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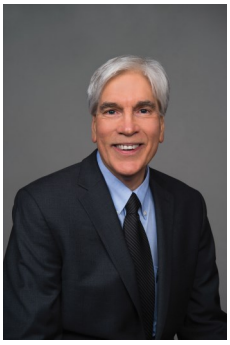
Bronchscopic lung volume reduction (BLVR): Past, Present and Promising Future



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Patients with severe and very severe COPD suffer from hyperinflation, a condition that occurs when gas volume in the lungs exceeds the normal state at the end of spontaneous expiration. The lung can be hyperinflated at rest (static hyperinflation) and/or during exercise (dynamic hyperinflation) when ventilatory demands are increased and expiratory times are reduced.[1, 2] Hyperinflation arises due to expiratory flow limitation[3] that is caused by the dual effects of emphysematous parenchymal destruction and airways abnormalities (e.g., mucus obstruction, airway edema, heightened bronchial tone, airway wall remodeling). Hyperinflation contributes to dyspnea,[4] [5-7]impaired exercise tolerance,[8] [9, 10] an increased number of hospitalizations,[11] development of respiratory failure [12]and increased mortality.[9, 11, 13] In patients with a predominant emphysema phenotype, static and dynamic hyperinflation are commonly present despite optimal medical management and significantly contribute to increased morbidity, mortality and a severely impaired quality of life.

Various interventions have been tried over the past century to reduce the size of the lung in patients with severe hyperinflation due to emphysema.[14] Most failed, or at best had short term success until Joel Cooper revised and modernized Otto Branigan's technique of bilateral lung volume reduction surgery (LVRS) and reported remarkable improvements in lung function, quality of life and exercise tolerance.[15, 16] Failure of others to duplicate Cooper's initial success led to the Center of Medicare and Medicaid Services to suspend financial coverage for the treatment based on an analysis by the Agency for Healthcare Policy Research (AHRQ) which fostered initiation of the National Emphysema Treatment Trial (NETT). NETT was a prospective, randomized and controlled multicenter trial of bilateral LVRS plus optimal medical therapy compared to optimal medical therapy alone.[17] The coprimary endpoints of NETT were exercise performance measured by a symptom limited maximal exercise test and survival with secondary endpoints of changes in lung function, quality of life and dyspnea.

NETT demonstrated that LVRS produces statistically significant and clinically meaningful improvements in exercise performance, breathlessness, and quality of life and in patients with upper lobe disease and ventilatory limited exercise performance, an improvement in survival. [18] NETT also demonstrated that hyperinflated emphysematous patients could be sub-phenotyped based on the pattern and extent of emphysema demonstrated on chest CT and post rehabilitation exercise performance into subgroups of with differential magnitudes of improvements in lung function, exercise performance quality of life dyspnea and even survival.[19] High risk for death was initially reported in a subgroup that had diffuse emphysema and $FEV_1 \leq 20$ % predicted or DLCO $\leq$ 20 % predicted and were further excluded from trial enrollment.[20] Patients with heterogenous emphysema, DLCO > 20% predicted and low exercise performance post rehabilitation had the largest and most durable improvements in all clinical outcomes. [21]When surgical resection was performed in the regions of the lung with the least perfusion, patients had the greatest magnitude and durability of improvement across all clinical outcomes. [22]Cardiopulmonary morbidity was encountered in ~ 50 % subjects, air leaks lasting was reported in 90 % (median duration 7 days) and mortality at 90 days post LVRS was 4.3% in the non-high-risk group of patients.[19] CMS approval of LVRS was announced in 2004, however the uptake of LVRS in the US has been very low relative to the number of patients with emphysema and hyperinflation (~140-185 Medicare recipi-

ents annually) and limited geographic availability.[23, 24] Explanations for the poor uptake of LVRS despite being approved therapy include higher than acceptable morbidity and mortality, lack of regional availability, complexity of patient workup, high procedural costs, need to refer to a specialty center and the need for a multidisciplinary team to evaluate and care for the patients being referred for this therapy.[25, 26]

Based on the above factors, work began on devising less invasive and costly alternatives that could use the bronchscopic route of performing lung volume reduction. Airway plugs or Watanabe spigots were reported to have some success in inducing atelectasis of the target lobe.[27] The Zephyr one-way endobronchial valve was developed by Emphasys Medical Inc (Redwood City, CA) to allow targeted lobar occlusion with simultaneous egress of secretions and air through the one-way valve. Early studies showed success with inducing atelectasis in patients with severe emphysema and hyperinflation.[28] The Intrabronchial Valve System was developed by Spiration using the airway wall as part of the valve system. Both endobronchial valves underwent early clinical trials that failed to achieve clinically meaningful and durable improvements in lung function or radiographic reduction in lung volumes.[29, 30] However, significant information was gleaned from these initial trials about the essential elements of successful endobronchial valve treatment for bronchscopic volume reduction in emphysematous patients. Based on post hoc analysis, the key elements for successful treatment with endobronchial valves was complete lobar occlusion and the degree of heterogeneity between the target lobe and the ipsilateral target lobe. The importance of lobar occlusion for successful bronchscopic lung reduction was confirmed in a prospective and controlled investigation.[31]

Subsequent multicentered prospective randomized and controlled trials have shown that endobronchial valves in hyperinflated patients with heterogenous and homogenous patterns of emphysema with intact fissures by chest CT imaging or lack of collateral ventilation by physiologic assessment produce clinically meaningful, statistically significant, and durable improvements in lung function, quality of life and exercise tolerance with acceptable side effects.[32-36] In contrast to LVRS, bronchscopic lung reduction has similar benefits in patients treated in the upper or lower lobes and in patients with homogenous disease. Pneumothorax, COPD exacerbations and pneumonia appear are the major complications with BLVR, however, the morbidity and mortality are less compared to LVRS.

What does the future hold for this therapy? I propose that BLVR can be made even safer, more effective, and durable by better patient selection, enhanced techniques, and device development. It should be noted that the current EBV devices are over 2 decades old since their introduction into the clinical arena. The need for total lobar occlusion with EBVs placed at the lobar or segmental or subsegmental levels results in an all or none phenomenon- all EBVs must remain in place at multiple points to ensure durable success with BLVR. Over time, displacement of an EBV by granulation tissue, cough or cardiorespiratory oscillation can occur and the likelihood increases with a greater number of implanted EBV devices. Newer devices that have different valve dynamics to allow slower deflation, sizes and shapes that better conform to the airway wall to cause less granulation tissue development, displacement, or even larger sizes to treat larger lobar regions with less valves are desirable features for new EBV products.

Patient selection is key to the procedure. Patients with dyspnea due to emphysema that precipitates static and/or dynamic hyperinflation is the target population. As mentioned earlier, airways disorders are common in patients with advanced emphysema and complicate the clinical picture of hyperinflation due to air trapping and contribute to poor outcomes in patients undergoing BLVR with EBV. Evaluating patients prior to BLVR with chest imaging to assess for airway wall thickening, mucus plugging, or airway wall inflammation may improve patient selection and avoid unnecessary complications. If current ingoing clinical trials demonstrate success in treating mucus plugging and airway wall inflammation associated with chronic bronchitis, or airways hyperresponsiveness with targeted lung denervation, then perhaps BLVR with EBV as a sequential, not initial therapy for these types of patients may show better outcomes.

Additionally routine assessment of lung perfusion to target areas for BLVR regardless of the patterns of emphysema (homogenous or heterogeneous) may improve patients' outcomes. NETT demonstrated that when the most oligemic sections of lung tissue were excised those patients had the greatest magnitude and durability of improvements in lung function, exercise tolerance, quality of life and survival.[22]

Not all patients have uniform lobar destruction with emphysema, removing the function of the entire lobe during BLVR with EBV sacrifices viable with the non-viable tissue. Having

the capability of "sculpting the lung" by just treating the disease segments may not only produce superior clinical outcomes in terms of lung function and gas exchange but also decrease the risk of pneumothorax by avoiding the need for total lobar occlusion.

Pneumothorax is the unique complication of concern that occurs ~ 24-34 % of the time in patients who are collateral ventilation negative or with an intact fissure undergoing BLVR with EBV and total lobar occlusion. With targeted lobe collapse, ipsilateral nontargeted lobe expansion occurs, the rate and extent of which is dependent upon the elastic recoil of the treated lobe and the plasticity of the nontargeted lobe to expand. This potential complication requires a mandatory 72-hour hospitalization for observation and treatment of a pneumothorax and limits the availability of BLVR at many community medical centers. Much more work needs to be done to predict the development of a pneumothorax based on pre procedural chest CT imagining by examining emphysema pattern and distribution in the targeted and ipsilateral nontarget lobe, estimating the potential volume shifts of the targeted lobe into the nontargeted lobe, the presence of pleural plaques and adhesions, and the textural properties of the lung being treated. Procedural technique such as pattern of mechanical ventilation, effects of high inspired oxygen inducing reabsorption atelectasis, choice of anesthetic approach (general vs conscious sedation) and procedural time may all contribute to its occurrence. Finally, EBV device and its inherent properties to function as a one-way endobronchial valve to facilitate air egress also needs to be evaluated as a contributing factor.

The only currently approved BLVR device in the U.S. and most of the world is the two FDA approved EBV devices. Only approximately 30% of the hyperinflated emphysematous patient population has sufficient fissure intactness or collateral ventilation negative status to use EBV to perform BLVR. Therefore, most of the patient population who could benefit from lung volume reduction can only be considered for LVRS or lung transplant- treatments that may not be feasible for many patients due to age or comorbid conditions. Lung coils, flowable adhesives and sclerosing agents and thermal ablation have been studied but have failed to meet clinical endpoints to allow approval or have never been studied in the U.S., respectively.[37-40] Early preliminary studies have suggested that fissure closure with airway delivered sealant may be successfully followed by EBV treatment, however, follow-up studies are in progress.[41] Other studies using lung tensing devices and techniques impervious to fissure integrity or collateral ventilation status are currently underway and hopefully will successfully produce applications to address this unmet clinical need.

The last 3 decades has shown significant progress in addressing hyperinflation in patients with advanced emphysema and irreversible airflow limitation who remain symptomatic despite optimal medical management. I believe the future is bright to take a therapy that currently has significant benefit to patients and make it better, safer, and more available to the patients that need it most.

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Technology Corner

Quantitative Computed Tomography of Emphysema

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Introduction

Patients with advanced emphysema often suffer from breathlessness despite optimal medical treatment. When pulmonary function test in these patients indicates significant hyperinflation, lung volume reduction (LVR) by bronchoscopy or surgery may be considered to improve the patient´s quality of life. Prior to such an invasive treatment modality, accurate patient selection is crucial to ensure optimal clinical outcomes. Besides pulmonary function tests, exercise tests, and echocardiography, multi-detector computed tomography (CT) is an essential diagnostic tool that confirms the presence of the emphysema, reveals emphysema extent and distribution, and detects the interlobar fissures and thus the interlobar collateral ventilation (CV). Depending on these results, a decision can be made whether a patient is likely to benefit from one of the lung volume reduction procedures and from which one, or whether the patient should be excluded from these invasive treatment modalities.

Background

Nowadays, various software techniques are available that support the CT emphysema evaluation referred to as quantitative computed tomography (QCT) [1]. One software technology is StratX, a cloud based QCT provided by PulmonX Inc. For StratX evaluation, the non-contrast, inspiratory CT scan should fulfil the following criteria: (a) all files in standard DICOM format, (b) supine position chest CT scans with arms positioned above the head, (c) slice thickness <1.5 mm or less and (d) slice pacing less than or equal to slice thickness [2].

StratX quantifies the inspiratory lobar volumes and emphysema extent and calculates the fissure integrity between the different lung lobes (Figure 1). Emphysematous parenchyma is evaluated for each lung lobe by applying a density threshold of -910 Hounsfield units (HU) and -950 HU. The best correlation between pathologically confirmed emphysema and CT measurements were shown for a voxel density less than -950 HU, so the -950 HU threshold seems to be the optimal cut-off. The difference between the lobar emphysema quantification scores indicates the emphysema distribution. Heterogeneity is the percentage difference in the emphysema

scores between ipsilateral lobes. Although there is no clear definition for heterogeneity, a > 10–20% difference in the proportion of pixels of less than −910 HUs or a > 10% difference in the proportion of pixels of less than –950 HU is used as the criterion for heterogeneity [4]. Moreover, the fissure completeness will be given in % between the adjacent lung lobes which is a surrogate for the interlobar CV.

The emphysema extent and the fissure integrity are also displayed graphically (figure 1): If the emphysema index (voxel density less than -910 HU) is ≥70%, 60-70%, 50-60% and <50%, the lung lobe is colored black, dark grey, light grey and white respectively. A fissure integrity ≥95; 80-90% and <8% are represented by a black solid line, a grey solid line, and a dotted light grey line respectively. This allows the physician to see at first glance whether there is a target lobe for a volume reduction treatment modality.

Clinical Application

For each patient with symptomatic advanced emphysema despite optimal medical treatment, a forced expiratory volume in 1 second (FEV_1) <50% and a residual volume >175% should be considered for an additional therapeutic modality that aims at LVR [4]. Thereby, a QCT analysis of an inspiratory slice thickness CT scan is an elementary part of the preceding diagnostics for patient selection prior to a lung volume reduction procedure. StratX provides the identification of the most emphysematous lung lobe that presents the target lobe for volume reduction and fissure integrity. Studies have shown that the quantitative analysis using the StratX software contributed to a more objective and efficient evaluation of collateral ventilation compared to a visual fissure analysis [5]. Overall, a fissure with >95%, 80-95%, and 80% completeness is defined as complete, partially complete, and incomplete, respectively [4; 6]. Patients with a target lung lobe, that is separated by a complete fissure from the adjacent lung lobes, will most likely benefit from endoscopic valve treatment. Patients with fissure integrity between 80 and 95% should undergo an invasive catheter-based measurement of the CV and should be treated by valve implantation in case of absent significant CV. Patients with a significant CV in the catheter-based measurement or fissure integrity <80% should be evaluated for alternative treatment approaches such as bronchoscopic thermal vapor ablation or lung volume reduction surgery.

Conclusion

Patient selection is crucial for beneficial outcomes following LVR procedures. QCT by using StratX or comparable software techniques provides emphysema quantification and automated fissure analysis that is superior to visual CT assessment. Therefore, QCT is recommended prior to LVR procedures to select patients who will benefit and to decide which LVR technique to use.

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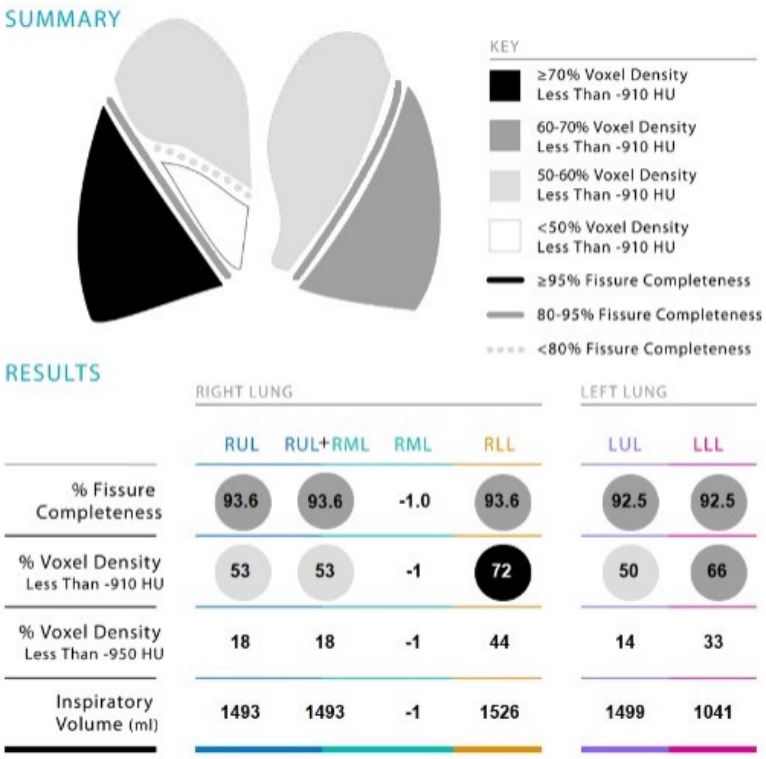

Figure 1. StratX analysis of a patient with lower lobe predominant emphysema. The right lower lobe is the most emphysematous lung lobe and thus target lobe for LVR. The fissure between the right lower lobe and the middle lobe/right upper lobe is 93.6%. The next step would be an invasive catheter-based measurement of CV. In case of an absent CV, the patient would most likely benefit from endoscopic valve implantation in the right lower lobe.

Bronchoscopic Lung Volume Reduction: Complications Happen!

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Introduction:

High complications of surgical lung volume reduction have led to multiple iterations (bypass stents, thermal vapor, sealants, coils, valves, etc.) of bronchoscopic lung volume reduction (BLVR). BLVR has been proven in clinical trials to benefit quality of life and improve lung function (FEV1, TLC, RV, 6-minute walk). These potential gains in patients with severe emphysema should be weighed with the potential for complications, and strict patient selection should be adhered to. Complications generally seen post-BLVR are acute, chronic obstructive pulmonary disease (COPD) exacerbation/respiratory failure, pneumonia, and pneumothorax.

We present a few unusual cases of BLVR endobronchial valve (EBV) complications to help pulmonologists elucidate the risk/benefit of BLVR in their patients.

Case 1: Pneumothorax gone WILD:

A 59-year-old female prior smoker with severe COPD on maximum medical therapy, on 3 liters of oxygen at rest/5, liters of oxygen on exertion, severe dyspnea with minimal exertion, without any thoracic surgeries/radiation, and no recent COPD exacerbations was evaluated for Bronchoscopic Lung Volume Reduction (BLVR). Her FEV1 was 33%, TLC 145%, RV 209%, DLCO 56%, 6MWT 265m, CT-chest without any nodules or bullae. StratX and V/Q scan with left upper lobe target. Chartis balloon occlusion/collateral ventilation evaluation in the left upper lobe/lingula showed no evidence of collateral ventilation. Zephyr valves were placed in the left upper lobe and lingula. Post-procedure chest x-ray showed atelectasis of the left upper lobe, elevation of left hemidiaphragm, and no pneumothorax.

One hour post-BLVR, the patient began to have chest tightness and dyspnea. Chest x-ray revealed a large left pneumothorax. Percutaneous left mid-axillary 14Fr chest tube placed with improvement in pneumothorax. She continued to have persistent bronchopulmonary fistula after multiple chest tubes. She had a CT chest with large left midfield bullae, severe generalized subcutaneous emphysema, and unclear positioning of the chest tube. She continued to have slowly progressive generalized subcutaneous emphysema without any change in oxygenation or dyspnea over two weeks. Thoracic surgery was consulted, and on post-BLVR day 18, our patient had left video-assisted thoracoscopic surgery with left lower lobe bullectomy/wedge resection and talc pleurodesis. Her chest tubes were removed in the following days, and she was discharged home. She returned for her 1-month follow-up in the office. She improved much from the pre-BLVR baseline with less dyspnea, improvement in exertional capacity, and decreased oxygen requirement. Her repeat pulmonary function tests are pending.

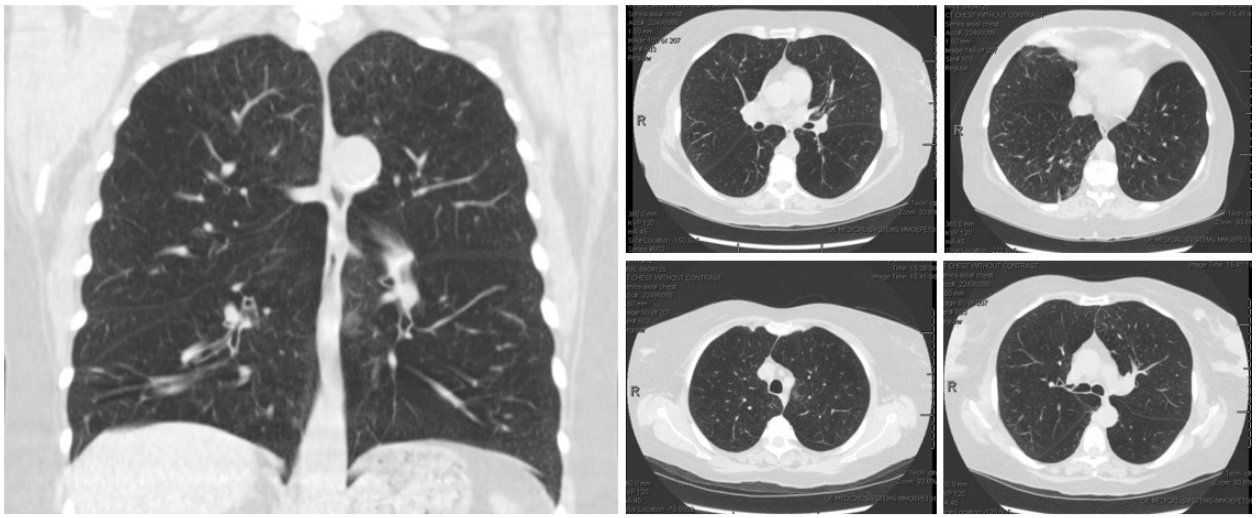

Figure 1: Case 1 - Computed Tomography Chest Pre-BLVR

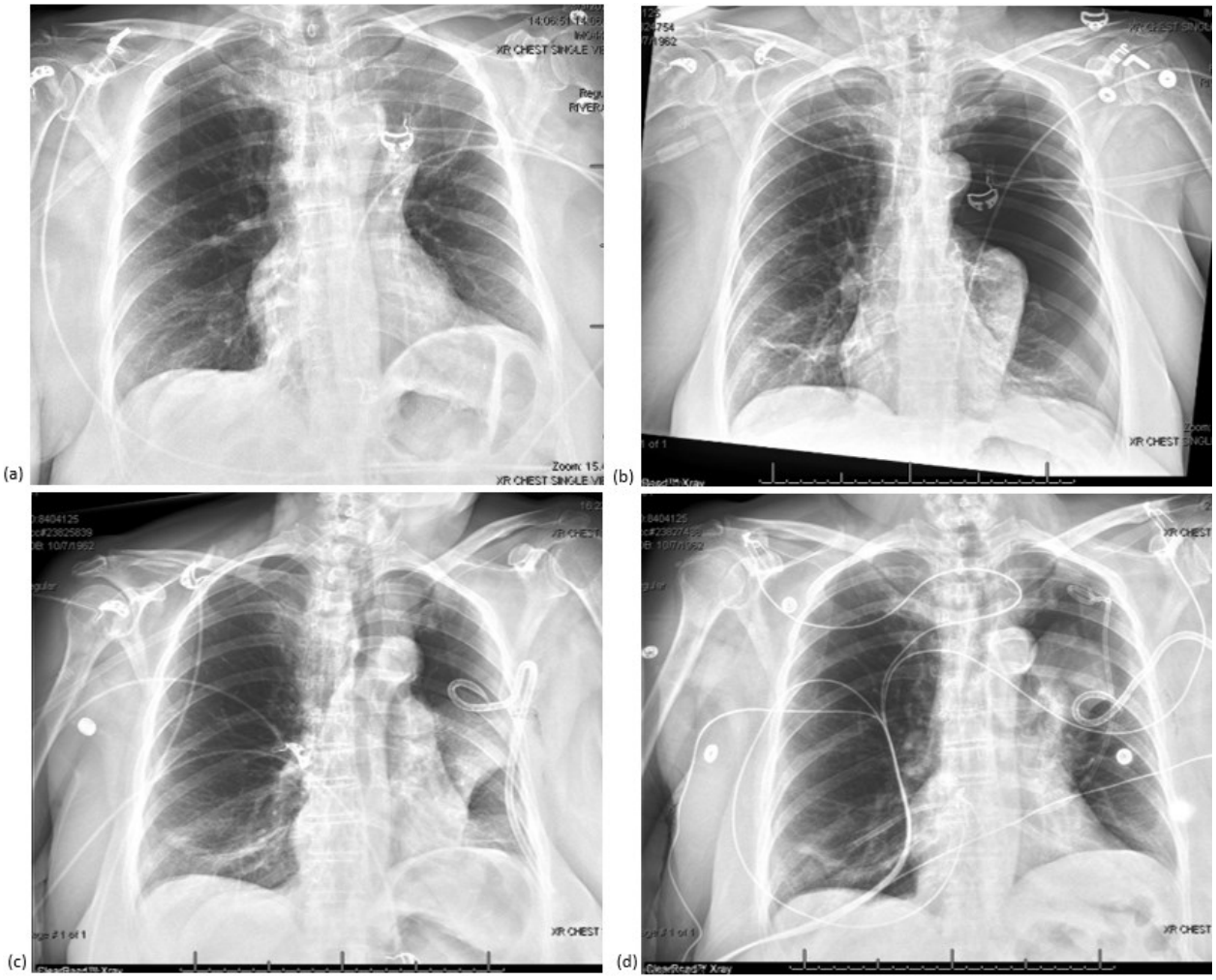

Figure 2: Case 1 - (a) Immediate Post-BLVR; (b) 1-hr Post-BLVR; (c)(d) Post-Chest Tube Placement

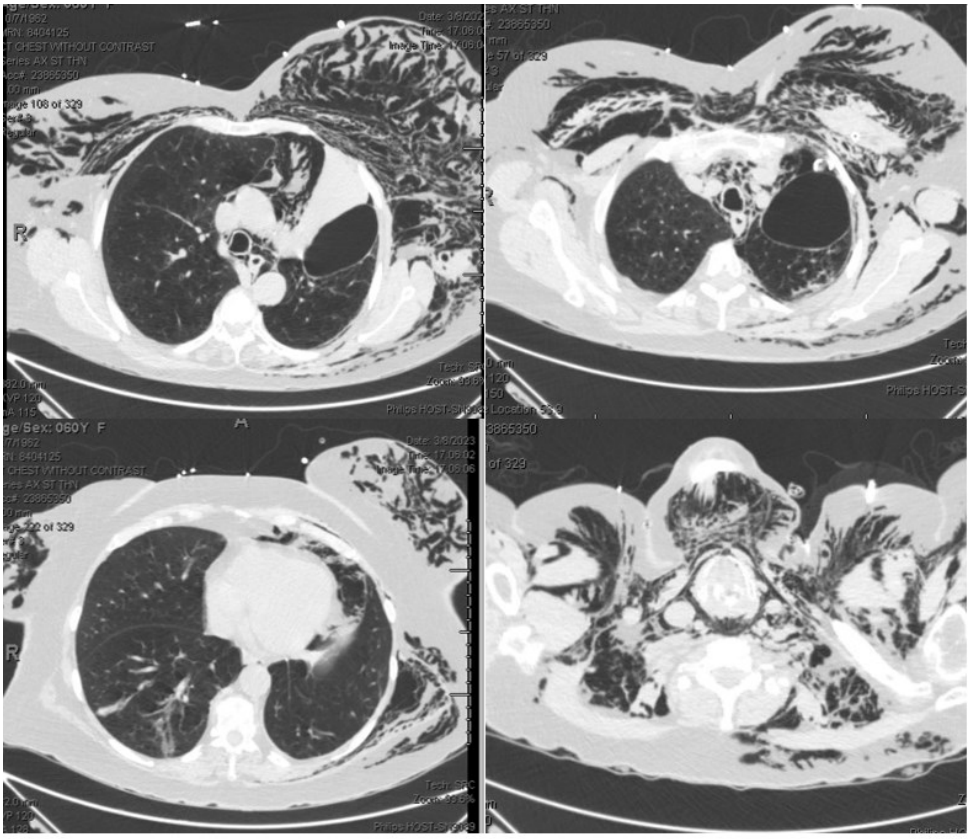

Figure 3: Case 1 - Computed Tomography Chest Post-BLVR Bullae and Subcutaneous Emphysema

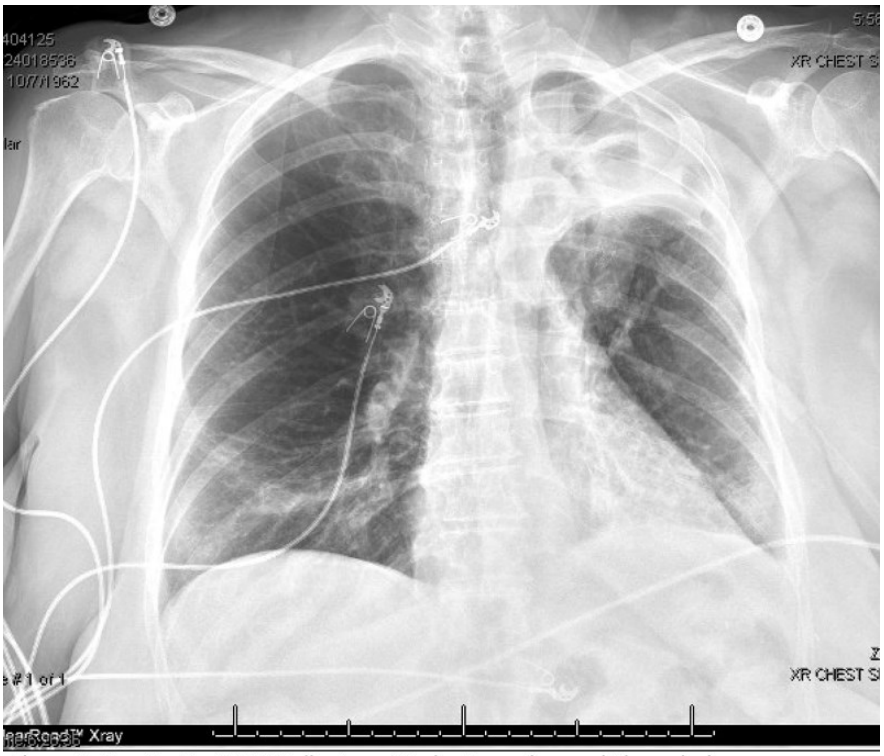

Figure 4: Case 1 - Post-VATS Bullectomy, Wedge Resection, and Pleurodesis

Commentary:

The causes of pneumothorax in post-BLVR patients include pleural adhesions, blebs, pleural scarring, and severely damaged/fragile lung tissue in the treated and untreated lobes. Expansion of tiny blebs into large bullae in the remaining (untreated) lobe is often noted due to the expansion of the lobe once the target lobe undergoes atelectasis. Persistent air leaks (Bronchopleural fistula) after BLVR requires careful management. We usually follow conservative management with small pigtail catheters and low suction. A multidisciplinary approach is warranted in the event of failure after a week. A CT chest and discussion with CT surgery is critical. In the presence of large bullae (not before the BLVR) and significant subcutaneous emphysema, the decision to remove the valves or do bullectomy with pleurodesis is considered. The final decision should be individualized with patients' input since some may vehemently oppose valve removal. In contrast, others would want to remove the valves immediately, citing the valve as the problem.

The management of post-BLVR pneumothorax is often stepwise, including removing just one valve first and observing for resolution of pneumothorax and re-expansion of the lung. But in case of failure, all the valves can be removed. The patients should be reassured that, in most cases, valves can be tried again. Below is an algorithm to guide the management of post-post-BLVR pneumothorax management.

Our patient had a pneumothorax, multiple chest tubes, and large bullae formed after the valve placement and atelectasis of the left upper lobe and lingula. With significant persistent bronchopleural fistula, unclear placement of chest tube, and large bullae, a successful VATS bullectomy and pleurodesis were performed. On follow-up, the patient received all the benefits from BLVR as expected.

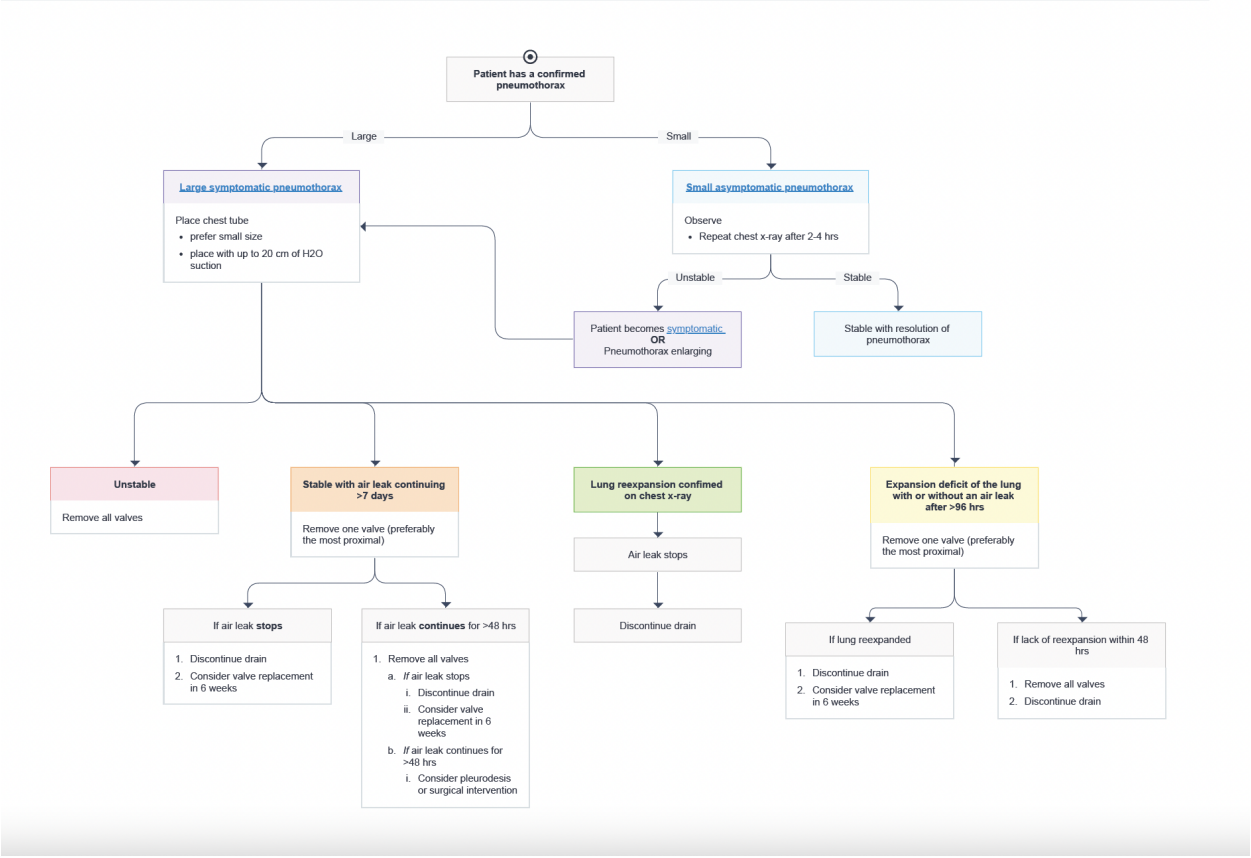

Figure Reference: van Dijk, M et al. Respiration. DOI: 10.1159/000516326

Case 2: Get them OUT

81-year-old male with a history of prior smoking and severe COPD was on maximum medical therapy. He also had obstructive sleep apnea, coronary artery disease, heart failure with preserved ejection fraction, on 2 liters of oxygen at rest, and severe dyspnea with minimal exertion. He had no thoracic surgeries/radiation history and no recent COPD exacerbations. His FEV1 was 45%, TLC 157%, RV 194%, DLCO 60%,

6MWT 202m, CT-chest without any nodules or bullae. StratX showed the left upper lobe as the best target. Pulmonx Zephyr valves were placed in the left upper lobe and lingula. Post-procedure chest x-ray showed atelectasis of the left upper lobe and elevation of the left hemi-diaphragm without pneumothorax. He was discharged without any immediate complications from the hospital on post-BLVR day 4.

He returned for a routine clinic follow-up at one month and three months post-BLVR with worsening dyspnea and oxygen requirements compared to pre-BLVR. His pulmonary function tests from pre-BLVR to 1-month post-BLVR and 3-month post-BLVR, respectively had consistent improvements in RV (194% → 153% → 151%) and TLC (157% → 111% → 117%), although worsening of FEV1 (45% → 37% → 39%), FVC (108% → 71% → 75%), DLCO (80% → 58% → 57%), and 6MWT (440m → 396m → 396m). CT-chest was completed, which showed atelectasis of the left upper lobe and lingula along with a tiny bulla. During this time, he had been given multiple courses of prednisone and antibiotics for possible COPD exacerbations without any improvement. He subsequently had all valves removed four months post-BLVR, with reinflation of his left upper lobe/lingula, and on a 1-month follow-up visit, he returned to his pre-BLVR baseline respiratory symptoms and PFTs and 6MW.

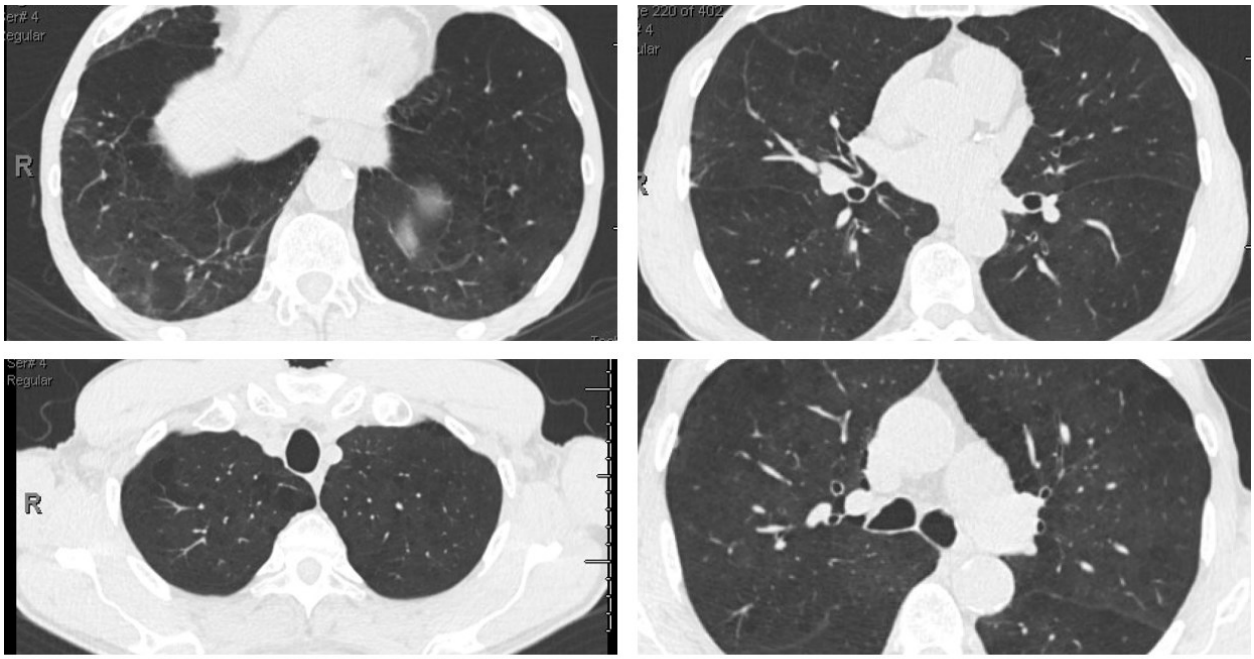

Figure 5: Case 2 - Computed Tomography Chest Pre-BLVR

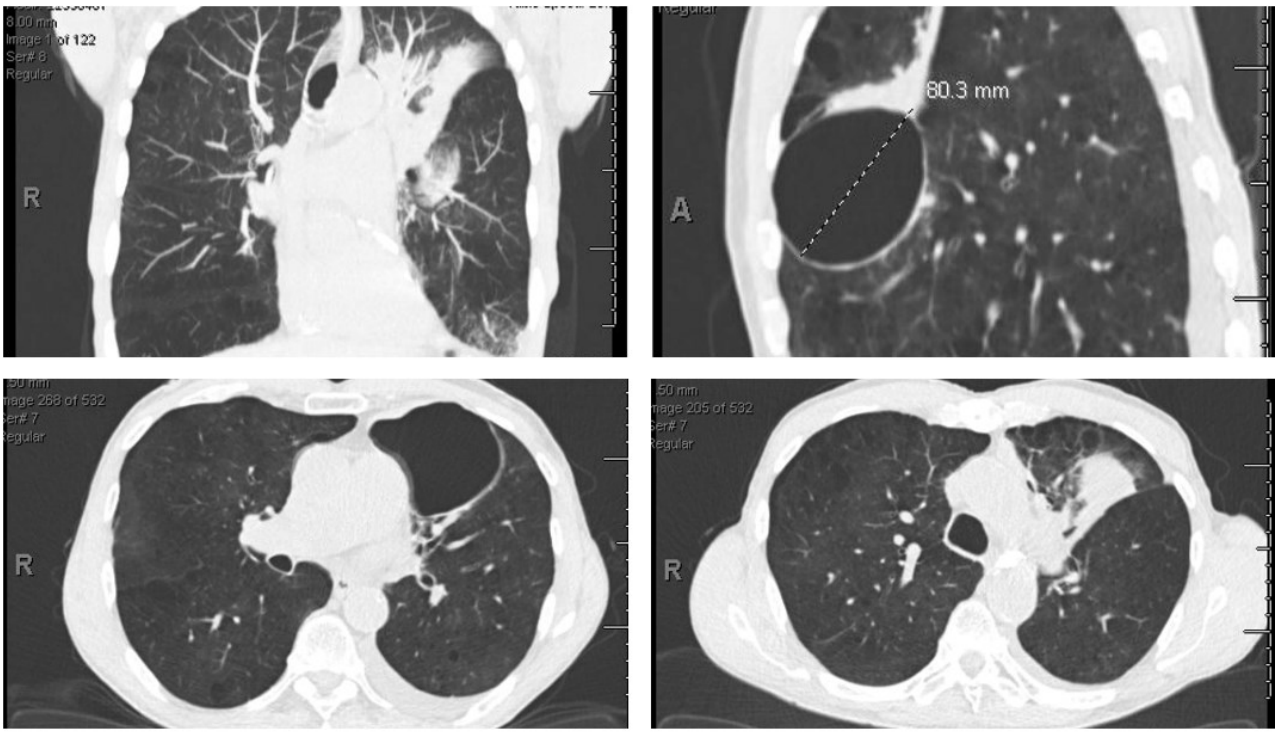

Figure 6: Case 2 - Computed Tomography Chest Post-BLVR

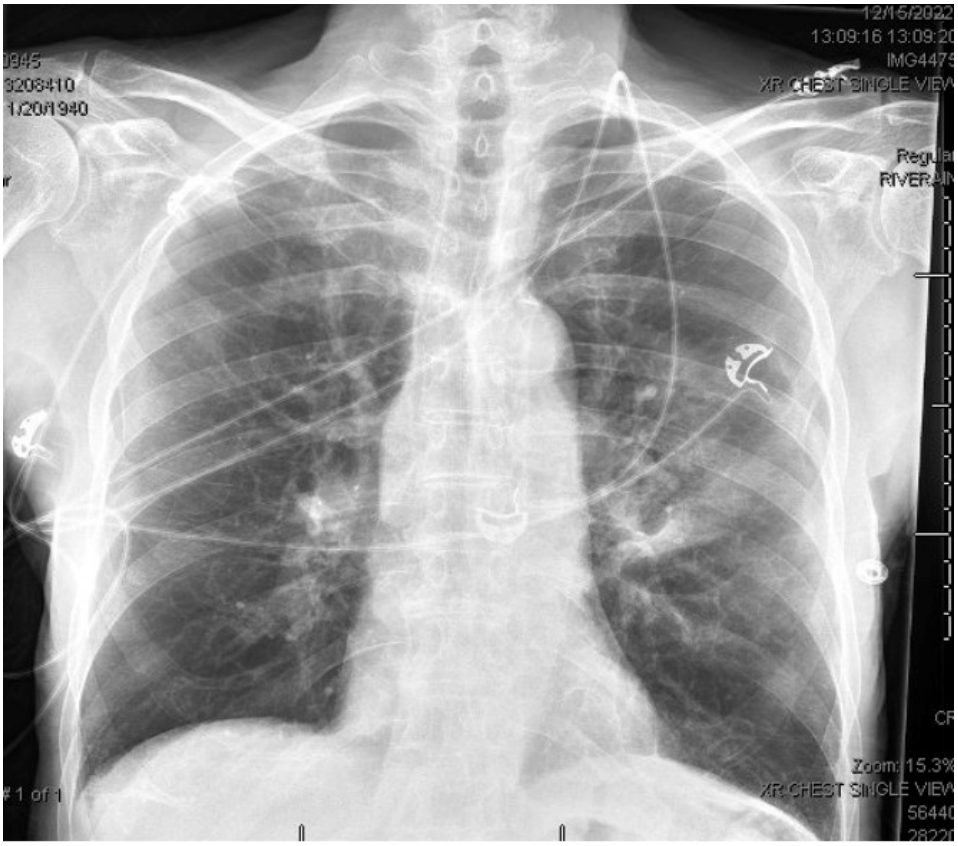

Figure 7: Case 2 - Post-EBV Removal

Commentary:

Our second case delineates the importance of a perfusion scan in BLVR. We now get perfusion scans in almost all cases to ensure that our target lobe has the lowest perfusion and that the lung left behind has good perfusion. This issue is even more critical in homogenous emphysema. Our patient most likely had good perfusion to the lobes, collapsed with valves, and suffered respiratory decline due to a decrease in ventilation perfusion. By understanding the lung volumes, perfusion, and physiologic principles of BLVR, we can avoid some of the complications, and if they do occur, we can reverse them, as in this case.

Conclusion:

The goal of endobronchial valve placement is atelectasis of the target lobe(s) in anticipation of allowing the remaining lung parenchyma to expand and provide objective and symptomatic benefits. With this goal, there can be repercussions; some unusual ones are described in the above cases. These complications are typically due to lung adhesions, rapid expansion of remaining lobes, rupture of bullae or blebs, and poor lung parenchyma. The complications can be devastating and should be clearly weighed with patient discussion before the valve placement. If these complications arise, contemplation of lung physiology and all possible treatment options should be reviewed. Having a strong suspicion of complications, thinking outside the box, and having multidisciplinary resources to deal with possible devastating complications are necessary for bronchoscopic lung volume reduction.

STRIKING A BALANCE: ADDRESSING INEQUITY IN THE FACE OF RISING DRUG COSTS AND BIG PHARMA'S COMMERCIAL INTERESTS

Healthcare providers are bound to make suboptimal treatment judgements. Healthcare professionals in most countries work within intricate and fragmented systems that often lack sufficient evidence. While it is true that every patient is unique, it is important to note that the majority of current research tends to concentrate on patient groups that share similar characteristics. The enhancement of the continuum of drug development, approval, funding, and prescription is crucial for medical researchers, regulatory bodies, insurance providers, and accountable care organizations, despite the challenges posed by these distinctions. The importance of this is especially significant when considering costly medications that have proven to be ineffective. In order to sustain the healthcare system in the long term, it is necessary to establish a thorough framework that supports fair and efficient therapeutic choices.

The increasing costs pose a challenge for funding innovative medications in this situation. One aspect to consider is the acquisition of sufficient financial resources to meet the increasing demand for drugs. Additionally, it is important to implement strategies that will improve the process of introducing new drugs. According to data from 2015, the total expenditure on pharmaceuticals by OECD countries exceeded $800 billion. The significant rise in spending on new hepatitis C and oncology drugs is the main factor behind this upward trend. The allocation of health expenditures to pharmaceuticals varies significantly between developing and transitioning nations, ranging from 20 to 60 percent. In comparison, OECD countries allocate a lower proportion of 18 percent towards pharmaceuticals. In low-income countries, a significant portion of the population, up to 90 percent, relies on personal funds to purchase medications. This implies that medicines rank as the second-largest household expense, following food. As a result, a considerable number of people around the globe face difficulties when it comes to obtaining affordable medications.

Over the course of the last decade, there has been a significant increase in the cost of novel cancer drugs, with prices multiplying by up to ten times their original value. The observed trend has played a significant role in the overall rise in the cost of cancer medications. Cancer therapies have become the primary focus of pharmaceutical spending in developed markets. The global sales of cancer medications in 2015 were $107 billion, which represented a significant increase of 11.4% compared to the previous year. The increase in question can be attributed to two main factors: the growing occurrence of cancer and the increasing expenses associated with pharmaceuticals. Projections indicate that there will be a significant rise in new cancer cases, reaching 21.4 million annually by 2030. This increase is expected to have a notable impact on the financial burden associated with cancer-related healthcare. The high costs of premium-priced medicines, especially in the field of oncology, are worrisome due to a lack in many new drugs of clear therapeutic benefits. According to independent drug information journals, the majority of new drugs are found to have limited or nonexistent health benefits compared to existing therapies. The evidence suggests that in the pharmaceutical industry, increases in prices do not always correspond directly to the level of benefits provided. The significant rise in oncology drug prices over the past decade serves as a notable example within the field of cancer research. The rise in costs, combined with the observation that a significant portion of new drugs offer minimal or no extra advantages, raises concerns about the sustainability and efficacy of existing pharmaceutical practices.

But not only cancer drugs have outraging prices. In the new scenario, the issue of funding for medications for orphan diseases is challenging due to the increasing costs involved and the lack of sufficient and trustworthy data in many diseases. The presence of emotional complexity within these disorders adds a layer of complication to the situation. Taking into account the proliferation of new costly drugs for low prevalence diseases, according to projections, the global expenditure on orphan pharmaceuticals was expected to reach $178 billion by 2020, which is equivalent to the amount spent on cancer treatment. That potential impact of orphan drugs worsens the current difficult situation.

A deliberate balance is needed due to price and financial constraints. The possible downsides of these issues in light of their benefits to pharmaceutical firms in stimulating the development of new treatments to satisfy unmet medical needs must be considered. Sovaldi and Harvoni, two hepatitis C drugs, have also garnered attention. Sovaldi costs $84,000 and Harvoni $95,000 for a 12-week course. Although they may cure Hepatitis C, their total impact is hard to assess. Since these therapies can avoid liver cancer, liver failure, transplants, and disease spread, their advantages are clear. Hepatitis C killed 20,000 people in 2013. Like the cancer medications discussed previously, patients who cannot pay or qualify for discounts face a difficult situation. Sofosbuvir, known as Sovaldi in the US, was once priced at $1,000 per tablet, making it expensive even for robust economies. Pharmaceutical firm Gilead charges £35,000 for a 12-week UK treatment cycle. Some people need a 24-

week therapy schedule. The persistent danger of hepatitis C and the transforming power of these drugs make universal access crucial. It became evident that no government had enough money to help everyone. The UK National Institute for Health and Care Excellence (NICE) authorized hepatitis C medications if Gilead offered a discount. Despite the potential cost savings from eliminating expensive National Health Service (NHS) operations like liver transplants, the UK government has been reluctant to cover 160,000 affected people. The NHS has tried an innovative approach by phasing in medicines. This method prioritizes the sickest and delays adoption for others. This remarkable move represents a new healthcare delivery model. The decision to delay NICE-approved medicine implementation is a major deviation from standards. The authorities' decision underlines the complexity of balancing healthcare goals with national healthcare systems' financial limits.

The annual growth rate of new medicine introductions from 2008 to 2021 was 20%. In 2020-2021, the market acquired 47% of the innovative medicines that had initial costs exceeding $150,000. Despite anticipated manufacturer discounts and alterations in drug characteristics, such as cancer and specialty drugs like injectables and biologics, the upward trend persisted with an annual growth rate of 11%. The cost of these newly developed drugs, which are safeguarded by 20-year patents, can amount to hundreds or even thousands of pounds per package. But government may implement strategies to decrease the impact. In 2015, the UK implemented the breast cancer medication Kadcyla, which had a price tag of £90,000 per patient annually. The outcome of the negotiations led to a substantial reduction in the NHS.

The challenge of escalating drug prices extends beyond newly developed medications, indicating a pervasive trend that surpasses the rate of price hikes observed in other healthcare services. A staggering 71% of pharmaceuticals acquired through Medicaid have witnessed price increases, highlighting a prevalent and persistent issue. Global healthcare systems are grappling with an escalating burden. According to NHS England, the estimated annual spending on pharmaceuticals in 2017 was £16 billion, with £9 billion specifically earmarked for general practitioners' prescriptions. Furthermore, this expenditure has been increasing at a rate of 7% per year, outpacing the overall growth rate of the NHS budget and significantly disproportionate to inflation.

Manufacturers commonly implement price hikes after the launch of pharmaceutical products, resulting in an average annual increase of 4.5% in net pricing from 2007 to 2018. A noteworthy case is the substantial price surge of Mylan's EpiPen, skyrocketing by over 500% from 2007 to 2016, escalating from just under $100 to over $600. AbbVie's rheumatoid-arthritis medicine Humira also experienced a significant price hike from $19,000 to $60,000 per year between 2012 and 2019, even with discounts factored in. Another distressing example is the threefold increase in insulin costs from 2002 to 2013. This surge in insulin prices has severe financial implications, leading to instances of self-rationing among certain patients, posing significant risks, some of which can be life-threatening. It is utterly unacceptable that a life-saving drug remains inaccessible to individuals in need. This example underscores the critical need to address the systemic issue of escalating medication costs, particularly for essential medications.

The influence of pharmaceutical pricing and regulations extends significantly to both patients and physicians. The imposition of prior authorization requirements not only hinders and delays access to healthcare but also results in adverse clinical outcomes. As indicated by a recent survey, a substantial 75% of physicians have reported instances where patients discontinued their treatment due to the onerous demands of prior authorization. Furthermore, 28% of physicians observed severe adverse events directly linked to these prior authorization requirements and the resulting unavailability of essential medications. Notably, 25% of diabetic patients chose to reduce their insulin intake below the prescribed amount in a cost-cutting effort, and approximately one-third of these patients opted not to disclose this information to their healthcare providers.

Exorbitant drug prices have not only affected patient care but have also added an extra burden on physicians. Physicians invest a significant amount of time, averaging 14.9 hours per week, in administrative tasks such as completing prior-authorization paperwork, making phone calls, and fulfilling procedural duties. Within this timeframe, physicians typically submit an average of 31 prior authorization requests. Physicians and their staff play a crucial role in interpreting coverage regulations and conveying them to patients, serving as the primary source of information as patients navigate their treatment choices within coverage plans.

What factors contribute to the determination of drug prices? How can we define is the price of a medication is fair?

The escalating and considerable costs of medications have sparked public apprehension across a spectrum of nations. A survey involving 1500 patient groups in 78 countries revealed that merely 9% considered pharmaceutical companies to possess "excellent or good" fair pricing policies. This percentage has fluctuated between 11% and 15% since the survey's initiation in

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2011.1 A heated discourse among politicians, experts, physicians, patients, and pharmaceutical executives has ensued, revolving around the equitable pricing of medicines, yet consensus on the definition of "fairness" remains elusive. The drug pricing debates revolve around the intricate calculations of costs and the inclusion of various factors.

Pharmaceutical corporations argue that the cost of a medicine includes expenses related to research and development (R&D), even for drugs that do not ultimately make it to market. Clinical trials, which are conducted to ensure the safety and effectiveness of medical interventions, require significant financial resources, often amounting to millions of dollars. The process of drug development is characterized by its unpredictability, as a significant number of potential candidates ultimately fail or exhibit adverse effects in human trials, despite initially showing promise in laboratory or animal studies. This inherent uncertainty in drug development poses a considerable financial burden. Pharmaceutical companies argue that incorporating the expenses of unsuccessful medications is essential for funding continuous research. The Tufts Centre for the Study of Medication Development in Boston agrees with this statement, highlighting the significant time and financial investments required for medication development.

But many disagree with its logic. Olivier Wouters, PhD, associate professor of economics and politics at the London School of Economics and Political Science, questions the idea that high R&D expenditures justify high medicine prices. Wouters and colleagues from UC San Diego's Skaggs School of Pharmacy and Pharmaceutical Sciences studied 60 new FDA-approved medications from 2009 to 2018. R&D costs did not affect medicine pricing, contrary to forecasts. The scientists also discovered no association between price and therapeutic value. These data challenge the idea that increasing R&D spending raise medicine pricing. “Our findings show that drug companies do not set prices based on R&D spending or drug quality. Instead, they charge what the market will bear”.

As an example the price of Zolgensma has sparked debate and disagreement. Pharmaceutical companies argue that the implementation of high prices is essential in order to recover the costs incurred during research and development. In 2019, Novartis introduced Zolgensma, a gene-altering injectable medication that is considered the most expensive in the world. It is priced at $2.1 million for a single treatment, targeting an uncommon genetic condition that is fatal for children. Critics argue that Novartis, the drug's marketer, should not be credited with the research and development of Zolgensma. In addition, the company strategically acquired AveXis, the developer of Zolgensma, with the expectation of achieving swift cost recovery. There is disagreement among parents of children who have benefited from Zolgensma. The cost of $2,100,000 is justified by their belief that it can potentially save their future generations. According to these parents, the expenses associated with in-home care, ventilators, and frequent hospitalizations could potentially surpass the overall cost of Zolgensma treatment over a person's lifetime.

Companies' claim that high medication prices are due to a competitive market is untrue since drug pricing does not follow free market principles. Medicine prices are higher in some nations due to monopoly-like safeguards. Patents protect against competition and encourage bargaining, extending market exclusivity. In the meanwhile, the secrecy of drug pricing is maintained. In order to share information relevant to the transparency of health product markets, including investments, incentives, and subsidies, WHO would need to "evaluate the feasibility and potential value of establishing a web-based tool." At the moment, manufacturers' prices are entirely subjective, opaque, and discretionary, with little accountability.

Commercial organizations, including BigPharma, are primarily driven by the desire to maximize their profits. But the acceptability of high profit margins, especially for necessities, raises a crucial moral question. Multiple studies have provided evidence of the impact of a financialized business model on pharmaceutical companies. These studies highlight the shift in priorities, where these companies have moved away from making investments that benefit a larger population and instead prioritize maximizing profits for their shareholders. The financial stability of a company can be assessed by analyzing various indicators such as the size of its balance sheet, the amount of dividends paid to shareholders, and the proportion of valuable assets held by the company. When these events take place, a company's approach shifts from focusing on manufacturing goods and providing services to prioritizing the generation of revenue. The negative impact of this situation can be observed in the hindered growth of productivity, investments in fixed capital, research and development (R&D), and labor force participation. The cash reserves of 27 companies experienced a significant increase over the span of 18 years, rising from US$83 billion in 2000 to US$219 billion in 2018. The allocation of funds to shareholders has experienced a significant increase over the years, rising from 88% of total R&D expenditure in 2000 to 123% in 2018, amounting to a substantial sum of US$146 billion. This growth can be attributed to dividends and share buybacks. The use of drugs is crucial for the well-being of individuals, and their availability directly impacts human lives. It is doubtful that pharmaceutical companies can sustain their pursuit

of profits, as they often rely on low-cost borrowing and monopolistic income from intangible assets. While some argue that high drug prices are necessary to offset research and development expenses, studies suggest that the significant price difference between the United States and other nations would enable companies to not only cover their R&D costs but also generate substantial profits.

Pharmaceutical corporations, like other businesses, prioritize shareholder profit while following laws. But prioritizing private profits over public well-being, especially when it threatens a fundamental human right like healthcare, raises grave ethical concerns. Turing Pharmaceuticals, founded by former hedge fund manager Martin Shkreli, was notorious for drastically raising Daraprim prices from $13.50 to $750 per pill. The annual treatment costs sometimes exceeded hundreds of thousands of dollars. The company's justification that the price raise was to fund toxoplasmosis therapeutic research and development has been criticized for hiding pharmaceutical greed. Daraprim's effectiveness and low side effects exacerbate this response. Shkreli's forthright statement at the Forbes Healthcare Summit that profit maximization took the topic to scandalous proportions. While Valeant and Rodelis Therapeutics have used similar pricing strategies to acquire specific medications, Shkreli's actions sparked widespread public outcry and heightened scrutiny on this issue, and his transparency in revealing the underlying objectives, pricing strategies, and operational mechanisms of a healthcare system often shielded from such candid discussions was notable. He proved that Turing Pharmaceuticals raised Daraprim's price from $18 to $750 per pill just because they could.

During his keynote address at the Medicine X conference, Peter Bach, MD, the director of Memorial Sloan Kettering's Centre for Health Policy and Outcomes, expressed concerns about the actions of pharmaceutical companies. According to Peter B. Bach, there is a general consensus that drug pricing in the United States lacks rationality, with the pharmaceutical industry having complete control over prices. This reflects a widespread appreciation of the issue. Pharmaceutical companies often establish prices and try to discourage discussions about costs by emphasizing the importance of innovation. This implies that any measures to restrict profits could potentially hinder the progress of creating life-saving medications. Implementing the framework for decision-making necessitates access to typically confidential information regarding research and development (R&D), manufacturing, and distribution costs. The absence of cost transparency impedes attempts to assess the reasonableness of drug prices and exacerbates the information asymmetry in favour of sellers. Nonetheless, disclosure may be mandated by law, regulation, judicial action, or as a condition for receiving public research funds, tax benefits, regulatory approval, or reimbursement formulary inclusion. In the absence of such disclosure, decision-makers may rely on publicly available information to make reasonable estimates. At least as ordinary citizens, physicians should advocate for greater cost structure transparency with their elected officials.-

Big Pharma has spent $2.5 billion lobbying for medication pricing policies over the previous decade (OpenSecrets, 2018). Pharmaceutical trade organizations like PhRMA and BIO spent $277 million on federal government lobbying in 2017. According to CREW, 153 firms lobbied on medicine prices in 2017, a fourfold rise from previous years, 22 of these companies were among Forbes' top 25 worldwide pharma/biotech corporations, demonstrating sector dominance. On the other hand, remarkably, pharmaceutical companies wield substantial influence over patient advocacy groups. For instance, the Leukemia and Lymphoma Society receives a staggering $50 million annually from drug makers, constituting approximately 16 percent of their funding. The National Patient Advocate Foundation relies on the pharmaceutical industry for 60 percent of its $2 million budget. This influence has the potential to stifle crucial voices in the policy discourse on escalating drug prices, particularly in the context of cancer or childhood potentially fatal diseases. Patients and their advocates are more concerned about the prospect of curing diseases than the specific costs associated with individual drugs, regardless of their financial implications, and their voice is a powerful one because the emotional impact of personal histories..

The expiration of drug patents can lead to the availability of inexpensive generic copies, which has the potential to reduce healthcare costs. In recent years, advancements in technology have made it possible to produce cheap copies even of complex biologics, which have demonstrated their effectiveness in various cases. For instance, the Royal Marsden cancer hospital in London saved £80 million in one year by using a biosimilar of rituximab for lymphoma treatment. Similarly, the NHS could potentially save £200 million to £300 million annually by utilizing a biosimilar version of trastuzumab (Herceptin). However, concerns arise for patients with life-threatening diseases who cannot afford to wait for patents to expire.

Organizations like Médecins Sans Frontières and the UN have been advocating for fair access to vital medicines, arguing that they should not be considered a luxury but a basic right. The World Health Organization (WHO) supports the idea of universal medication access and maintains a list of critical drugs that all countries should have in stock.

Humanitarian News

Pharmaceutical corporations are profit-driven, only one aspect of the problem. Drug price is systemic, and payers and providers share responsibility. The government is crucial in ensuring access to expensive drugs that increase survival or quality of life. This obligation arises from the government's commitment to public health, citizen rights, and fair and equal access to critical healthcare. The degree of regulation imposed by the laws and the proportion of the national budget allocated to health care are also government prerogatives (at least in middle or high income countries). The accessibility of new pharmaceuticals and technologies is directly impacted by decisions regarding the level of taxes levied on exceedingly high income or non-productive activities (such as the financial sector) and whether tax payers' money will primarily fund armed conflicts or social security. As regular people, physicians should include as a reason for their political elections their policies on the matter.

Efforts to address exorbitant drug prices have given rise to numerous policy solutions, a detailed analysis of which goes beyond the scope of this column. Multiple factors contribute to the problem of (excessively) high prices, which can only be resolved through a combination of targeted policies, regulatory measures, and stakeholder cooperation. Achieving substantial change is undeniably challenging. Meanwhile, physicians grapple with a fundamental ethical dilemma: finding a balance between advocating for cancer or orphan disease patients and responsibly managing social resources. While ethical scholars are divided on whether physicians should always prioritize their patients, considering the direct impact on patient care prompts reflection on how to make conscientious and responsible decisions.

Physicians may have limited political influence, but professional organizations have the ability to effect change. Pharmaceutical companies that engage in price profiteering should be held accountable. Ignoring the cost of cancer or rare diseases care may ease the consciences of medical professionals, but it would be unethical and fiscally irresponsible, potentially burdening taxpayers or other insured individuals. Since the majority of new targeted cancer medicines are only marginally effective, the cost-benefit ratio of drugs is substantial. Different payers and mainly health care authorities could negotiate substantial reductions, so healthcare systems, governments, and medical societies should advocate to influence legislation and regulations. When existing laws limit such considerations, advocacy and policy changes are necessary. To ensure equity, allocation, and patient welfare, scientific societies should establish benchmarks for cost-effective benefits, such as requiring expensive pharmaceuticals to increase life expectancy. Doctors must collaborate with professional associations and provide individualized patient counselling in order to fulfil their moral obligations and protect patients from preventable medical and financial damage.

The Hippocratic Oath binds physicians as advocates for their patients' health, but their economic role is frequently overlooked. Doctors are responsible for controlling prices and helping patients afford treatments. Due to their ignorance of drug costs, physicians' economic contributions are undervalued. Physicians frequently misestimate prescription costs due to a lack of communication between healthcare entities. Oncologists and specialists in uncommon diseases may be incentivized to recommend particular treatments, jeopardizing their dual role as patient advocates and healthcare organization representatives. Capitated payment systems may force physicians to juggle patient and organization obligations. Because physicians regulate demand, pharmaceutical corporations target them for promotional expenditure. Promotion that is persuasive rather than informative increases prices, prescribing frequency, and quality decline. The lack of cost knowledge among physicians, particularly for insured patients, impedes prudent patient expenditure. System-level reforms to opaque medication pricing, coverage decisions, and challenging prescription coverage are needed to enhance patient care in the healthcare system. It can be argued that physicians are often influenced by pharmaceutical corporations' persuasive promotions that increase prices and prescribing frequency. Physicians must engage in critical thinking and make well-informed decisions, followed by appropriate actions. Ignoring the current topic is not a viable strategy as they are urged to fulfill their moral obligations by protecting patients from both unnecessary medical and financial harms, necessitating collaboration with professional organizations and individualized patient guidance.

The research conducted in Norway reveals that there is widespread support for explicit criteria-based priority setting, which aligns with the country's legal framework that guarantees access to essential healthcare. The participants in the study recognized the significance of prioritization and understood the need to allocate resources carefully. But the discussions surrounding the role of physicians as patient advocates and gatekeepers raised concerns about potential conflicts of interest. The lack of trust in the rationing process can be attributed to various factors, including limited involvement, inconsistencies in rationing standards, and doubts about the transparency and effectiveness of dispute resolution mechanisms. In general, physicians do not wish to be involved in the design of health care policy, cost-controlling strategies, or rationing discussions. But they

must acknowledge that de facto rationing is already widespread and decisions are being made by people who do not necessarily prioritize the benefit of the patients. Teen suicide rates exceed the combined age-related fatalities of main health conditions, however, the majority countries do not invest significantly in mental health coverage or programs. Millions of children are affected by adverse emotional or physical traumatic childhood events, and it has been known for a decade that multiple adverse childhood events increase mortality risk. Even when childhood trauma shortens a victim's life and affects future generations, few nations allocate a portion of their health care budget to preventing these events or their consequences. Overall, the obesity epidemic, which kills 300,000 people yearly, is a significant public health issue, predominantly (although not only) in highly developed countries . Not surprisingly, there are few programs and no large-scale initiatives to make a difference. These pressing concerns at hand require prompt intervention, although they are mostly overlooked, along with the majority of preventive actions, due to a lack of comparable lobbying as compared to expensive pharmaceutical interventions.

Healthcare and pharmaceutical manufacture are complex and expensive difficulties, creating moral quandaries for governments entrusted with providing healthcare to their inhabitants. Coverage systems differ between nations due to differences in historical circumstances, ethical beliefs, and priority classifications. While practically every country recognizes healthcare as a core human right, medical treatment cost and affordability vary. Globally, physicians agree that it is unacceptable that patients risk terrible consequences, including death, owing to the inability to buy critical prescriptions such as insulin. Insulin, which was designed to be widely available, has regrettably become a tragic symbol of a system in which business often takes precedent above human wellbeing.

Physicians have the ethical obligation to ensure that their patients have access to safe and effective medications that can improve their lives. It is our responsibility as members of a professional community to advocate for the formulation and execution of national policies in our nations that improve the availability and cost of vital medications. Furthermore, we should urge medical associations to implement strict ethical norms for scientific information sharing, ensuring that pricey medications provide meaningful advantages that justify their revolutionary prices. Most importantly, as individual practitioners, we must make educated and responsible judgements that prioritize patient well-being over possible unspoken gains linked with choosing more expensive pharmaceuticals or overusing therapies with minor benefits. Physicians act as demand gatekeepers, they must use their power to protect their patients' rights while minimizing harm to the healthcare system's sustainability and prevent the amplification of unacceptable inequities in healthcare access.

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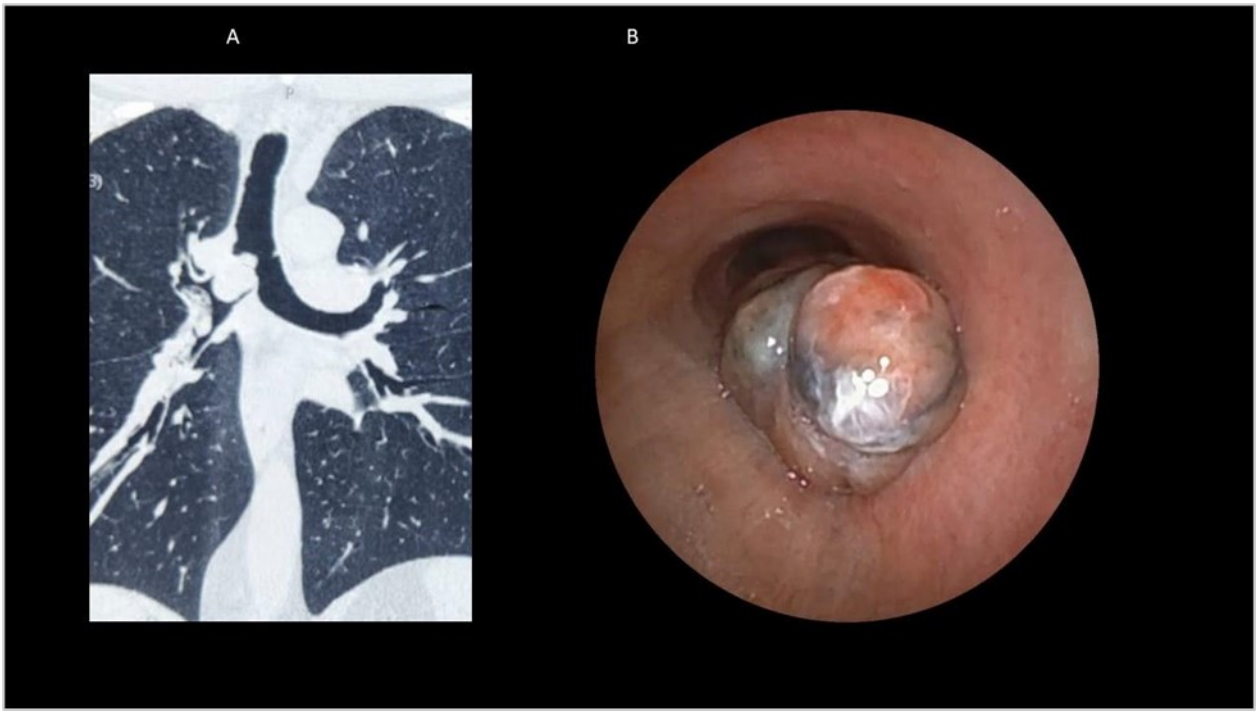
**The views expressed in this article are those of the author (Silvia Quadrelli) and do not necessarily reflect the official positions of the Executive Board or International Board of Regents of the WABIP.*

Best Image Contest

Best Image Contest 2023 (3 of 3)



Description: ENDOBRONCHIAL TB - TUMOR TYPE

Central Airway Obstruction due to endobronchial tumorous type of tuberculosis

A. CT scan showing RMB polypoid mass with extraluminal extension

B. Mobile large growth in the distal trachea on the right side causing ball valve effect at the carinal level . The histopathology suggestive of Granulomatous inflammation with necrosis

Submitter(s): Harikishan Gonuguntla, Preeti Vidyasagar, Sai Samrat

This image is 1 of 3 selected among 100+ submissions to our Best Image Contest held in late 2022. Our next Image Contest will open later this year. We look forward to receiving your image submissions.

WABIP News

Inviting you to Bali Indonesia for WCBIP 2024

Dear Colleagues,

On behalf of the World Congress of Bronchology and Interventional Pulmonology (WCBIP) in Conjunction with National Congress of Indonesian Society of Respirology (ISR), it is my great pleasure to invite you to join us in Bali, Indonesia for the upcoming the 23rd Congress of the WCBIP, October 23rd – 27th, 2024 organized by WABIP, Indonesia Society of Bronchoscopy, and Indonesian Society of Respirology.

World Congress of Bronchology and Interventional Pulmonology (WCBIP) in Conjunction with National Congress of Indonesian Society of Respirology will convene about 500 participants from Indonesia and 1000 participants from all around the world. This meeting will be attended by the expert in the field of Bronchology and Interventional Pulmonology. Furthermore, in National Congress of Indonesian Society of Respirology will be attended by the expert in pulmonology infection, thoracic oncology, asthma and chronic obstructive pulmonary disease, and also interstitial lung diseases. In this meeting, we are developing an attractive programme with enhanced scientific and educational sessions to explore the latest developments, medical advances and breakthrough in the management of pulmonology and respiratory illness. Recognizing the value of closer industry cooperation, this congress will also provide opportunities for meaningful engagements between you and key opinion leaders, high prescribers, and other respiratory medicine professionals.

WCBIP and ISR National Congress 2024 thus represents an opportunity to share your products and services with a captive medical community. As a congress sponsor, you not only have the chance to broaden your reach, but you also will find more information on strategic opportunities to gain valuable facetime with your target audience and to achieve the depth of scientific exchange that we aim to achieve.

We look forward to partnering with you in our endeavors to promote clinical excellence in the field of respiratory medicine. Visit the congress website at **https://www.WCBIP.org** for more details.

Yours Sincerely,

Menaldi Rasmin
Congress President
WCBIP-ISR National Congress 2024
https://www.WCBIP.org

WABIP News

Join us for a webinar on Bronchoscopic Lung Volume Reduction (BLVR): A standard of care treatment option for patients with severe COPD/emphysema

October 30, 2023
5:00 p.m. PST
Register Here:

https://bit.ly/3LNEzjw

Chaired by
Stefano Gasparini, MD

During this interactive webinar, attendees will learn about:

- COPD - the burden of disease
- Treatment options for advanced COPD
- Bronchoscopic Lung Volume Reduction (BLVR)
- Clinical evidence supporting BLVR
- International COPD guidelines recommending BLVR
- Patient selection
- BLVR program development

Ali I. Musani MD, FCCP
Professor of Medicine and Surgery
Director, Complex Airway Pillar of the Comprehensive Lung and Breathing Program

Director, Interventional Pulmonology
University of Colorado, Denver

This webinar is sponsored by Pulmonx Corporation.

Research

The Bronchoscopic Revolution Continues!

Bronchoscopic Treatment of Emphysema

Ali I. Musani MD, FCCP
University of Colorado School of Medicine, Denver

Emphysema, a debilitating and often life-threatening condition, has long challenged the medical community. For decades, patients with upper lobe dominant emphysema and low exercise tolerance found a glimmer of hope in Lung Volume Reduction Surgery (LVRS), as shown by the National Emphysema Treatment Trial (NETT), a procedure that promised improved mortality and quality of life. However, the widespread application of LVRS has been hampered by its high morbidity and mortality rates. In the United States, less than 150 patients receive LVRS annually, leaving millions of emphysema sufferers without effective treatment options. Globally, the situation is even more dire due to continued smoking and limited access to transplantation and alternative treatments.

Over the past two decades, the pulmonary community has dedicated significant efforts to developing minimally invasive Bronchoscopic Lung Volume Reduction (BLVR) techniques. BLVR operates on a concept akin to surgical lung volume reduction but achieves the damaged lobe's atelectasis (lung collapse) by blocking its airway. This process redirects air to relatively healthier lung regions, enhancing gas exchange and reversing the debilitating symptoms of Chronic Obstructive Pulmonary Disease (COPD).

Traditionally, LVRS has held the "Gold Standard" status for emphysema treatment despite mounting evidence suggesting otherwise. BLVR has emerged as a less morbid and mortal alternative, with shorter hospital stays and conceivably reduced costs. Moreover, BLVR is often reversible when conducted with valves, a feature that adds to its appeal. It is not uncommon for the medical community to take time to embrace paradigm-shifting modalities, even when the evidence clearly supports their efficacy.

One approach to demonstrating the effectiveness of a new treatment modality is to conduct a head-to-head comparison with the established "Gold Standard." Such a study was undertaken by Buttery SC et al. in the UK (1). This multicenter, single-blind, parallel-group study involved patients eligible for both LVRS and BLVR. The study aimed to compare outcomes at the one-year mark using the i-BODE (body mass index, airflow obstruction, dyspnea, and exercise capacity) score.

Eighty-eight participants (48% female, age 64.6±7.7 years, FEV1 predicted 31.0±7.9%) were recruited at five specialist centers and randomized to either LVRS (n=41) or BLVR (n=47). At 12 months follow-up, the complete i-BODE was available in 49 participants (21 LVRS/28 BLVR). Neither improvement in the i-BODE score (LVRS −1.10±1.44 versus BLVR −0.82±1.61; p=0.54) nor its individual components differed between groups. Both treatments produced similar improvements in gas trapping (residual volume percent predicted: LVRS −36.1% (95% CI −54.6– −10%) versus BLVR −30.1% (95% CI −53.7– −9%); p=0.81). There was one death in each treatment arm.

The study conducted by Buttery SC et al. underscores no significant difference in the outcomes of LVRS and BLVR after one year of follow-up in patients eligible for both procedures. BLVR, in this study conducted with endobronchial Zephyr valves from Pulmonx, CA USA, demonstrates its effectiveness as a treatment option for emphysema, challenging the traditional "Gold Standard" of LVRS.

However, it is essential to acknowledge that BLVR may not be suitable for all patients, particularly those with positive collateral ventilation. In such cases, alternative BLVR modalities or LVRS may be more appropriate.

The benefits of BLVR, including lower morbidity and mortality, shorter hospital stays, and reversibility (in cases using valves), position it as the preferred option for many patients. Moreover, the potential for patients to remain on the lung transplant candidacy list after BLVR offers them an improved quality of life while potentially delaying the need for transplantation.

In conclusion, Bronchoscopic Lung Volume Reduction has the potential to revolutionize the treatment of emphysema, offering hope and relief to millions of patients who have long suffered from this debilitating condition. As more studies and clinical experience accumulate, BLVR will likely continue to gain recognition as a viable alternative to the traditional surgical approach, ultimately reshaping the landscape of emphysema treatment.

Reference:

1. Buttery SC et al. Eur Respir J 2023; 61: 2202063 [DOI: 10.1183/13993003.02063-2022].

WABIP ACADEMY- WEBCASTS

The WABIP has started a new education project recently: *THE WABIP ACADEMY.* The WABIP Academy will provide free online webcasts with new and hot topics that will interest pulmonologists and interventionalists.

Current webcast topic: **Tissue acquisition for biomarker directed therapy of NSCLC**

You can reach these webcasts by using this link: http://www.wabipacademy.com/webcast/

Links

www.bronchology.com	Home of the Journal of Bronchology
www.bronchoscopy.org	International educational website for bronchoscopy training with u-tube and facebook interfaces, numerous teachiing videos, and step by step testing and assess ment tools
www.aabronchology.org	American Association for Bronchology and I nterventional Pulmonology (AABIP)
www.eabip.org	European Association for Bronchology and Interventional Pulmonology
www.chestnet.org	Interventional Chest/Diagnostic Procedures (IC/DP) NetWork
www.thoracic.org	American Thoracic Society
www.ctsnet.org	The leading online resource of educational and scientific research information for cardiothoracic surgeons.
www.jrs.or.jp	The Japanese Respirology Society
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This article has summarized the historical advances in the design and performance of needles used for EUS-guided procedures. Since the early 1990s, EUS-FNA has played a clear and vital role in oncological care and has become the standard procedure for sampling tissues with high diagnostic accuracy.

Reference:
Current Status of Needles in the Optimization of Endoscopic Ultrasound-Guided Procedures.

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