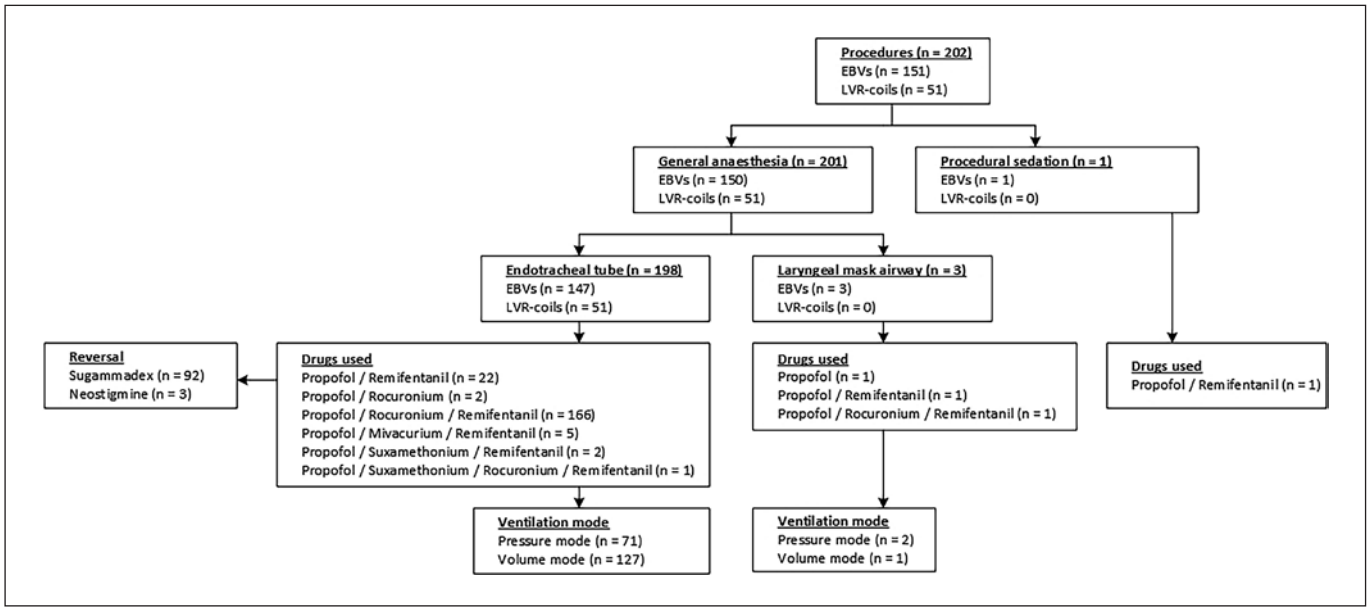

Fig. 1. Flowchart. EBVs, endobronchial valves; LVR-coils, lung volume reduction coils.

event. One case of the hypotension was severe, and all others were either significant (n = 40, 20%) or moderate (n = 48, 24%). To prevent hypotension, noradrenaline, phenylephrine, and/or ephedrine were administered in the majority of the procedures (n = 179, 89%). Desaturation was the second most common anaesthesia-related event (severe, n = 0, 0%; significant, n = 5, 2%; and moderate, n = 37, 18%). All anaesthesia-related events are shown in Table 3.

During the hospitalization period, 20 complications, in 18 patients that underwent EBV treatment, occurred. There were no cases of in-hospital death within 30 days after the procedure, and there were no ICU admissions. One patient died in-hospital more than 30 days after the initial EBV procedure. This patient suffered a pneumothorax with a prolonged air leak for which EBVs were removed. The patient refused surgery and eventually died from respiratory failure, in a palliative setting. The other post-procedural complications included pneumothorax (n = 12), acute COPD exacerbation (n = 3), influenza A infection (n = 1), urinary retention requiring a ureteral catheter (n = 1), and atrial fibrillation de novo (n = 1).

Conclusion

General anaesthesia is the recommended method of sedation for BLVR treatments since it provides optimal bronchoscopic conditions and reduces procedure time [7, 10]. This study confirms that general anaesthesia with IPPV is feasible and safe for severe COPD patients undergoing an EBV or LVR-coil procedure. No catastrophic anaesthesia-related events were encountered and only one case of severe hypotension. All anaesthesia-related events were manageable and did not lead to premature termination of the procedure or ICU admission. All patients were extubated in the bronchoscopy suite and subsequently transmitted to the post-anaesthesia care unit. After stable recovery, all patients were transferred to the general ward.

The finding that these severe COPD patients can safely undergo general anaesthesia and mechanical ventilation is possibly related to the strict selection criteria for EBV and LVR-coil treatment. Eligible patients have no or limited other comorbidities and have a low frequency of infectious COPD exacerbations. They are optimally prepared by receiving optimal pharmacological treatment, smoking cessation for a minimum of 6 months, and completing a pulmonary rehabilitation program and/or are following a structured physical therapy program. Finally, we prescribe all patients a short course of prophylactic

Table 3. Anaesthesia events

	Overall (n = 202), n (%)	Volume (n = 128), n (%)	Pressure (n = 73), n (%)
Catastrophic			
Same day death	0 (0)	0 (0)	0 (0)
Cardiopulmonary resuscitation	0 (0)	0 (0)	0 (0)
Unplanned ICU admission	0 (0)	0 (0)	0 (0)
Re-intubation	0 (0)	0 (0)	0 (0)
Severe			
Hypotension: mean arterial pressure <40 mm Hg for more than 5 min, requiring medication	1 (1)	0 (0)	1 (1)
Desaturation: peripheral oxygen saturation <85% for more than 5 min	0 (0)	0 (0)	0 (0)
Bradycardia: heart rate <20/min for any duration of time	0 (0)	0 (0)	0 (0)
Tachycardia: heart rate >200/min for any duration of time	0 (0)	0 (0)	0 (0)
Hypercapnia: $EtCO_2$ >13 kPa (100 mm Hg) for any duration of time	0 (0)	0 (0)	0 (0)
Aspiration: aspiration of gastric content evidenced by bronchoscopy	0 (0)	0 (0)	0 (0)
Anaphylaxis: allergic reaction requiring adrenaline and antihistamine	0 (0)	0 (0)	0 (0)
Significant			
Hypotension: mean arterial pressure <65 mm Hg for more than 10 min, requiring medication	40 (20)	23 (18)	17 (23)
Desaturation: peripheral oxygen saturation <90% for more than 5 min	5 (2)	4 (3)	1 (1)
Bradycardia: heart rate <40/min for more than 5 min	0 (0)	0 (0)	0 (0)
Allergic reaction not requiring adrenaline or antihistamine	0 (0)	0 (0)	0 (0)
Moderate			
Hypotension: mean arterial pressure <65 mm Hg for more than 5 min, requiring medication	48 (24)	31 (24)	17 (23)
Desaturation: peripheral oxygen saturation <90% for more than 1 min	37 (18)	21 (16)	16 (22)
Bradycardia: heart rate <40/min for any duration of time	4 (2)	4 (3)	0 (0)
Hypercapnia: $EtCO_2$ 8–13 kPa (60–100 mm Hg) for any duration of time	0 (0)	0 (0)	0 (0)

Results are shown as number (percentage). $EtCO_2$, end-tidal carbon dioxide; ICU, intensive care unit.

prednisolone and antibiotics starting the day before and the day of the procedure, respectively, to possibly prevent peri- and post-procedural pulmonary complications. Thus, this patient population might not be as "high-risk" as the general severe COPD patient can potentially be.

Both volume- and pressure-controlled ventilation were safely used to mechanically ventilate the patients. During BLVR procedures, the airway is shared with the bronchoscope, increasing airway resistance and limiting airflow. This should be taken into consideration while determining the appropriate ventilatory settings [17, 18]. In our opinion, volume-controlled ventilation has a practical advantage since it allows for an easier and more reliable method to ensure that the desired tidal volume is delivered to the patient. Movement of the bronchoscope in the ETT causes changes in airflow resistance which in turn can cause the delivered tidal volume to vary drastically when pressure-controlled ventilation is used [19]. As in volume-controlled ventilation the required inspiratory and plateau pressure is determined by the ventilator, it would be reasonable to expect increased, or even undesirably high pressures, subsequently increasing the risk of barotrauma [17, 20]. The average plateau pressure was higher during volume-controlled ventilation but remained well within acceptable limits and was not associated with an increased risk of peri- or post-procedural complications. When a rigid bronchoscope is used to perform the procedure, high-frequency jet ventilation possibly is a suitable ventilation option [21].

Ventilatory parameter settings should be optimized to maintain adequate ventilation and oxygenation while minimizing the risk of undesirable events. During mechanical ventilation, patients with advanced COPD are prone to develop progressive dynamic hyperinflation and subsequent development of auto-PEEP. This can cause a ventilation-to-perfusion mismatch or impaired venous return, which in turn can lead to hypoxemia, hypercapnia, and/or hemodynamic instabilities [22–24]. Allowing enough time for complete expiration by reducing respiratory rate, increasing the I:E ratio, and using relatively low

tidal volumes are the most important measures, preventing undesirable anaesthesia-related events. In the evaluated procedures, an average respiratory rate of 10 breaths per minute with an I:E ratio of 1:2.8 was used and the tidal volume was kept relatively low at 5.8 mL/kg, thereby reducing the volume that needs to be exhaled and thus reducing the time needed for complete expiration. In addition, we use a 9-mm ETT, allowing for a considerable diameter difference with the bronchoscope, thereby minimizing the increase in airway resistance [17]. To illustrate, using a 9-mm ETT and a 6.2 mm-flexible bronchoscope, the surface available for ventilation is 34 mm^2, which is equal to a 6.5-mm ETT. Using an 8- or 7- mm ETT reduces the available surface to be comparable to a 5.0- or 3.0-mm ETT, respectively. In our experience, most patients tolerate a 9-mm ETT, but if this is not the case an 8 mm-ETT also provides an adequate sized working channel, but it should be taken into account that the airway resistance is significantly higher. Alternatively, a laryngeal mask airway can be used with the same ventilatory settings, which in some centres is the preferred choice. However, we prefer using an ETT since this provides a larger and more stable working channel for the bronchoscope.

Hypotension was the most frequent anaesthesia-related event. During general anaesthesia, hypotension is a common event and associated with unfavourable patient outcomes, nevertheless, no widely accepted definition is available [14, 25]. Based on our definitions, severe hypotension was only encountered during one procedure. Significant and moderate hypotensions were more frequent with event rates of 20% and 24%, respectively. In all procedures, propofol was the anaesthetic of choice, which is known to have a vasodilatory effect, which can result in hypotension [26]. This effect might be more pronounced in patients eligible for EBV or LVR-coil treatment due to some factors that limit their cardiac reserves, such as a long history of smoking, advanced age, the use of antihypertensive medication, and an overnight fast possibly inducing some fluid depletion. Since these patients might be more susceptible to anaesthesia-related hypotension, vasopressor infusion was frequently started before hypotension occurred. Despite the frequent occurrence of significant and moderate hypotension, none of the patients were diagnosed with ischemic complications, such as myocardial infarction, stroke, or acute kidney injury in the peri- or post-procedural period.

Desaturations were the second most frequently encountered anaesthesia-related events. Although desaturations were classified as anaesthesia-related, we believe that most, if not all, are either because of permissive hypoxemia or procedure-related. Hypoxemia might have been accepted in patients with a low baseline saturation causing it to be scored as a desaturation event based on our pre-defined criteria. Procedure-related desaturation will likely be associated with the Chartis measurement. During the Chartis measurement, the target lobe is fully blocked to evaluate collateral ventilation. Generally, this will not result in a desaturation because the target lobe should have a low perfusion. However, in some cases, the Chartis measurement of the target lobe is inconclusive, and the adjacent lobe, which is usually less affected by emphysema, is evaluated as a surrogate, which can therefore be associated with a temporary and accepted desaturation during the procedure [3].

This study has some strengths and limitations. The anaesthetic data used were automatically recorded during the procedures and was analysed using scripts with predefined definitions and criteria, minimizing interpretation bias, recall bias, and missing data while allowing for detailed analysis. Furthermore, a relatively large number of procedures were included in the analysis, giving a realistic overview of management used in our high-volume BLVR treatment hospital with anaesthesiologists experienced in the anaesthetic management during EBV and LVR-coil procedures. A limitation is the retrospective nature of this study which resulted in several different combinations of used medication, ventilation modes, and ventilatory settings. Therefore, a direct comparison of different anaesthetic management techniques was not possible.

In conclusion, although providing general anaesthesia and mechanical ventilation to patients with advanced COPD can be challenging, the results of this study indicate that it is well tolerated by patients selected for EBV or LVR-coil treatment with hypotension being the most frequent anaesthesia-related event. The strict selection criteria and patient preparation are presumably the main reason these patients could safely undergo general anaesthesia. Based on our findings, we recommend the following guidelines for anaesthetic management during BLVR when IPPV is used: (1) use a large size, preferably 9-mm ETT, (2) use low tidal volumes, 6–8 mL/kg body weight, and (3) allow for long expiration times by using a low respiratory rate, 9–11 breaths/min, and an I:E ratio around 1:3. Lastly, we recommend using volume-controlled over pressure-controlled ventilation to allow for a stable tidal volume delivery with the changing airway resistances following bronchoscope introduction and removal. If alternatively a rigid bronchoscope is used, high-frequency jet

ventilation is the more suitable ventilation approach. A short-course of prednisolone and antibiotics can be considered to reduce the risk for peri- and post-procedural pulmonary complications, although strong scientific evidence for this approach is lacking.

Statement of Ethics

The participants included in this study are included in the BREATHE-NL registry or the ELEVATE study. The ELEVATE study protocol was revised and approved by all participating site's Medical Local Ethics Committees. The BREATH-NL registry has been granted an exemption from requiring ethics approval due to the non-invasive nature of the registry by the Local Medical Ethics Committee of the University Medical Center Groningen. Written informed consent was obtained from all participants. The current study does not fall within the scope of the Dutch Medical Research Involving Human Subjects Act (WMO), and therefore, no formal ethics approval was needed.

Conflict of Interest Statement

Sharyn Roodenburg, Clemens Barends, Grita Krenz, and Eelco Zeedijk report no conflict of interest. Dirk-Jan Slebos has reported grants or contracts, support for attending meetings and/or travel, and attendance on a data safety monitoring board or advisory board from/at PulmonX, USA, and PneumRx/BTG, USA, outside the context of the current study.

Funding Sources

No funding was received for the conduction of this study.

Author Contributions

Sharyn Roodenburg: study conceptualization, design of methodology, data collection, data analysis, and drafting of the manuscript. Clemens Barends and Dirk-Jan Slebos: study conceptualization, design of methodology, data collection, and critical review of the manuscript. Grita Krenz and Eelco Zeedijk: data collection and critical review of the manuscript. All authors read and approved the final version of the manuscript.

Data Availability Statement

All data generated or analysed during this study are included in this article and its online supplementary material. Further enquiries can be directed to the corresponding author.

References

1 Shah PL, Slebos DJ. Bronchoscopic interventions for severe emphysema: where are we now? Respirology. 2020;25(9):972–80.
2 van Geffen WH, Slebos DJ, Herth FJ, Kemp SV, Weder W, Shah PL. Surgical and endoscopic interventions that reduce lung volume for emphysema: a systemic review and meta-analysis. Lancet Respir Med. 2019;7(4):313–24.
3 Slebos DJ, Shah PL, Herth FJ, Valipour A. Endobronchial valves for endoscopic lung volume reduction: best practice recommendations from expert panel on endoscopic lung volume reduction. Respiration. 2017;93(2):138–50.
4 Slebos DJ, Ten Hacken NH, Hetzel M, Herth FJF, Shah PL. Endobronchial coils for endoscopic lung volume reduction: best practice recommendations from an expert panel. Respiration. 2018;96(1):1–11.
5 Klooster K, ten Hacken NH, Hartman JE, Kerstjens HA, van Rikxoort EM, Slebos DJ. Endobronchial valves for emphysema without interlobar collateral ventilation. N Engl J Med. 2015;373(24):2325–35.
6 Klooster K, Slebos DJ. Endobronchial valves for the treatment of advanced emphysema. Chest. 2021;159(5):1833–42.
7 Welling JBA, Klooster K, Hartman JE, Kerstjens HAM, Franz I, Struys MMF, et al. Collateral ventilation measurement using Chartis: procedural sedation vs general anesthesia. Chest. 2019;156(5):984–90.
8 Chandler D, Mosieri C, Kallurkar A, Pham AD, Okada LK, Kaye RJ, et al. Perioperative strategies for the reduction of postoperative pulmonary complications. Best Pract Res Clin Anaesthesiol. 2020;34(2):153–66.
9 Pietzsch JB, Busca R, Rott C, Geisler BP, Weber SA, Slebos DJ, et al. Adoption patterns of bronchoscopic lung volume reduction procedures in Germany and predicted procedure volumes for other European countries. Respiration. 2019;97(1):34–41.
10 Thiruvenkatarajan V, Maycock T, Grosser D, Currie J. Anaesthetic management for endobronchial valve insertion: lessons learned from a single centre retrospective series and a literature review. BMC Anesthesiol. 2018;18(1):206.
11 Klooster K, Valipour A, Marquette CH, Boutros J, Mal H, Marceau A, et al. Endobronchial coil system versus standard-of-care medical management in the treatment of Subjects with severe emphysema. Respiration. 2021;100(8):804–10.
12 Barends CRM, Driesens MK, van Amsterdam K, Struys MMRF, Absalom AR. Moderate-to-deep sedation using target-controlled infusions of propofol and remifentanil: adverse events and risk factors: a retrospective cohort study of 2,937 procedures. Anesth Analg. 2020;131(4):1173–83.
13 Cheng Q, Zhang J, Wang H, Zhang R, Yue Y, Li L. Effect of acute hypercapnia on outcomes and predictive risk factors for complications among patients receiving bronchoscopic interventions under general anesthesia. PLoS One. 2015;10(7):e0130771.
14 Salmasi V, Maheshwari K, Yang D, Mascha EJ, Singh A, Sessler DI, et al. Relationship between intraoperative hypotension, defined by either reduction from baseline or absolute thresholds, and acute kidney and myocardial injury after noncardiac surgery: a retrospective cohort analysis. Anesthesiology. 2017;126(1):47–65.
15 R Core Team. R. A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2021.
16 American Society of Anesthesiologists'. ASA physical status classificantion System. https://www.asahq.org/standards-and-guidelines/asa-physical-status-classification-system2020.

17 Lawson RW, Peters JI, Shelledy DC. Effects of fiberoptic bronchoscopy during mechanical ventilation in a lung model. Chest. 2000; 118(3):824–31.
18 Nay MA, Auvet A, Mankikian J, Herve V, Dequin PF, Guillon A. Evaluation of a flexible bronchoscope prototype designed for bronchoscopy during mechanical ventilation: a proof-of-concept study. Anaesthesia. 2017; 72(6):719–28.
19 Rittayamai N, Katsios CM, Beloncle F, Friedrich JO, Mancebo J, Brochard L. Pressure-controlled vs volume-controlled ventilation in acute respiratory failure: a physiology-based narrative and systematic review. Chest. 2015;148(2):340–55.
20 Hsia D, DiBlasi RM, Richardson P, Crotwell D, Debley J, Carter E. The effects of flexible bronchoscopy on mechanical ventilation in a pediatric lung model. Chest. 2009;135(1):33–40.
21 Pathak V, Welsby I, Mahmood K, Wahidi M, MacIntyre N, Shofer S. Ventilation and anesthetic approaches for rigid bronchoscopy. Ann Am Thorac Soc. 2014;11(4):628–34.
22 Antonogiannaki EM, Georgopoulos D, Akoumianaki E. Patient-ventilator dyssynchrony. Korean J Crit Care Med. 2017;32(4):307–22.
23 Blanch L, Bernabe F, Lucangelo U. Measurement of air trapping, intrinsic positive end-expiratory pressure, and dynamic hyperinflation in mechanically ventilated patients. Respir Care. 2005;50(1):110–23; discussion 123-4.
24 Junhasavasdikul D, Telias I, Grieco DL, Chen L, Gutierrez CM, Piraino T, et al. Expiratory flow limitation during mechanical ventilation. Chest. 2018;154(4):948–62.
25 Sudfeld S, Brechnitz S, Wagner JY, Reese PC, Pinnschmidt HO, Reuter DA, et al. Post-induction hypotension and early intraoperative hypotension associated with general anaesthesia. Br J Anaesth. 2017;119(1):57–64.
26 Robinson BJ, Ebert TJ, O'Brien TJ, Colinco MD, Muzi M. Mechanisms whereby propofol mediates peripheral vasolidation in humans. Anesthesiology. 1997;86(1):64–72.