Lung volume reduction surgery is safe and leads to functional improvement in patients who fail or cannot undergo bronchoscopic lung volume reduction

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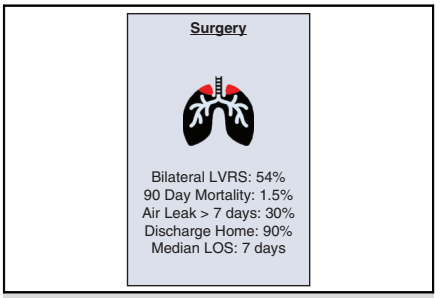
ABSTRACT

Background: Bronchoscopic lung volume reduction (BLVR) has supplanted surgery in the treatment of patients with advanced emphysema, but not all patients qualify for it. Our study aimed to investigate the outcomes of lung volume reduction surgery (LVRS) among patients who either failed BLVR or were not candidates for it.

Methods: We conducted a retrospective analysis of patients who underwent LVRS for upper lobe–predominant emphysema at a single tertiary center between March 2018 and December 2022. The main outcomes measures were preoperative and postoperative respiratory parameters, perioperative morbidity, and mortality.

Results: A total of 67 LVRS recipients were evaluated, including 10 who had failed prior valve placement. The median patient age was 69 years, and 35 (52%) were male. All procedures were performed thoracoscopically, with 36 patients (53.7%) undergoing bilateral LVRS. The median hospital length of stay was 7 days (interquartile range, 6-11 days). Prolonged air leak (>7 days) occurred in 20 patients. There was one 90-day mortality from a nosocomial pneumonia (non–COVID-related) and no further deaths at 12 months. There were mean improvements of 10.07% in forced expiratory volume in 1 second and 4.74% in diffusing capacity of the lung for carbon monoxide, along with a mean decrease 49.2% in residual volume ($P < .001$ for all). The modified Medical Research Council dyspnea scale was improved by 1.84 points ($P < .001$).

Conclusions: LVRS can be performed safely in patients who are not candidates for BLVR and those who fail BLVR and leads to significant functional improvement. Long-term follow-up is necessary to ensure the sustainability of LVRS benefits in this patient population. (JTCVS Open 2024;18:369-75)



LVRS is a viable therapeutic option for patients who fail or are not eligible for BLVR.

CENTRAL MESSAGE

Lung volume reduction surgery (LVRS) can be safely performed in patients who are not candidates for bronchoscopic lung volume reduction (BLVR) and those who fail BLVR. It is associated with significant functional improvement that is comparable to primary LVRS.

PERSPECTIVE

Few studies address the safety and efficacy of lung volume reduction surgery (LVRS) in patients who fail bronchoscopic lung volume reduction (BLVR) or do not qualify for BLVR. We demonstrate that LVRS can be performed with low mortality and acceptable morbidity in this patient population. The functional improvement is comparable with primary LVRS. Surgery remains a viable therapeutic option for patients with advanced chronic obstructive pulmonary disease and no other interventional option.

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Abbreviations and Acronyms

6MWT = 6-minute walk test
BLVR = bronchoscopic lung volume reduction
CMS = Centers for Medicare & Medicaid Services
COPD = chronic obstructive pulmonary disease
CPET = cardiopulmonary exercise testing
DLCO = diffusing capacity of the lung for carbon monoxide
FEV1 = forced expiratory volume at 1 second
IQR = interquartile range
LVRS = lung volume reduction surgery
MRC = Medical Research Council
NETT = National Emphysema Treatment Trial
PFT = pulmonary function tests
RV = residual volume

Chronic obstructive pulmonary disease (COPD) is a debilitating disease with devastating clinical, financial, and social impacts. In the United States, COPD it affects more than 12 million people and is currently the sixth-leading cause of death overall.[1] Lung volume reduction surgery (LVRS) was first proposed by Brantigan in the 1950s as a method of removing the most emphysematous diseased portion of the lung, leading to improved lung function due to increased elastic recoil pressure and better chest wall and diaphragmatic mechanics due to reduced hyperinflation.[2,3]

LVRS was not widely adopted until Cooper reintroduced the surgery in the 1990s using reinforced staplers through a sternotomy.[4] Widespread uptake of this surgery lad to varied results until the landmark National Emphysema Treatment Trial (NETT) established that upper lobe–predominant emphysema patients with low exercise capacity showed the greatest improvement in survival and symptoms.[5]

Despite these promising findings, there has been a nationwide underuse of LVRS for treating emphysema. A 2014 analysis of the Society of Thoracic Surgeons database found that only 538 patients underwent the procedure over an 8.5-year period.[6] Possible reasons for underuse include concerns about safety and efficacy, a limited patient pool due to strict qualifying criteria, and uncertainty regarding the long-term outcomes and sustainability of benefits, as well as the introduction of less invasive modalities, such as bronchoscopic lung volume reduction (BLVR).

Several randomized controlled studies have demonstrated the benefits of endoscopic valve placement in the treatment of end-stage emphysema.[7-11] However, BLVR still carries a substantial risk of morbidity and mortality. Furthermore, some patients do not qualify for the endoscopic approach, mainly because of a lack of fissure integrity and the ensuing potential for collateral ventilation, and many others do not exhibit sustainable improvement after the procedure.[7] Here we report our single-center tertiary experience with LVRS in patients with severe emphysema and hyperinflation who previously failed BLVR or were not candidates for BLVR.

METHODS

Patient Population

We performed a retrospective review of all patients who underwent bilateral or unilateral LVRS between March 1, 2018, and December 31, 2022. All patients were evaluated by a multidisciplinary team of pulmonologists, respiratory therapists, radiologists, physical therapists, and thoracic surgeons. The study population consisted of all patients who either had previously failed BLVR or did not meet the criteria for the procedure (Figure 1). All patients were selected based on Center of Medicare & Medicaid Services (CMS) inclusion and exclusion criteria. As such, only patients with upper lobe–predominant emphysema and low exercise capacity were offered surgical intervention.

Approval from the Temple University Hospital Institutional Review Board was obtained (approval 29700; August 8, 2022). Consent was waived for this retrospective review.

Preoperative Testing

Patients considered for LVRS underwent an extensive preoperative workup at our institution. This included multiple outpatient visits, full pulmonary function testing (PFT) prior to intervention, arterial blood gas analysis, the 6-minute walk test (6MWT), high-resolution computed tomography scan with quantification of the percentage of emphysematous destruction and volumetric lobar measurement, evaluation of fissure integrity, and qualitative inspection for the presence of lung nodules, bronchiectasis, bulla, and pulmonary artery dilatation. Patients also underwent ventilation-perfusion scan or strict perfusion scan, a baseline echocardiogram, cardiac nuclear stress test, cardiopulmonary exercise testing (CPET), and cardiopulmonary rehabilitation prior to the operation. Patients were offered surgery if they failed BLVR or did not meet criteria based on the interlobar fissure integrity score of <80% as measured by StratX (Pulmonx) and the intraprocedural Chartis measurement.

Surgical Procedure and Hospital Care

All patients underwent unilateral or bilateral video-assisted thoracoscopic surgery (VATS) with three 12- to 15-mm ports and a plan to remove 20% to 30% of the lung, mainly underperfused regions. All parenchymal divisions were performed with reinforced staples (Medtronic). Following pneumectomy, gentle mechanical pleurodesis was performed limited to the apical chest region, and 2 chest drains (24-28 Fr) were placed on each operative side.

All patients had planned disposition to a telemetry monitored medical/surgical nursing unit postoperatively, where they followed a post-LVRS care protocol. This included early mobilization on day 1, proactive pulmonary toilet with mucolytics, incentive spirometry and flutter valves. Chest drains were connected to conventional drainage system maintained at −10 cm water suction for the first 48 hours and water seal thereafter as deemed safe by the surgeon. All procedures were performed by 2 surgeons (C.B. and A.A.).

Follow-up

Patients were evaluated in the clinic at 2 weeks postoperatively, before undergoing repeat cardiopulmonary rehabilitation according to CMS

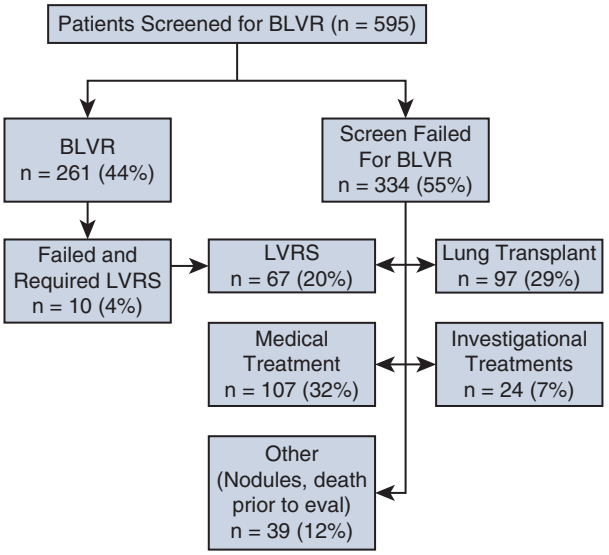

FIGURE 1. Algorithm for patient evaluation for lung volume reduction surgery (*LVRS*) during the study period (March 2018-December 2022) at our center. *BLVR*, Bronchoscopic lung volume reduction.

guidelines. They were reevaluated at 3 to 6 months and at 1 year and underwent repeat PFT and imaging and completed pulmonary questionnaires.

Statistical Methods

The main outcomes measures were perioperative mortality and morbidity, in addition to preoperative and postoperative respiratory parameters. Descriptive values are given as actual number with percentage, mean with standard deviation, or median with interquartile range (IQR), as appropriate. Categorical and continuous variables were analyzed using the Fisher exact test and Student *t* test, respectively, as appropriate. Preoperative and postoperative functional outcomes were compared using paired *t* tests. Functional outcomes are reported as the mean change from preoperative as reported in the paired *t* tests. *P* values (2-tailed) $< .05$ were considered significant. Statistical analysis was done using Stata version 17 (StataCorp).

RESULTS

A total of 67 patients underwent LVRS during the study period, of whom 35 (52%) were male. The mean age was 68 ± 6 years (range, 48 to 84 years). BLVR was previously performed in 10 patients (15%) who failed to show clinical or functional improvement. Eleven patients underwent bronchoscopy under anesthesia for BLVR, but the preprocedural examination with balloon occlusion of the targeted lobe (eg, Chartis test) showed the presence of collateral ventilation. In those patients, BLVR was aborted, and they were referred for LVRS. The remaining patients (n = 46) did not meet imaging criteria for the procedure (ie, incompleteness of the fissure, paraseptal or nonhomogenous emphysematous lobar destruction, prepleural emphysema). Table 1 shows the baseline demographics and characteristics of the patient population, and Table 2 presents the perioperative outcomes.

TABLE 1. Baseline patient characteristics

Characteristic	Value
No. of patients	67
Age, y, median (IQR)	69 (64-72)
BMI, kg/m^2, median (IQR)	25 (22-27)
Sex, n (%)	
Female	32 (48)
Male	35 (52)
Left ventricular ejection fraction, %, median (IQR)	60 (55-60)
Prior bronchoscopic valve, n (%)	10 (15)
6MWT, m, median (IQR)	267 (210-320)
FEV1 prior to bronchodilator, %, median (IQR)	30 (25-34)
FEV1 prior to bronchodilator, L, median (IQR)	0.71 (0.62-0.88)
RV, % of predicted value, median (IQR)	180 (157-210)
RV after bronchodilator use, absolute value, L, median (IQR)	3.97 (3.21-4.97)
DLCO, % of predicted value median (IQR)	34.5 (30-42)
pCO_2, arterial, mm Hg, median (IQR)	38 (36-41)
pO_2, arterial, mm Hg, median (IQR)*	75 (70-83)
Use of home	
Prednisone, n (%)	12 (18)
Prednisone dose, mg, median (IQR)	10 (7.5-10)
CPAP/BiPAP, n (%)	2 (3)
History of, n (%):	
Pulmonary hypertension (mild)	15 (22)
Pneumonia	14 (21)
Pneumothorax	5 (7)
Prior lung surgery	8 (12)
Chest wall radiation	7 (10)

IQR, Interquartile range; *BMI*, body mass index; *6MWT*, 6-minute walk test; *FEV1*, forced expiratory volume in 1 second; *RV*, residual volume; *DLCO*, diffusion capacity of the lung for carbon monoxide; *CPAP*, continuous positive airway pressure; *BiPAP*, bilevel positive airway pressure. *Includes patients on supplemental oxygen therapy at baseline.

Bilateral LVRS was performed in 36 patients (53.7%). The median time to final chest tube removal was 6 days (IQR, 5-10 days). Among the 20 patients with prolonged air leak, 3 underwent successful surgical reexploration, and 13 were discharged to home with a Heimlich valve. Two patients had incidental adenocarcinoma in the removed portions of the lung on final pathology, and 1 patient had planned concomitant resection of a biopsy-proven adenocarcinoma (T1aN0). There was 1 (1.5%) inpatient death, from nosocomial pneumonia (non–COVID-related). At a 12-month follow-up, there were no additional deaths.

Functionality Improvement

Table 3 shows the changes in functional outcomes at 6 months follow-up. The median postoperative FEV1 was 0.95 L (IQR, 0.72-1.24 L), and the median postoperative residucal volume (RV) was 2.71 L (IQR, 2.13-3.79 L). The

TABLE 2. Operative details and perioperative outcomes

Parameter	Value
No. of patients	67
Laterality of procedure, n (%)	
Bilateral	36 (53.7)
Left	4 (6.0)
Right	27 (40.3)
Estimated blood loss, mL, median (IQR)	50 (25-100)
Right specimen weight, g, median (IQR)	60.5 (47.5-75)
Left specimen weight, g,	59.5 (54-76)
Extubated in OR, n (%)	64 (95.5)
Pulmonary complications, n (%)	
Pneumonia	5 (7.5)
Chest tube or pigtail placement	4 (6.0)
Mucus plugging or need for bronchoscopy	4 (6.0)
Reintubation	4 (6.0)
Tracheostomy	1 (1.5)
Other complications, n (%)	
Atrial fibrillation	11 (16.4)
AKI	8 (11.9)
DVT/PE	2 (3.0)
ICU transfer	16 (23.9)
Return to OR	3 (4.5)
Prolonged air leak (>7 d), n (%)	20 (29.9)
Hospital length of stay, d, median (IQR)	7 (6-11)
Discharge disposition, n (%)	
Rehabilitation	6 (9.0)
Home	60 (89.5)
Deceased	1 (1.5)

IQR, Interquartile range; *OR*, operating room; *AKI*, acute kidney injury; *DVT*, deep venous thrombosis; *PE*, pulmonary embolism; *ICU*, intensive care unit.

mean improvement in FEV1 was 0.32 L ($P < .001$), and the mean decrease in RV was 1.15 L ($P < .001$). Subjectively, the dyspnea exertion score (during the 6MWT) and the Medical Research Council (MRC) dyspnea score were significantly improved, by 1.76 points ($P = .016$) and 1.84 points ($P < .001$), respectively. There was no significant change in the distance travelled during the 6MWT.

DISCUSSION

The landscape and practice of lung volume reduction have changed significantly since the NETT results were published more than 20 years ago.[5] The narrow eligibility criteria and the quest for a less invasive approach led to the advent of endoscopic techniques, mainly one-way bronchoscopic valve placement. With multiple randomized studies demonstrating the benefits of BLVR,[7-11] the endoscopic approach became the first line of therapy in many institutions, including ours. However, not all patients are eligible for BLVR based on anatomic considerations discussed earlier, and many others undergo but fail the endoscopic approach. This can be due to multiple factors, including loss of atelectasis, valve migration, infectious complications, hyperinflation of the remaining lung, and overall COPD progression. The role of surgery in this rather distinct patient population has not been well defined.

In this study, we found that patients who either failed BLVR or were not candidates for the procedure can still undergo surgery and achieve outcomes at least comparable to those reported in other series of primary LVRS, in terms of perioperative morbidity, mortality, and functional improvement. Here we report a 1.5% 90-day mortality rate, compared to a 2.9% mortality rate reported in similar patients with upper lobe–predominant emphysema and low exercise capacity in the NETT.[5] We also report excellent clinical and functional improvement in most patients. We attribute this to multiple factors, including a better understanding of the degree of disease and the optimal extent of resection, guided by better imaging and perfusion scanning.[12] In addition, the surgical technique has been refined with enhanced stapling technology, and patients benefit from dedicated multidisciplinary evaluation and postoperative management. Moreover, our series reflects the accrued experience of a limited number of surgeons in one center, with an exclusive minimally invasive thoracoscopic approach compared to 70% sternotomy in the NETT.

Our results compare favorably with more contemporary series of primary LVRS. Ginsburg and colleagues[13] reported their 10-year experience in a series of 91 patients

TABLE 3. Change in functional outcomes

Functional outcome	N	Mean change (95% CI)	*P* value
FEV1 (% predicted)	46	10.07 (7.03-13.1)	<.001
RV (% predicted)	41	−49.20 (−65.63 to −32.75)	<.001
DLCO (% predicted)	39	4.74 (2.3-7.19)	<.001
6MWT (meters)	44	19.95 (−16.82 to 56.73)	.28
Dyspnea exertion score*	31	−1.76 (−3.16 to −0.35)	.016
Modified MRC dyspnea scale	49	−1.84 (−2.25 to −1.42)	<.001

CI, Confidence interval; *FEV1*, forced expiratory volume in 1 second; *RV*, residual volume; *DLCO*, diffusion capacity of the lung for carbon monoxide; *6MWT*, 6-minute walk test; *MRC*, Medical Research Council. *Measured during the 6MWT.

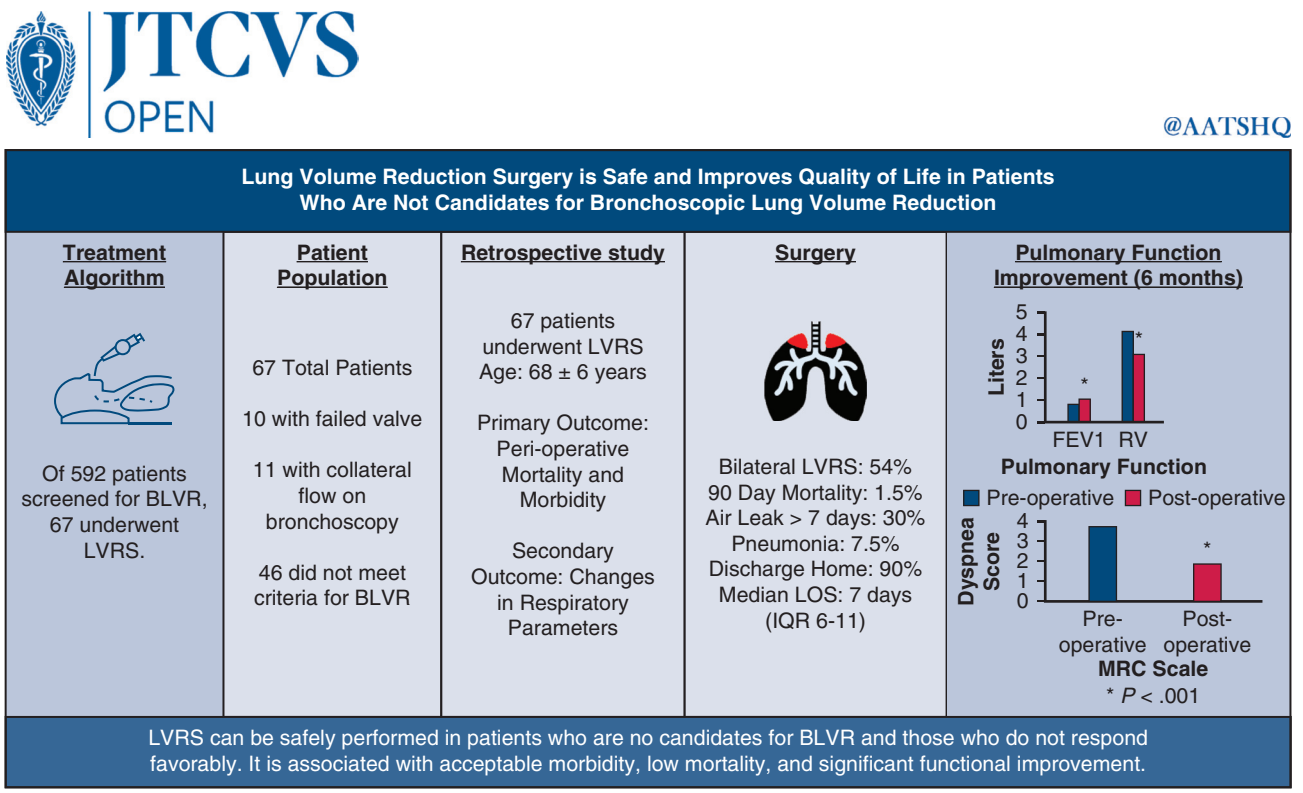

FIGURE 2. Graphical abstract. *LVRS*, Lung volume reduction surgery; *BLVR*, bronchoscopic lung volume reduction; *LOS*, length of stay; *IQR*, interquartile range; *PFT*, pulmonary function tests; *MRC*, Medical Research Council.

who underwent LVRS between 2004 and 2014. At a 1-year follow-up, they reported an 11% improvement in FEV1 (% predicted) with a corresponding mean relative change of 43%, and a 64.4% improvement in RV (% predicted), as well as improvement in respiratory questionnaires. They also reported a median hospital length of stay of 8 days, a median intensive care unit stay of 2 days, an incidence of prolonged air leak (>7 days) of 52%, and no mortality at 6 months. In our series, patients were mostly extubated in the operating room and transferred to the telemetry floor postoperatively, where they received dedicated care that emphasized early mobilization and advanced pulmonary toilet. Approximately one-quarter of patients required later transfer to the intensive care unit. Our median hospital length of stay was 7 days, and the incidence of prolonged air leak was 30%.

Regarding the PFTs, we found a significant improvement in FEV1, RV, and DLCO, as well as improvement in the modified MRC scale. Of note, 54% of our patients underwent bilateral LVRS, compared to almost 98% in the series reported by Ginsburg and colleagues.[13] This can partially explain why the 6MWT was not statistically different after surgery in our study, although patients reported significantly less dyspnea during the assessment.

Another recent series of 135 patients by Horwood and colleagues[14] reported a 2.2% 90-day mortality rate and mean improvements in FEV1 (% predicted) from preoperative baseline of 5.3% at 1 year and 4.3% at 2 years. Most patients (>96%) underwent bilateral thoracoscopic LVRS, and the mean baseline FEV1 was 1.54 L (29.1% of predicted) in their cohort, compared to 0.78 L (31.7%) in ours. The authors reported comparable discharge disposition, as most patients (93%) were sent home after a median length of stay of 8 days. On the national level, a recent Society of Thoracic Surgeons database review of 1617 patients who underwent LVRS between 2001 and 2017 found decreasing mortality rates over the years, with a risk-adjusted mortality of 3.1% in 2016.[15]

These results highlight the role of LVRS in patients with advanced emphysema who do not have other interventional options. In addition, there is more evidence demonstrating the long-term durability and the functional improvement after LVRS compared to the endoscopic approach, for which very little of the controlled follow-up data extends beyond 1 year.[7-11,13,14,16-18] When considered exclusively as a salvage option, there is currently a paucity of data on the outcomes of LVRS for patients who fail the endoscopic approach. Caviezel and colleagues[19] recently

reported a series of 38 patients who underwent LVRS after having failed BLVR either primarily or secondarily. They considered secondary failure as those patients whose benefit faded over time as opposed to those who never achieved the intended valve-induced atelectasis of the diseased area. They reported no 90-day mortality and a 12.5% improvement in FEV1, from 640 to 720 mL, with more pronounced improvement in the primary failure group.

Additionally, Eichhorn and colleagues[20] from Germany reported an interesting series of 20 patients who underwent a lobectomy as a consolidating procedure after failed BLVR. Most of the patients (90%) underwent lower lobectomy, and although there was one 90-day mortality, the authors reported improved respiratory parameters (FEV1 and RV), exercise tolerance, and relief of dyspnea (modified MRC score). In our series, we performed LVRS only in patients with upper lobe–predominant emphysema, strictly following the CMS guidelines and NETT selection criteria.

Although comparing the outcomes of LVRS and BLVR was not our goal, we believe that some patients are more suited for one modality than others. Besides fissure integrity, patients with marked intralobar heterogeneity or predominance in the apical or paraseptal region may be better served by LVRS. The latter factor was considered when determining the eligibility for BLVR at our institution. Of note, the recent randomized CELEB trial showed comparable 1-year outcomes between BLVR and LVRS, and another ongoing prospective trial, SINCERE, is investigating the same topic.[21]

This study has multiple limitations, related to its retrospective nature and slightly heterogeneous population, as some patients failed BLVR while others did not qualify for it. Our outcomes might not be generalizable, as they reflect the experience of a tertiary center with a high volume of LVRS referrals that currently performs 20 to 25 procedures annually. We also acknowledge the lack of longer-term follow-up and the issue of missing data, although the latter is not exclusive to our series and has been reported by other LVRS studies.[5,13,14] It is possible that some of the patients who were lost to follow-up may not have exhibited the same functional improvement. Of note, to best assess the impact of surgery, paired testing was used to compare patients with their own values preoperatively. Therefore, only patients with complete preoperative and postoperative data were included in each individual statistical test. In addition, the COVID-19 pandemic significantly impaired our ability to follow up with patients and perform the necessary studies, mainly PFTs and CPET. In fact, some of our patients did contract COVID-19 viral pneumonia after the surgery, and they subjectively reported that their improvement was impeded by the infection. It is quite possible that other patients also contracted the disease without being tested for it, and that could have influenced their pulmonary testing and/or questionnaires. Finally, we did not include the Saint George Respiratory Questionnaire or the COPD Assessment Test in this series, both of which may better reflect patients' quality of life than the modified MRC scale.

CONCLUSIONS

Despite these limitations, our findings support the safety and efficacy of LVRS in patients with severe emphysema who are not candidates for BLVR and those who fail BLVR (Figure 2). Careful patient selection and a multidisciplinary evaluation are paramount to achieve favorable outcomes. Long-term follow-up with objective respiratory and exercise capacity assessment are still necessary to demonstrate the sustainability of LVRS benefits in this challenging patient population.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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