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ORIGINAL RESEARCH

A Novel Percutaneous Volume Reduction Technique for Giant Emphysematous Bullae: Combined Percutaneous Erythromycin Sclerotherapy With Bronchoscopic Occlusion

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Objective: To evaluate the efficacy and safety of a novel percutaneous volume reduction technique combining erythromycin sclerotherapy with bronchoscopic occlusion for giant emphysematous bulla (GEB) patients unsuitable for surgery.

Methods: This retrospective study analyzed 70 patients with GEB who underwent a novel percutaneous volume reduction technique. Outcomes including St. George's Respiratory Questionnaire (SGRQ), 6-minute walk test (6MWT), modified Medical Research Council (mMRC) score, pulmonary function, and blood gas analysis were assessed before the procedure, at discharge, and 6 months post-procedure. The primary endpoint was improvement in mMRC grade. Related complications were also recorded.

Results: The average GEB size of 70 patients was 14.91±2.68cm (10–21cm). The mMRC grade improved in 43 patients, and the efficacy of volume reduction was 61.4%. The forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC), residual volume (RV), total lung capacity (TLC), PaO_2/FIO_2, $PaCO_2$, 6MWT, total SGRQ, mMRC grades before discharge showed significant improvement compared to those before the procedure. FEV_1, FVC, 6MWT, total SGRQ score, and PaO_2/FIO_2 continued to improve at 6 months after the procedure compared to those before discharge. There was significant correlation between mediastinal displacement and postoperative efficacy of GEB volume reduction (OR=3.609, 95% CI: 1.263–10.316, p=0.017). In addition, the major postoperative complications included pneumothorax (36 cases, 51%) and pleural effusion (44 cases, 63%). Most of the symptoms were mild and improved after symptomatic treatment for the involved patients. There were no deaths during the perioperative period.

Conclusion: The novel percutaneous bulla volume reduction technique represents a safe and effective non-surgical alternative for patients with inoperable GEB, demonstrating sustained therapeutic benefits lasting at least six months. The procedure appears particularly beneficial for patients with mediastinal displacement. However, the study has limitations, including its retrospective design and lack of long-term efficacy data, which may affect the generalizability of the findings.

Keywords: giant emphysematous bulla, percutaneous puncture, bulla volume reduction, non-surgical strategy

Introduction

Bullae are defined as emphysematous spaces of over 1 cm in diameter in the lungs when distended.[1] Giant pulmonary bulla (GEB), with no accepted definition so far, is generally a bulla occupying more than one-third of the hemithorax.[2] It is still a clinical challenge to profile the natural history of GEB. GEB is usually secondary to chronic obstructive pulmonary disease (COPD), and its spontaneous resolution or natural elimination occurs infrequently clinically.[3] Patients often experience exacerbated symptoms, poor pulmonary function, disturbed mechanical ventilation, low quality of life, and limited efficacy of drug therapy, requiring surgical treatment usually.[4,5] Open thoracotomy or video-assisted thoracic

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surgery (VATS) is currently the main surgical option for GEB, which, however, proposes some requirements for the overall health status of patients as some patients cannot tolerate the risks of surgery.[5,6]

Non-surgical strategies have gained increasing attention in recent years; however, their clinical application remains constrained by notable limitations. Bronchoscopic techniques, such as endobronchial valve (EBV) placement, offer a minimally invasive approach for bulla volume reduction.[7] Nevertheless, their utility is restricted by stringent eligibility criteria (eg, absence of collateral ventilation in the target lobe) and potential long-term complications, including valve migration, pneumonia, and hemoptysis.[7–9] Current evidence is predominantly limited to small-sample case reports or single-center experiences, underscoring a pressing need for large-scale cohort studies and extended follow-up to rigorously validate both efficacy and safety. Percutaneous bulla volume reduction, first pioneered by Takizawa et al,[10] has emerged as a promising therapeutic option due to its broader applicability in high-risk populations. However, the widespread adoption of this technique has been impeded by persistent technical challenges, notably postoperative persistent air leakage, heterogeneity in closure protocols, and insufficient robust evidence supporting its long-term efficacy.[10,11] Historically, this approach has been documented only in small-scale case series or anecdotal reports,[10,11] reflecting clinicians' reservations regarding procedure-related complications (eg, pneumothorax) and the absence of standardized operational protocols.

Since 2013, our team has systematically optimized a percutaneous bulla volume reduction protocol by integrating three core components: CT-guided targeted catheterization, erythromycin-induced aseptic inflammation combined with high-negative-pressure continuous suction, and bronchoscopic autologous blood-thrombin occlusion. This refined approach has partially mitigated historical limitations, including inadequate air-leakage control and the absence of standardized procedures. To further validate its clinical utility, this study aimed to evaluate the efficacy and safety of this modified percutaneous technique in GEB patients deemed ineligible for surgical intervention.

Materials and Methods

Study Population

This study retrospectively reviewed the clinical data of patients who underwent bulla volume reduction via percutaneous puncture in the Respiratory and Critical Care Medicine Department of Hunan Provincial People's Hospital (the First Affiliated Hospital of Hunan Normal University) from January 2013 to December 2023. All the enrolled patients were diagnosed with COPD in other hospitals. The definition of GEB should conform to the following criteria: (1) the presence of giant bullae in unilateral or bilateral lobes; (2) occupying at least one-third of the hemithorax; and (3) compressing the surrounding normal lung parenchyma. The presence of GEB with space occupying over 1/3 of the hemithorax was confirmed by high-resolution CT (HRCT) of the chest, with the well-defined boundary between GEB and surrounding lung tissues. Exclusion criteria of patients in this study were described as follows: individuals with complex arrhythmias, a six-month history of myocardial infarction or chronic heart failure, and those who could not tolerate examination under bronchoscope; patients with severe asthma; and patients with severe pulmonary infection or coagulation dysfunction. Specifically, patients with complex arrhythmias, a history of myocardial infarction within the preceding six months, or chronic heart failure were excluded due to significantly elevated perioperative cardiovascular risks. These conditions may compromise procedural tolerance and postoperative recovery, particularly given the potential for procedurally induced tension pneumothorax. This life-threatening complication could precipitate fatal outcomes in this high-risk cohort. The criterion of inability to tolerate bronchoscopy ensures patient compliance during bronchoscopic interventions, which are integral to our protocol. Severe asthma or pulmonary infection was also an exclusion criterion, as acute exacerbations of asthma or active infections could confound postoperative outcomes (eg, worsening dyspnea or inflammatory responses). In addition, patients with severe bronchial asthma were excluded due to their heightened risk of bronchoscopy intolerance. Coagulation dysfunction was another exclusion criterion to minimize bleeding complications during percutaneous puncture and subsequent interventions. With the exclusion of patients who were not suitable for surgical volume reduction or were unwilling to undergo surgery due to high surgical risks, 70 patients were ultimately enrolled in this study, including 67 males and 3 females. All patients were admitted to the Hospital in the stable phase of COPD and had long-term standardized inhaled medication, but still exhibited suboptimal symptom control. This study

was approved by the Ethics Committee of Hunan Provincial People's Hospital (Approval No.: [2024]-322). Patients were instructed to sign an informed consent form and were informed in detail of the expected efficacy and possible complications of bulla volume reduction via percutaneous puncture.

Therapeutic Protocols

Main Equipment and Drugs

Main equipment: SOMATOM high-resolution CT scanner (Siemens Healthineers, Erlangen, Germany), Disposable triple-lumen thoracic drainage system (YY0583-1500, Tiantai Kangsheng Medical, Zhejiang, China), Flexible electronic bronchoscope (Olympus BF-1T260, Japan), disposable triple lumen stone retrieval balloon (Olympus B-V232P-A, Japan), and disposable single lumen central venous catheter kit (C0201-16G, PUYI MEDICAL, Shanghai, China). Main drugs: Erythromycin Lactobionate for Injection (0.25g each; H43020028, KELUN Pharmaceutical, Hunan), and Thrombin Freeze-dried Powder (1000U each; H43020123, YIGE Pharmaceutical, Hunan).

Preoperative Preparation and Evaluation

The preoperative evaluation was conducted according to the criteria related to lung volume reduction proposed in a previous study.[12] Patients were instructed to complete lung capacity measurement, plethysmography, 6-minute walk test (6MWT), modified Medical Research Council (mMRC) questionnaire, St. George's Respiratory Questionnaire (SGRQ), PaO_2 (measured under oxygen inhalation in some patients with severe respiratory distress), $PaCO_2$, as well as chest HRCT of GEB characteristics (eg, number, size, and position, etc.) before the procedure. Routine tests such as routine blood tests, coagulation function, myocardial enzymes, pre-transfusion examination, electrocardiogram, etc. were also required to be completed by the enrolled patients preoperatively. Some patients had severe dyspnea and could not or refused to receive pulmonary function tests and 6MWT. After preoperative examinations, experts in thoracic surgery were invited to assess the indications and risks of surgical volume reduction for GEB.

Procedures

The studied bulla volume reduction via percutaneous puncture involved three key steps. Firstly, GEB catheterization was performed using the Seldinger technique under CT guidance.[13] All patients underwent CT scans to determine the puncture site (Figure 1A), followed by local anesthesia and insertion of a 16G puncture needle into the GEB at the site of position. Subsequently, the guide wire was inserted into the GEB through the puncture needle, and a 1.7mm single-lumen central venous catheter (16G) was inserted into the GEB along the guide wire (Figure 1B). The three-way connector was connected to the proximal end of the central venous catheter and a 50mL syringe was used to exhaust air through the connector. Patients should be closely monitored during the process and air exhaust should be withdrawn in case of the aggravation of dyspnea in some patients. The air exhaust volume should be controlled at 1,000–2,000mL. After air exhaust, CT re-examination should be performed to accurately grasp the degree of GEB reduction, the position after reduction, and the depth of the catheterization. The occurrence of pneumothorax should also be monitored in the process, and the depth of the drainage tube should be adjusted accordingly. In case of pneumothorax, a single-lumen central venous catheter (16G) should be immediately placed for drainage; and if tension pneumothorax occurs, a chest drainage tube (24Fr) should be urgently placed for drainage.

Afterward, 1g of erythromycin lactylate (dissolved in 50 mL of 50% glucose) was injected into GEB through the central venous catheter. The three-way connector should be closed immediately after injection, and CT should be performed 10 min later to observe the location of drug deposition and whether there was delayed pneumothorax. Patients should be subjected to continuous electrocardiogram and vital sign monitoring after the procedure. After 4–6 h, the three-chamber closed thoracic drainage bottle was connected for continuous negative pressure suction, with negative pressure set at −12 cmH_2O to −18 cmH_2O, for 3–5 days (Figure 1C). Notably, 1g of erythromycin lactobionate could be injected again in case of no significant reduction in GEB air leakage. The injection should not exceed three times.

Finally, selective bronchial occlusion[14] under bronchoscopy was performed three days after the completion of the infusion through the central venous catheter (Figure 1D). The target bronchus for drainage was determined by analyzing the preoperative HRCT, the position after GEB reduction, and the location of drug deposition within the GEB. A triple

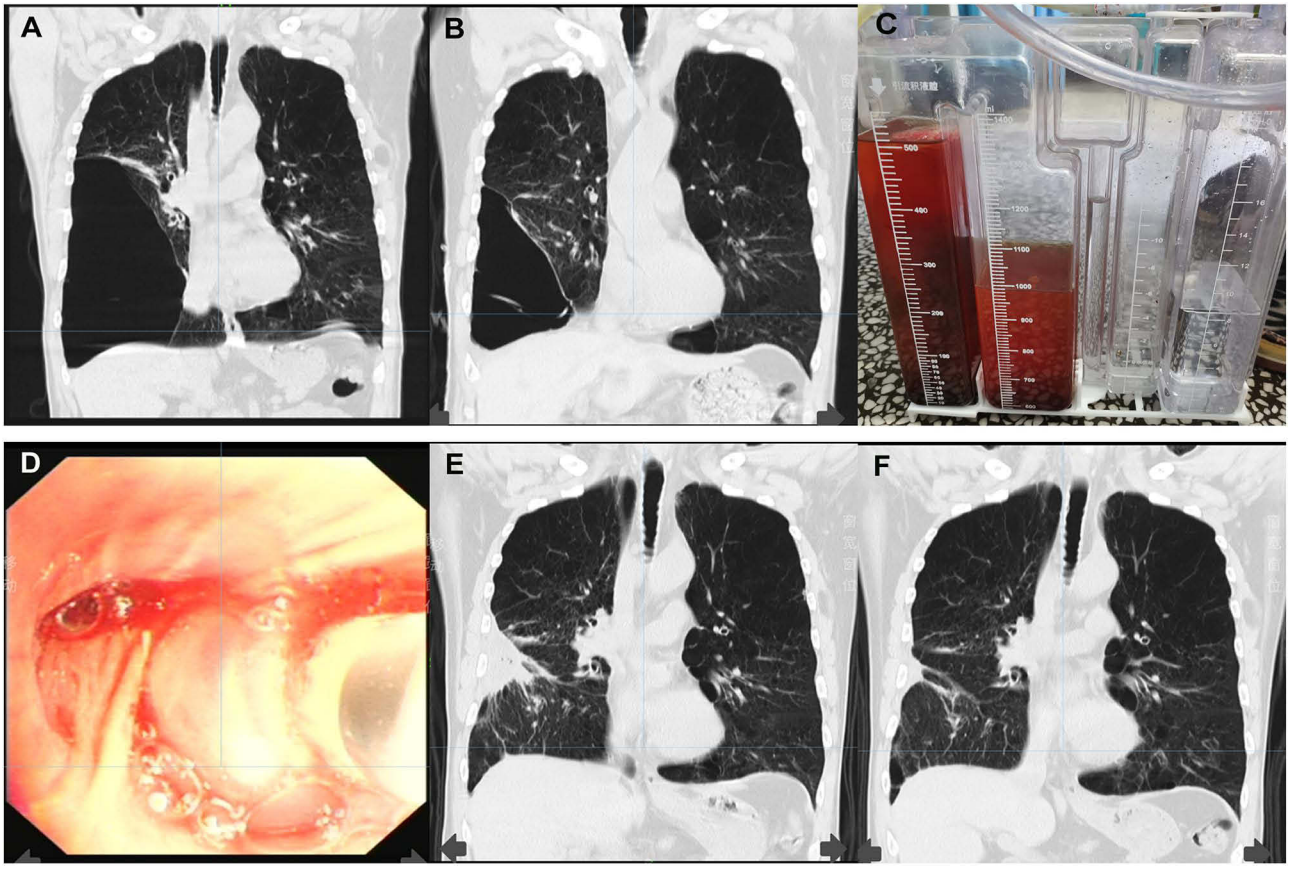

Figure 1 The operational flowchart of volume reduction of giant emphysematous bulla (GEB) for Case 1 and the chest CT images of the 6-month follow-up after the procedure. (**A**) Pre-treatment chest CT revealed a GEB occupying the entire right lower lobe. (**B**) Under CT guidance, a central venous catheter was inserted into the GEB and connected to a connector for suction. (**C**) Continuous negative pressure suction was performed by connecting a three-chamber closed thoracic drainage bottle to extract bloody fluid, which was caused by erythromycin stimulation of the GEB and inflammation of the target bronchial wall for draining. (**D**) Autologous blood and thrombin were injected into the bronchus of the anterior basal segment of the right lower lobe through bronchoscopy for occlusion. (**E**) Follow-up chest CT before discharge demonstrated near-complete closure of the GEB. (**F**) Postoperative chest CT at 6-month follow-up demonstrated no recurrence of pulmonary bullae.

lumen stone retrieval balloon was utilized to insert into the target bronchus through bronchoscopy, with the infusion of autologous blood and thrombin mixture synchronously. Each lung segment could be injected with 30 mL of autologous blood and 5 mL of thrombin solution (100 U/mL). The drainage continued after the procedure. If GEB stopped air leakage, CT would be scheduled 24 hours later and the catheter could be withdrawn as appropriate. Moreover, special attention should be given to postoperative complications (eg, pneumothorax, subcutaneous emphysema, pleural effusion, etc), with corresponding treatment measures taken. For patients with prolonged and persistent pulmonary air leakage, autologous blood and thrombin should be injected through a thoracic drainage tube to promote healing at the site of pneumothorax rupture. If necessary, pleurodesis should be performed. Before discharge, we will review the chest CT to assess the shrinkage of the bulla (Figure 1E), and we will do so again 6 months after surgery (Figure 1F). The patient enrollment flowchart and procedural workflow for percutaneous bulla volume reduction are illustrated in Figure 2.

Methods of Study

General Data Collection

This study collected the general data of all the included patients, including gender, age, height, weight, smoking status, underlying disease status, and chest HRCT images. Meanwhile, this study also recorded the length of stay in the hospital of all patients, drainage time of postoperative pneumothorax patients, various postoperative complications, and follow-up data at 6 months after the procedure.

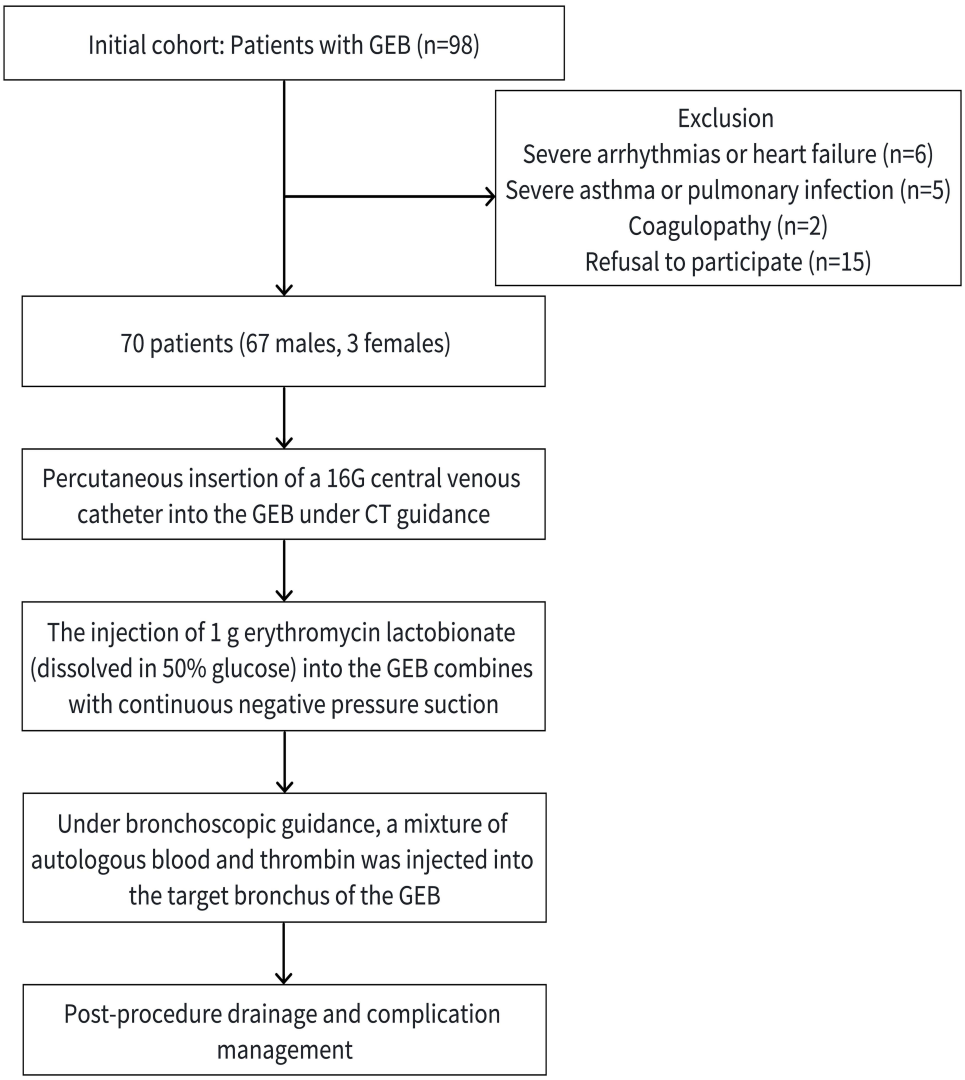

Figure 2 Patient enrollment flowchart and procedural workflow of percutaneous bulla volume reduction.
Abbreviation: GEB, giant emphysematous bulla.

Measurements

This study evaluated relevant indicators before the procedure, before discharge, and 6 months after the procedure. The mMRC grade was regarded as the primary indicator considering that some patients were unable or refused to complete pulmonary function tests and 6MWT due to severe respiratory distress. GEB volume reduction was defined to be effective if the mMRC grade was improved by one grade after the procedure. Simultaneously, the secondary indicators included SGRQ score, indexes of blood gas analysis (PaO_2/FIO_2 and $PaCO_2$), 6MWT results, pulmonary function examination [forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC), residual volume (RV) and total lung capacity (TLC)], as well as the maximum diameter of GEB via cross-sectional measurement of chest HRCT images (improvement in pulmonary bulla size).

Statistical Analysis

Considering that this study investigated the therapeutic effect of GEB volume reduction via percutaneous puncture, FEV_1 has been accepted to be the most commonly evaluated indicator domestically and internationally, which was usually compared in terms of its improvement before and after surgery (before discharge). According to previous research on GEB volume reduction,[5] preoperative FEV1 of patients with GEB was 1.8±0.9L, and it increased to an average of 0.4L at

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6 months postoperatively, assuming α=0.05 (two-tailed), and the power of the test of 1-B=0.9. In this study, sample size estimation was conducted in PASS 2021 software, with a test level of x=0.05 and a test power of 1-B=0.9, with u=1.8 and S=0.9 set based on the above clinical data. Based on the results of the above clinical research, pulmonary bulla volume reduction could improve by 0.4L. As a result, the required sample size was calculated as N=55 using a paired sample *t*-test. Considering a dropout rate of 20%, the corrected sample size was N=69.

All analyses of relevant data were completed in SPSS 29.0 software. Based on the test of normality prior to data analysis, quantitative data that conformed to normal distribution was expressed by $\bar{x} \pm s$, quantitative data not conforming to normal distribution was represented by M (Q_1, Q_3), and qualitative data was described as the number of cases (%). For normally distributed quantitative variables, paired *t*-tests were performed to evaluate mean differences between pre-operative and postoperative time points. Wilcoxon signed-rank tests were applied for ordinal data to assess distributional differences across these temporal intervals under paired measurement conditions. Univariate binary logistic regression analysis was employed to clarify factors affecting the efficacy of GEB volume reduction and the risk of postoperative complications. A two-tailed $P<0.05$ was used to indicate the presence of a statistically significant difference.

Results

General Data

A total of 70 patients were enrolled in this study, including 67 males (96%), with their ages ranging between 37–73 years old and body mass index (BMI) between 14.6~28.7 kg/m^2, with an average age of (59.36 ±7.83) years and an average BMI of (19.98 ±3.03) kg/m^2. Meanwhile, 67 cases (96%) of patients have been smoking for a long time, with an amount of cigarette smoking of 0~86 (36.00±24.05) pack-years.

All patients received chest HRCT to determine the target GEB for volume reduction and measure the GEB size to be 10~21 (14.91±2.68) cm. There were 31 patients (44.29%) with GEB accompanied by mediastinal displacement and 62 patients (88.57%) with diffuse emphysema. In addition, the length of stay in the hospital was 6~42 (21.83±7.93) days, and the drainage time of postoperative pneumothorax patients was 6 (4, 15) days, with the longest drainage time being 33 days. Table 1 shows the general data of all the 70 patients.

Table 1 Demographic Characteristics and Clinical Data of 70 COPD Patients With GEB

Clinical Characteristics	Data
Age (years)[a]	59.36 ±7.83
Gender (male, cases, %)	67 (95.71%)
BMI (kg/m^2)[a]	19.98 ±3.03
Smoking (cases, %)	63 (90.00%)
Pack-years[a]	36.00±24.05
Underlying disease	
Coronary heart disease (cases, %)	8 (11.43%)
Hypertension (cases, %)	11 (15.71%)
Type 2 diabetes (cases, %)	5 (7.14%)
Hypoxemia	48 (68.57%)
Hypercapnia	34 (48.57%)
GEB size (cm)[a]	14.91±2.68
Mediastinal displacement (cases, %)	31 (44.29%)
Concurrent diffuse emphysema (cases, %)	62 (88.57%)
Length of stay in the hospital (days)[a]	21.83±7.93

(*Continued*)

Table 1 (Continued).

Clinical Characteristics	Data
Drainage time for postoperative pneumothorax patients (days)[b]	6 (4, 15)
mMRC	
Grade 0	0
Grade 1	0
Grade 2	0
Grade 3	36 (51.43%)
Grade 4	34 (48.57%)

Notes: [a]$\bar{x} \pm s$; [b]$M(Q_1, Q_3)$.
Abbreviations: BMI, body mass index; GEB, giant emphysematous bulla; mMRC, modified Medical Research Council.

Evaluation of the Clinical Effect

For the evaluation of the clinical effect of volume reduction via percutaneous puncture for GEB patients, this study took into consideration mMRC grade, total SGRQ score, blood gas analysis results, pulmonary function test indicators, 6MWT, and improvement in pulmonary bulla size. To be specific, among the 70 patients after the procedure, 43 cases showed improvement in mMRC grade, and the effective rate of GEB volume reduction was 61.43%. The total SGRQ score, mMRC grade, PaO_2/FIO_2, and $PaCO_2$ all showed significant improvement before discharge compared to those before the procedure (all $p<0.001$).

At the same time, considering the actual evaluation results of the included patients, a pulmonary function test and 6MWT evaluation were completed in 54 patients before the procedure and before discharge (Table 2). Compared with the data before the procedure, FEV_1, FEV_1%, FVC, FVC%, RV, RV%, TLC, TLC%, and 6MWT were all significantly improved in 54 patients before discharge (all $p<0.001$). The mean FEV_1 increased from 0.81 ± 0.33 L/s preoperatively to 1.03 ± 0.39 L/s before discharge ($p<0.001$). This improvement (ΔFEV_1= 0.22 L/s) exceeds the minimal clinically important difference (MCID) threshold of 0.10–0.15 L, which is associated with reduced dyspnea and enhanced functional capacity in COPD patients.[15]

Table 2 Comparison of Lung Function, Blood Gas Analysis, Dyspnea, and Quality of Life Scores in GEB Patients Before Surgery and Before Discharge ($\bar{x} \pm s$)

Variables	N (cases)	Before Surgery	Before Discharge	*t*	*p*
FEV_1 (l/s)	54	0.81±0.33	1.03±0.39	−6.91	<0.001
FEV_1(% pred)	54	28.28±11.36	36.59±13.37	−7.15	<0.001
FVC (l)	54	1.99±0.59	2.31±0.63	−6.05	<0.001
FVC (% pred)	54	55.46±14.84	64.64±17.05	−5.98	<0.001
RV (l)	54	5.96±1.49	4.91±1.54	6.71	<0.001
RV (% pred)	54	270.64±68.00	224.11±72.02	6.62	<0.001
TLC (l)	54	7.48±1.11	6.57±1.36	6.60	<0.001
TLC (% pred)	54	124.65±23.4	109.50±27.19	6.73	<0.001
6MWT (m)	54	274.03±106.36	344.93±109.37	−7.07	<0.001
$PaCO_2$	70	44.56 ±11.86	41.39 ±10.28	4.97	<0.001
PaO_2/FIO_2	70	274.18±33.43	298.02±40.55	−7.68	<0.001
Total SGRQ score	70	67.13±16.22	57.37±19.56	7.15	<0.001
mMRC score[a]	70	3 (3, 4)	3 (2, 3)	−6.63[b]	<0.001

Notes: [a]$M(Q_1, Q_3)$; [b]Wilcoxon signed-rank test.
Abbreviations: FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; RV, residual volume; TLC, total lung capacity; 6MWT, 6-min walking testing; SGRQ, St. George's Respiratory Questionnaire; mMRC, modified Medical Research Council; PaO_2, partial pressure of oxygen; $PaCO_2$, partial pressure of carbon dioxide; %pred, % predicted.

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In addition, 7 (10.00%) of the enrolled 70 patients achieved closure of target GEB (ie, GEB reduction by ≥90%); 20 patients (28.57%) had a significant reduction in target GEB (ie, GEB reduction by 50–90%); and 16 patients (22.86%) realized reduction of target GEB to some extent (ie, GEB reduction by 25–50%).

Complications

Table 3 presents postoperative complications in 70 COPD patients with GEB undergoing bulla volume reduction via percutaneous puncture. Specifically, 44 cases (62.86%) had ipsilateral pleural effusion after the procedure, of which 39 cases (55.71%) had a small amount of effusion and 5 cases (7.14%) required drainage. Pleural effusions in these patients were ultimately absorbed voluntarily or eliminated through thoracic puncture and drainage. There were 36 cases (51.43%) of ipsilateral pneumothorax after the procedure, of which 29 cases (41.43%) had tension-free pneumothorax, which was improved by drainage using a single-lumen central venous catheter. Another 7 cases (10.00%) had tension pneumothorax and were given immediate drainage using a chest drainage tube (24Fr), with satisfactory outcomes achieved. Notably, among the 36 patients with pneumothorax described above, 21 cases (30.00%) had drainage time of less than 7 days. The remaining 15 cases (21.43%) had drainage time of ≥7 days, which were defined as prolonged and persistent pulmonary air leakage. All patients with concurrent pneumothorax were discharged from the hospital with successful withdrawal of chest drainage tubes. For patients with prolonged and persistent pulmonary air leakage, 10 cases were successfully treated by injecting autologous blood and thrombin through chest drainage tubes, another 3 cases recovered well after pleurodesis, and the remaining 2 cases recovered spontaneously after drainage.

In addition, 22 cases (31.43%) of postoperative subcutaneous emphysema were mild in symptoms and relieved by promoting absorption with appropriate symptomatic oxygen treatment. In addition, 4 patients (5.71%) experienced arrhythmia, including 2 cases of atrial fibrillation and 2 cases of supraventricular tachycardia, but none of them occurred hemodynamic disorders. All these patients recovered sinus rhythm after treatment using antiarrhythmic agents. In addition, there were 3 patients (4.29%) of secondary bacterial pneumonia, with improvement after switching to advanced antibiotics. Additionally, 8 patients (11.43%) developed drug-induced pneumonia and recovered well after receiving anti-infective and/or glucocorticoid therapy. No deaths occurred during the perioperative period.

Follow-up

Among 70 patients, 44 cases were followed up via outpatient examination. The specific follow-up data included SGRQ score, mMRC grade, blood gas analysis, pulmonary function test, 6MWT, and chest HRCT for 6 months after the

Table 3 Postoperative Complications in 70 COPD Patients With GEB

Postoperative Complications	N (Cases)	Incidence (%)
Ipsilateral pleural effusion	44	62.86%
A small amount	39	55.71%
Drainage required	5	7.14%
Ipsilateral secondary pneumothorax	36	51.43%
Tension pneumothorax	7	10.00%
Tension-free pneumothorax	29	41.43%
Drainage time <7 days	21	30.00%
Drainage time ≥7 days	15	21.43%
Subcutaneous emphysema	22	31.43%
Arrhythmia	4	5.71%
Atrial fibrillation	2	2.86%
Supraventricular tachycardia	2	2.86%
Bacterial pneumonia	3	4.29%
Drug-induced pneumonia	8	11.43%
Death	0	0

procedure. Among patients who completed the 6-month follow-up after the procedure (n=44), 6 cases did not receive pulmonary function tests and 6MWT before the procedure, with no further comparison of corresponding measurement data. In addition, for the remaining 26 patients who were unable to complete follow-up, 14 patients refused to visit the Outpatient Department owing to the presence of severe respiratory distress symptoms; and the other 12 cases were unable to complete follow-up due to loss of contact.

Six months after the procedure, total SGRQ score, mMRC grade, PaO_2/FIO_2, $PaCO_2$, FEV_1, FEV_1%, FVC, FVC%, RV, RV%, TLC, TLC% and 6MWT showed significant improvement compared to those before the procedure (all $p<0.001$). Compared with the results before discharge, total SGRQ score, PaO_2/FIO_2, FEV_1, FEV_1%, FVC, FVC%, and 6MWT also exhibited continuous improvement 6 months after the procedure ($p<0.05$), as shown in Table 4. Among the 44 patients followed up for 6 months after the procedure, 15 cases (34.09%) showed continuous shrinkage of GEB, while the remaining 29 cases (65.91) maintained stable GEB. No late-onset complications were observed in these patients.

Long-term follow-up assessments were conducted via chest CT re-examinations or telephone consultations to obtain external hospital CT reports for evaluating bulla changes. Among the 43 patients who achieved effective giant emphysematous bulla (GEB) volume reduction, 22 (51.16%) were followed for 12–72 months (mean: 30 months). Of these, 18/22 (81.8%) maintained stable bullae without recurrence, while 4/22 (18.2%) experienced recurrence within 12–24 months. During the follow-up period, no delayed complications (eg, empyema or chronic pain) were observed in these patients. Among the four recurrent cases, one patient (25%) developed mild pneumothorax, which was successfully managed with conservative treatment.

In contrast, among the 27 patients who did not achieve significant GEB volume reduction, 8 (29.63%) were followed for 12–40 months (mean: 20 months). Of these, 5/8 (62.5%) exhibited progressive bulla enlargement, while 3/8 (37.5%) remained stable One patient in this subgroup developed pneumothorax, which resolved after closed thoracic drainage.

We now present a case with an excellent long-term prognosis. A 67-year-old male patient with a two-year history of GEB in the right lung and an 11-year history of COPD presented to our department. The patient had been regularly taking inhaled medications and required home noninvasive ventilator support owing to the severity of his condition.

The radiologist analyzed the preoperative HRCT results and identified the target bronchus of the GEB in the right middle lobe (Figure 3A). Subsequently, the patient underwent a procedure for bulla volume reduction via percutaneous puncture. Eleven days post-procedure, the patient reported a notable reduction in dyspnea and a significant enhancement in mobility. A follow-up chest CT examination at this juncture demonstrated a marked decrease in the size of the GEB

Table 4 Comparison of Lung Function, Blood Gas Analysis, Dyspnea, and Quality of Life Scores in GEB Patients Before Surgery, Before Discharge, and 6 months After Surgery ($\bar{x} \pm s$)

Variables	N (Cases)	Before Surgery	Before Discharge	Follow-up at 6 Months After Surgery
FEV_1 (l/s)	38	0.82±0.33	1.10±0.38	1.18±0.42[ab]
FEV_1(% pred)	38	28.67±10.98	38.70±15.54	41.07±14.48[ab]
FVC (l)	38	2.05±0.65	2.43±0.61	2.53±0.62[ab]
FVC (% pred)	38	57.41±16.05	68.05±15.17	70.07±14.97[ab]
RV (l)	38	5.71±1.35	4.41±1.13	4.25±1.59[a]
RV (% pred)	38	259.34±59.95	200.49±53.27	193.00±73.07[a]
TLC (l)	38	7.3±0.92	6.16±1.00	6.12±1.56[a]
TLC (% pred)	38	122.97±19.36	103.76±20.30	99.60±32.22[a]
6MWT (m)	38	275.70±106.49	367.63±102.70	390.95±103.64[ab]
$PaCO_2$	44	44.43±10.84	39.68±8.25	38.34±7.99[a]
PaO_2/FIO_2	44	277.17±29.85	311.94±32.02	324.77±40.84[ab]
Total SGRQ score	44	65.52±15.04	51.61±17.51	47.02±19.02[ab]
mMRC score[c]	44	3 (3, 4)	3 (2, 3)	2.5 (2, 3)[a]

Notes: [a]Statistically significant difference in indicators in follow-up at 6 months after surgery compared to those before surgery, $p<0.001$; [b]Statistically significant difference in indicators in follow-up at 6 months after surgery compared to those before discharge, $p<0.05$; [c]$M(Q_1, Q_3)$; All abbreviations are explained in the footnotes of Table 2.

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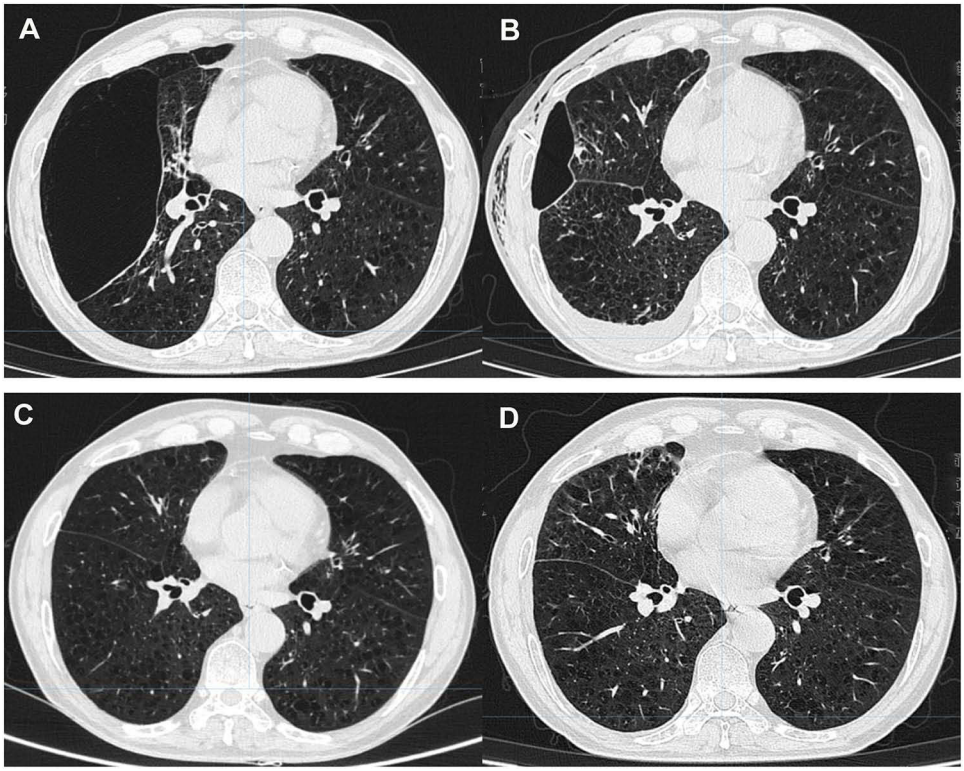

Figure 3 Chest CT images of Case 2 before the procedure, before discharge, at a 6-month and 3-year follow-up. (**A**) Chest CT before the procedure showed that giant emphysematous bulla (GEB) was located in the right lobe. (**B**) Pre-discharge chest CT demonstrated a ≥90% volume reduction in the GEB. (**C**) Chest CT showed that the GEB had been completely closed during a follow-up examination 6 months after the procedure. (**D**) Chest CT showed no recurrence of pulmonary bullae during a follow-up examination 3 years after the procedure.

(Figure 3B). Six months following discharge, a CT scan review confirmed that the GEB had been completely closed (Figure 3C). Moreover, a chest CT conducted three years post-procedure revealed no signs of pulmonary bullae recurrence (Figure 3D).

Analysis of Influential Factors of the Efficacy of GEB Volume Reduction

This study divided patients into an effective group (n=43) and an ineffective group (n=27) based on the postoperative efficacy of volume reduction. According to the results of univariate binary logistic regression analysis (Table 5), mediastinal displacement was a significantly correlated factor with the postoperative efficacy of volume reduction in GEB patients (OR=3.609, 95% CI: 1.263–10.316, p=0.017).

Table 5 Univariate Analysis of Factors Related to Postoperative Efficacy in 70 Patients With GEB

Variables	OR (95% Confidence Interval)	*p*
Age (years)	1.042 (0.978–1.109)	0.205
Smoking (pack-years)	1.006 (0.986–1.027)	0.576
BMI (kg/m^2)	1.068 (0.906–1.260)	0.433
GEB size (cm)	1.042 (0.870–1.248)	0.657
Mediastinal displacement	3.609 (1.263–10.316)	0.017
Diffuse emphysema	0.493 (0.092–2.644)	0.409
mMRC score	0.807 (0.308–2.117)	0.664

(*Continued*)

Table 5 (Continued).

Variables	OR (95% Confidence Interval)	*p*
Total SGRQ score	0.969 (0.938–1.001)	0.059
6WMT (m)	1.000 (0.994–1.006)	0.959
$PaCO_2$	0.978 (0.939–1.020)	0.301
PaO_2/FIO_2	1.005 (0.991–1.020)	0.475
FEV_1 (l/s)	0.521 (0.089–3.046)	0.469
FEV_1 (% pred)	0.991 (0.940–1.045)	0.744
FVC (l)	1.102 (0.386–3.147)	0.857
FVC (% pred)	1.024 (0.979–1.072)	0.301
RV (l)	0.862 (0.574–1.293)	0.472
RV (% pred)	0.996 (0.987–1.005)	0.387
TLC (l)	0.817 (0.478–1.396)	0.460
TLC (% pred)	0.996 (0.971–1.021)	0.746

Notes: All abbreviations are explained in the footnotes of Tables 1 and 2.

Table 6 Analysis of Risk Factors for Postoperative Pneumothorax in 70 Patients With GEB

Variables	OR (95% Confidence Interval)	*p*
Age (years)	1.020 (0.960–1.084)	0.517
Smoking (pack-years)	1.007 (0.988–1.028)	0.463
BMI (kg/m^2)	0.984 (0.841–1.150)	0.835
GEB size (cm)	0.945 (0.792–1.128)	0.530
Mediastinal displacement	1.013 (0.394–2.604)	0.978
Diffuse emphysema	1.897 (0.417–8.635)	0.408
mMRC score	1.416 (0.552–3.630)	0.469
Total SGRQ score	1.014 (0.984–1.044)	0.372
6WMT (m)	0.999 (0.994–1.004)	0.632
$PaCO_2$	1.018 (0.977–1.060)	0.396
PaO_2/FIO_2	0.997 (0.983–1.011)	0.689
FEV_1 (l/s)	1.141 (0.228–5.714)	0.873
FEV_1 (%pred)	1.004 (0.958–1.053)	0.856
FVC (l)	1.809 (0.692–4.731)	0.227
FVC (% pred)	1.029 (0.990–1.070)	0.151
RV (l)	1.222 (0.841–1.775)	0.293
RV (% pred)	1.003 (0.995–1.011)	0.424
TLC (l)	1.231 (0.750–2.021)	0.412
TLC (% pred)	1.023 (0.999–1.049)	0.064

Notes: All abbreviations are explained in the footnotes of Tables 1 and 2.

Analysis of Risk Factors of Pneumothorax After GEB Volume Reduction

Considering the occurrence of pneumothorax after volume reduction, this study divided patients into a pneumothorax group (n=36) and a non-pneumothorax group (n=34). Univariate binary logistic regression analysis revealed that none of the risk factors listed in Table 6 were significantly associated with the occurrence of pneumothorax after volume reduction for GEB.

Discussion

So far, the etiology of GEB remains undefined. It is mostly secondary to COPD, and long-term smoking is also an important risk factor.[16,17] Similarly, in our study, 67 patients (96%) had a long-term smoking history. At present, open thoracotomy or VAST for bullectomy is the preferred surgical option for GEB, with definite efficacy as well as significant

improvement in clinical symptoms and pulmonary function.[18–23] However, for GEB patients with preoperative FEV_1% <35%, accompanied by hypoxemia and hypercapnia, the benefits and risks of surgical volume reduction are not proportional, also revealing obviously increased postoperative mortality.[24,25] In this study, the average preoperative values for all patients were as follows: FEV_1% of 28.28%, PaO_2/FIO_2 ratio of 274.18, and $PaCO_2$ of 44.56 mmHg. Based on these considerations, all patients in our study group were deemed unfit for bullectomy due to their severely compromised preoperative functional exams. Therefore, it is particularly important to explore non-surgical strategies for the treatment of patients with GEB.

There are two major non-surgical strategies for the volume reduction of GEB so far. One of the strategies is the transbronchial volume reduction of GEB. Santini et al[8] reported the treatment of GEB in 9 consecutive patients via endobronchial placement of EBVs, and 8 patients achieved good short-term results. However, it may be less effective for GEB patients with collateral ventilation,[26] and EBV-induced atelectasis may cause damage to some potentially functional lung tissues. Moreover, long-term implantation of EBV may cause pneumonia and hemoptysis, and lead to some patients undergoing valve removal.[12,27] Lin et al[28] applied another bronchoscopic approach with the placement of endobronchial silicone plugs for treating GEB, showing a similar principle and effect as that reported by Santini et al.[8] So, the proposed method remains to be validated concerning its long-term outcome and the best indications based on large-scale studies in the future. The other strategy is bulla drainage via percutaneous puncture, a technique proposed by Takizawa et al.[10] In one case reported by them, a thin tube (6F balloon catheter) was inserted through a puncture of the GEB under a CT scan and connected to a water-sealed tube with negative pressure for continuous suction. Subsequently, OK-432, an immune activator as an adhesive agent, and minocycline were injected into the bulla through a drainage tube to promote inflammatory response. Takizawa et al[10] reported the treatment of two cases with this strategy in total, with some effect achieved. However, postoperative persistent pulmonary air leakage was the major complication, and it continued to bother one of the two patients until 37 days of intervention postoperatively. It is worth acknowledging that Takizawa et al[10] pioneered a minimally invasive technique of volume reduction for GEB via percutaneous puncture. However, persistent lung leakage was the major complication and continued to trouble one of the patients until an intervention was carried out on the 37th day after the surgery, bringing improvement. The type and dosage of adhesive agent injected into GEB were considered to be responsible for the air leakage as it was difficult to achieve the closure of the bronchial communication with GEB completely.

Uyama et al[29] have proposed speculation that the existence of bacterial inflammation would benefit the closure of the communication of bullae with the target bronchus for drainage, thereby leading to the shrinkage of bullae. Similarly, Chandra et al[11] also reported a case of GEB with concurrent infection successfully treated via catheter drainage through GEB puncture. It further supported the role of airway inflammation in blocking the bronchial communication with GEB, which enabled GEB to be a closed cavity where air was gradually absorbed over time. Our research team proposed another idea that injecting erythromycin, a potent solidifying agent,[30] and hypertonic glucose into GEB can stimulate the production of aseptic inflammation. In our hypothesis, by continuously applying high negative pressure suction and repeatedly injecting a solidifying agent, the inflammatory response within the GEB can be maintained to solidify GEB and the bronchial wall for drainage, thereby achieving the reduction or closure of GEB. However, the challenge remains for GEB with abundant collateral ventilation, which may be difficult to shrink using the above method, accompanied by the risk of prolonged air leakage, thus complicating GEB solidifying and bonding. To address this challenge, selective bronchial occlusion by bronchoscopy was applied to block the target bronchus for drainage, thereby preventing persistent air leakage or its recurrence after treatment. The key technical difficulties in implementation were determining the target bronchus for drainage and selecting appropriate agents for closure.

In actual practice, owing to the compression of GEB, the target bronchus for drainage may undergo twisting deformation and distribution alteration, increasing the difficulty of positioning. Preoperative analysis of the location of the target bronchus for drainage can be performed through chest HRCT across the sagittal and coronal planes, yet with relatively low accuracy. Meanwhile, the Chartis system and virtual navigation technology were also used to improve the accuracy of positioning,[26,28] which, however, were performed and described in case reports that require further validation with large-scale data. According to our discovery, through puncture-assisted aspiration or continuous negative pressure aspiration on GEB, pulmonary bullae would shrink towards the direction of the target bronchus for drainage. At the same time, the solidifying agent would deposit at

the base of the pulmonary bulla after injection through the drainage tube. These two signs would be crucial for positioning the target bronchus for drainage. Furthermore, there have been several case reports on the treatment of GEB by injecting autologous blood injection transbronchoscopically,[31,32] with the achievement of some short-term therapeutic effects. Indeed, it is a novel cost-saving strategy based on the biological adhesion characteristics of blood, which causes pulmonary bulla atrophy through blood clot blockage and scar formation. After determining the target bronchus for drainage, the present study used bronchoscopic injection of autologous blood and thrombin, and even extended the range of injection to the entire lung lobe, aiming to block the collateral ventilation of GEB as much as possible, thereby preventing or significantly reducing persistent air leakage from pulmonary bullae. We adopted continuous negative pressure suction and drainage technique simultaneously, which further increased the success rate of GEB solidifying and bonding. After that, the blood products remaining in the target lung lobes were gradually absorbed or degraded, allowing some lung tissues showing atelectasis changes to be re-expanded. It can also explain that some patients experienced continuous improvement in clinical symptoms during the 6-month follow-up after the procedure.

Among the 70 patients who underwent GEB volume reduction via percutaneous puncture, 43 patients showed improvement in mMRC grade, with an effective rate of 61.4%. Similarly, Krishnamohan et al[4] reported in their study that among 43 patients who had dyspnea before the procedure, 29 patients (67.4%) experienced relieved symptoms after undergoing surgical volume reduction for GEB. Further data collected in patients before discharge also exhibited obvious improvement in FEV_1, FVC, RV, TLC, PaO_2/FIO_2, $PaCO_2$, 6MWT, total SGRQ score, and mMRC grade when compared to those before the procedure. These improvements are primarily attributed to the elimination of the GEB occupying effect, which increases the ventilation/blood flow ratio, and promotes the re-expansion of compressed lung tissues and the upward movement of the diaphragm while restoring small airway elasticity and reducing airway obstruction.[33] It consequently significantly enhanced the exercise endurance and quality of life of these patients. Continuous improvements were observed in FEV_1, FVC, 6MWT, total SGRQ score, and PaO_2/FIO_2 6 months after the procedure when compared to those before discharge, which were in line with those reported by Santini et al.[8] In our speculation, it may be related to several reasons. Firstly, among the 44 patients followed up for 6 months after the procedure, 15 patients (34%) continued to experience a reduction in GEB. Secondly, as mentioned earlier, the blood products remaining in the target lung lobe were gradually absorbed, allowing the restoration of some lung tissues showing atelectasis changes previously. Thirdly, the subjects of the study were COPD patients with GEB who had poor pulmonary function at baseline. After undergoing GEB volume reduction via percutaneous puncture, most patients still did not recover to the stable stage of COPD before discharge, but continued to improve after discharge. Further analysis of efficacy-related factors showed that GEB with mediastinal displacement was significantly correlated with postoperative outcomes. In general, mediastinal displacement is a common clinical clue indicating the presence of high tension in pulmonary bullae. As a result, patients with tension GEB are more likely to benefit from GEB volume reduction via percutaneous puncture. It can be interpreted that due to the rapid decrease in tension after the contraction or closure of the tension GEB, it allows the severely compressed adjacent lung tissues to dilate again, while the diaphragm moves upward, thereby facilitating the improvement of pulmonary function.

Despite being minimally invasive, GEB volume reduction via percutaneous puncture may still induce some complications worthy of attention, such as pleural effusion (44 cases, 62.86%), ipsilateral pneumothorax (36 cases, 51.43%), and subcutaneous emphysema (22 cases, 31.43%). At the same time, these complications require further discussion of their mechanism, management, and impact. Ipsilateral pleural effusion (62.86%) was primarily an aseptic inflammatory response, secondary to erythromycin-induced pleuritis. While 55.71% resolved spontaneously, 7.14% required thoracentesis. Notably, no cases evolved into empyema or required long-term intervention. Prophylactic measures, such as limiting erythromycin dosage or combining anti-inflammatory agents, could reduce effusion severity.

In the current study, pneumothorax developed postoperatively in 36 patients (51.43%), with 15 cases (21.43%) exhibiting persistent air leakage lasting >7 days. The elevated incidence of pneumothorax was primarily due to sustained air leakage from the punctured giant emphysematous bulla (GEB), especially in those with extensive collateral ventilation. These rates align with those documented in prior surgical GEB volume reduction studies.[4,22] In terms of the causes, firstly, a few GEB patients with abundant collateral ventilation experienced persistent occur air leakage after puncture, requiring multiple injections of erythromycin into the pulmonary bulla for drainage to stop the leakage. Secondly, some

patients still experienced incomplete healing of pneumothorax even after the relief of air leakage of pulmonary bullae, with a similar mechanism of pneumothorax as that after EBV placement. In other words, after GEB shrinks or closes, the compressed lung tissue rapidly expands, which may lead to tearing of the lung parenchyma with existing emphysema-induced damage or tearing of the lung tissue caused by pleural adhesions. Anyway, these patients were eventually cured by injecting autologous blood and thrombin through chest drainage tubes or undergoing pleurodesis. Notably, 7 patients (10%) developed tension pneumothorax after GEB puncture, which required emergency placement of a 24Fr thoracic drainage tube for drainage. It thus proposes a high requirement for surgeons to be proficient in surgical thoracic closed drainage technology. Collectively, for GEB with abundant collateral ventilation and difficulty in shrinkage, it is necessary to modify and improve the type, dosage, and frequency of injection of solidifying agents to promote rapid shrinkage and stop air leakage of GEB under high negative pressure continuous suction, thereby reducing the incidence of pneumothorax and shortening its duration. In addition, pleural adhesions and diffuse emphysema are considered to increase the risk of pneumothorax after lobectomy.[34,35] While in our study, the size of pulmonary bullae, presence of mediastinal displacement, diffuse emphysema, and other factors were not significantly correlated with the occurrence of postoperative pneumothorax. The reason for this difference may lie in that the mechanisms by which pneumothorax occurs after the procedure are different between the two procedures. Pneumothorax after GEB volume reduction via percutaneous puncture in our study may be related to continuous air leakage from the pulmonary bulla, namely, air within the bulla continuously enters the pleural cavity through the puncture site.

Postprocedural complications also included Subcutaneous emphysema, observed in 22 patients (31.43%), predominantly arose from air dissection along fascial planes during catheter insertion or drainage maneuvers. All cases were mild and resolved spontaneously with conservative measures (eg, supplemental oxygen and rest), underscoring the critical role of meticulous catheter positioning and controlled negative pressure application to mitigate tissue trauma. Transient arrhythmias, including atrial fibrillation and supraventricular tachycardia, occurred in 4 patients (5.71%). These events were closely linked to pre-existing cardiovascular comorbidities (eg, coronary artery disease), emphasizing the imperative for comprehensive preoperative cardiac risk stratification. In addition pneumonia developed in 11 patients (15.71%), comprising 3 cases (4.29%) of bacterial pneumonia and 8 cases (11.43%) of drug-induced pneumonitis. Bacterial pneumonia mandates rigorous adherence to aseptic techniques during invasive procedures, while drug-induced pneumonitis necessitates vigilant monitoring for inflammatory responses to sclerosing agents (eg, erythromycin). Both subtypes resolved promptly with targeted interventions, including antibiotics for bacterial infections and corticosteroids for hypersensitivity reactions.

Compared to EBV therapy, percutaneous bulla reduction exhibited distinct differences in safety profiles, particularly in complication types and management strategies. EBV placement, which involves prolonged foreign-body implantation, is associated with device-related complications, including pneumothorax (18%), valve replacement (12%), valve removal (15%), and pneumonia (6%).[9] In contrast, transient pneumothorax (51%) and pleural effusion (63%) were the primary complications in our cohort, both of which were predominantly managed conservatively. Notably, no persistent infections or long-term device-related complications occurred in our study, whereas EBV trials reported valve removal in approximately 15% of cases due to adverse events.[9] However, the higher incidence of postoperative pneumothorax in our cohort emphasizes the necessity for meticulous intraoperative monitoring. Additionally, 3 patients (10%) experienced pneumothorax during long-term follow-up, which highlights an area for procedural refinement in future iterations of this technique. These differences emphasize the importance of individualized treatment strategies tailored to patient-specific risks, particularly for those deemed ineligible for surgery.

Our findings suggest that percutaneous bulla volume reduction may offer sustained clinical benefits for inoperable GEB patients, with improvements in dyspnea, pulmonary function, and quality of life lasting up to 72 months in responders. Among the subset of patients available for long-term assessment, 81.8% (18/22) maintained stable bullae over a mean follow-up of 30 months, while 34.1% (15/44) demonstrated ongoing bulla regression at 6 months. These trends, though promising, require cautious interpretation given the progressive loss to follow-up affecting 37% of the cohort, which may introduce selection bias toward patients with favorable outcomes. The sustained therapeutic effects may arise from the synergistic actions of our protocol: erythromycin-induced sterile inflammation promotes adhesion of the bulla walls, while autologous thrombin-induced occlusion targets collateral ventilation to reduce air leakage.[32]

However, recurrence occurred in 18.2% (4/22) of responders within 12–24 months, potentially due to incomplete bulla adhesion or residual collateral ventilation. Comparable recurrence rates have been reported in bronchoscopic valve studies (15–20%),[9,27] suggesting that technical refinements, such as repeated sclerosing agent injections or refined sclerosing agents, may further enhance long-term efficacy.

The minimally invasive nature of percutaneous bulla volume reduction may confer advantages in healthcare resource utilization. Compared to traditional surgical bullectomy, which often requires general anesthesia, prolonged hospitalization, and intensive postoperative care,[4] our technique utilizes readily available equipment, including CT guidance for precise puncture localization, flexible bronchoscopy for selective bronchial occlusion, central venous catheters for drainage, and closed thoracic suction systems. These tools are standard in most tertiary hospitals, minimizing additional infrastructure costs. Furthermore, in contrast to bronchoscopic EBV placement, percutaneous bulla reduction demonstrates significant cost-effectiveness. Data from recent studies indicate that EBV placement imposes substantial economic strain, as each GEB patient typically requires implantation of three valves on average,[8] with valve costs alone approaching $15,000 per procedure in China.[28] This financial burden is particularly prohibitive in resource-limited settings. Although complications such as pneumothorax necessitating drainage occurred in 51% of patients in our cohort, these were managed with simple interventions, avoiding costly surgical or bronchoscopic re-interventions.

This study has several limitations. First, its retrospective design introduces inherent biases, including reliance on historical data with potential inconsistencies in patient selection, incomplete documentation, and unmeasured confounders. For instance, the lack of a control group limits our ability to isolate the specific effects of percutaneous puncture from natural disease progression or concurrent therapies. Second, the predominantly male population (96%) raises concerns about generalizability. While this gender imbalance may reflect the higher prevalence of smoking-related COPD and GEB in males within our regional cohort, it also introduces selection bias, as physiological or comorbid differences between genders could influence treatment outcomes. Future studies should prioritize balanced enrollment to validate these findings across genders. Third, the long-term efficacy evaluation was limited by a high dropout rate during follow-up (37% lost to follow-up at 6 months), potentially skewing results toward patients with better outcomes. Lastly, the single-center nature and modest sample size may restrict broader applicability. Prospective, multicenter randomized controlled trials with standardized protocols and matched control groups are warranted to confirm these findings and establish causal relationships.

Conclusion

The novel percutaneous bulla volume reduction technique appears to represent a viable, minimally invasive therapeutic option for surgically ineligible patients with giant emphysematous bullae (GEB). Our findings suggest that this approach may improve dyspnea, exercise tolerance, quality of life, and pulmonary function, with benefits persisting for at least six months—particularly in patients exhibiting mediastinal displacement. While postoperative complications such as pneumothorax and pleural effusion were frequently observed, these were largely manageable through conservative interventions or catheter drainage, supporting the procedural feasibility in high-risk populations.

However, the interpretation of long-term outcomes should be tempered by several limitations, including a substantial loss to follow-up (37% at six months), recurrence in a subset of cases, and the inherent biases of a retrospective, single-center design. These constraints highlight the need for cautious optimism and further investigation.

Data Sharing Statement

The data are available from the corresponding authors upon reasonable request.

Ethics Approval and Informed Consent

The research was conducted in adherence to the principles outlined in the Helsinki Declaration and received approval from the Ethics Committee of Hunan Provincial People's Hospital (the First Affiliated Hospital of Hunan Normal University) with Approval Number [2024]-322. The authors affirm that all participants have provided written informed consent and have granted permission for the publication of images and all associated clinical information.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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