Surgical Therapies for Chronic Obstructive Pulmonary Disease

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Summary

Surgical procedures for treating emphysema were first developed nearly 100 years ago. Despite a wide range of surgical procedures performed over the years, only three appear to have true clinical benefit: bullectomy, lung volume reduction surgery (LVRS), and lung transplantation. Lung volume reduction surgery has been reintroduced in the past decade and is currently under active research. A recent large, multicenter trial showed LVRS to improve quality of life, exercise capacity, and even survival in certain highly selected patients. Some individuals with emphysema may be candidates for either LVRS or lung transplantation. Patient-selection criteria for these procedures are being developed. Key words: chronic obstructive pulmonary disease, COPD, emphysema, lung-volume reduction, lung transplantation, bullectomy.

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unpredictable results.\textsuperscript{4,5} These operations have been abandoned.

Interruption of portions of the autonomic nervous system was performed in an attempt to reduce bronchospasm, with the understanding that the autonomic nervous system in part controls bronchial tone. Sympathectomy, glomectomy, vagotomy, and total lung denervation were all attempted in asthma and emphysema patients, unfortunately with poor results.\textsuperscript{6,7} These operations were in use up through the 1950s for the treatment of asthma and COPD.

\textbf{Bullectomy}

Bullectomy for giant bullae is one procedure that is based on sound physiologic principles and has withstood the rigor of scientific evaluation and time. Bullae are markedly dilated (> 1 cm) air spaces within the lung parenchyma. They commonly occur in emphysema patients, often in the upper lung zones. The etiology of bullae in emphysema patients has not been precisely defined, but the most widely accepted theory is that of a ball-valve mechanism, in which obstruction of a bronchiolo or bronchus leads to progressive distention of areas of lung tissue where alveolar walls are already damaged. Gas can flow into these areas but is unable to escape, resulting in increased pressure and further enlargement of the air space.

Bullae in emphysema patients generally range from 1 to 4 cm in diameter, but occasionally much larger “giant bullae” can occupy a third or more of the hemithorax. These giant bullae may exert substantial compressive effects on underlying normal lung tissue, which may reduce blood flow and ventilation to potentially functioning lung. Bullectomy is considered when compression of underlying lung is thought to contribute to dyspnea and exercise limitation. Bullectomy is believed to improve lung function and reduce symptoms by allowing expansion of underlying compressed lung, which may not have been contributing effectively to either ventilation or perfusion.\textsuperscript{8} Bullectomy may also improve elastic lung recoil and decrease pulmonary vascular resistance.\textsuperscript{9} Bullectomy is also considered when bullae are associated with hemoptysis, complicated or repeated pneumothorax, or repeated infection.

Selection of patients who will benefit from bullectomy is difficult because dyspnea and reduced pulmonary function may be due to the bulla compressing more normal lung or to diffuse disease elsewhere in the lung, in which case bullectomy would have no impact on lung function or symptoms. Preoperative evaluation to identify the patients best suited for bullectomy should include plain chest radiograph, computed tomography (CT), full pulmonary function testing (including plethysmographic determination of lung volumes), ventilation/perfusion scan, and, for some patients, angiography of the pulmonary circulation. Testing is designed to determine the extent of gas trapped in the giant bulla, evidence of compressed normal lung underlying the bulla, and the extent of disease elsewhere in the chest. CT is the most accurate method of determining the size of bulla, and most experts suggest that the bulla must occupy at least one third, preferably one half, of the hemithorax.\textsuperscript{10} Both CT and pulmonary angiography have been standard tests used to identify the presence or absence of relatively normal underlying compressed lung tissue.\textsuperscript{8,11} Chest CT is now the preferred method for evaluation of compression of underlying lung. Pulmonary function testing helps in determining the volume of gas trapped in the bulla, and ventilation/perfusion scan and CT can assess disease elsewhere in the lung.

The surgical approach for bullectomy is either standard lateral thoracotomy,\textsuperscript{12} midline sternotomy,\textsuperscript{13} or video-assisted thoracoscopy, with stapling of bullae.\textsuperscript{14} Video-assisted thoracoscopy is less invasive and may be offered to patients previously considered to be at excessive risk with thoracotomy.\textsuperscript{15} Surgeries are designed for maximum preservation of the lung, and therefore full anatomic resection (ie, lobectomy and segmentectomy) are generally avoided.\textsuperscript{16} Single-lung ventilation is commonly employed dur-

\begin{table}[h]
\centering
\caption{Surgical Procedures for Treating Emphysema}
\begin{tabular}{|c|c|c|}
\hline
Procedure & Year Introduced & Theory Supporting the Procedure \\
\hline
Chostochondrectomy & 1906 & Restore thoracic mobility and reduce intrathoracic pressure \\
(disarticulation of ribs) & & \\
Autonomic denervation & 1923 & Interrupt neural pathway of bronchospasm \\
Thoracoplasty & 1935 & Reduce the volume of the distended thorax and lungs \\
Bullectomy & 1940s & Re-expand compressed lung and reduce size of thorax \\
Intraperitoneal air injection & 1950 & Increase curvature of flattened diaphragm \\
Partial pleurectomy & 1952 & Increase vascularity of the hypovascular lung \\
Lung volume reduction surgery & 1953 & Increase lung recoil pressure and reduce size of thorax \\
& Reintroduced in 1994 & \\
Nissen tracheal stabilization & 1954 & Prevent tracheal collapse during exhalation \\
Lung transplantation & 1970 & Replace diseased lung \\
\hline
\end{tabular}
\end{table}
ing the procedure because of substantial technical advantages. Effort is directed at reducing air leaks from the lung during the postoperative period. Buttressing of suture lines has been accomplished by everting and stapling the interior walls of the bullae and the use of bovine pericardial strip reinforcement. Teflon pledget reinforcement, biologic fibrin glues, and blood patches (using the patient’s own blood) are used to seal small air leaks. Following resection, pleurodesis to appose the pleural surfaces is sometimes employed, using a variety of techniques.

The outcomes of bullectomy in carefully selected patients appear to be positive and durable in terms of symptom relief and improvement of pulmonary function. In one of the largest series, FitzGerald et al reported the long-term results of 84 patients who underwent surgical procedures for bullous emphysema, over a period of 23 years. There were 2 operative deaths (2.1%). The greatest improvement (50–200% increase in FEV₁) was seen in patients with bullae that occupied >50% of the hemithorax and less emphysema elsewhere in the lung. Improvement in pulmonary function in that group lasted for up to 20 years and frequently for more than 5 years. Poorer results were seen in cases where the bulla occupied less than one third of the hemithorax, and with chronic bronchitis or diffuse emphysema. Unfortunately, all of the published results are case series with incomplete follow-up. Surgical mortality ranged from 0 to 22.5% in the series reported. Long-term follow-up of physiologic and clinical status is difficult because of incomplete reporting and multiple methods of data presentation. Despite these limitations, it appears that bullectomy results in subjective and objective improvement in patients with bullae occupying ≥30% (preferably ≥50%) of the hemithorax, with evidence of compressed lung tissue underlying the bullae and otherwise relatively preserved underlying lung function.

**Lung Volume Reduction Surgery**

The resection of giant bullae for the purpose of improving the function of underlying compressed lung is an accepted form of surgery for emphysema. Individuals with diffuse emphysema were generally thought to be poor candidates for resection surgery. However, nearly 50 years ago Brantigan and his colleagues performed pioneering work in this field when they performed resection of lung tissue in 33 patients with more homogeneous emphysema, in an attempt to reduce dyspnea and improve exercise capacity. Their procedure consisted of a unilateral thoracotomy with resection of 20–30% of the most diseased-appearing portion of the lung, coupled with lung denervation, with a radical hilar stripping. This was followed by the same procedure on the contralateral lung once the patient recovered. Brantigan hypothesized that removal of a portion of the emphysematous lung would increase radial traction on the airways, improve expiratory flow, and improve the mechanical function of the respiratory system, and thereby reduce symptoms. He documented subjective improvement in the majority of his patients, but there were no objective data in the form of physiologic measurement to substantiate the results. However, the procedure never gained widespread acceptance, perhaps because of the surgical mortality rate (16%) reported in Brantigan’s initial series.

In the early 1990s reports were published of lung volume reduction surgery (LVRS) conducted via video-assisted thoracoscopy with carbon dioxide laser or yttrium-aluminum-garnet laser. Large numbers of patients were reported, but incomplete follow-up made objective evaluation of the data very difficult. Lung volume reduction surgery in patients with diffuse emphysema gained a great deal of momentum in 1994, when Cooper et al presented their findings on 20 patients who had undergone bilateral LVRS via median sternotomy, with resection of 20–30% of each lung. Their patients showed significant increases in FEV₁ (mean increase 82%) and forced vital capacity (mean increase 27%). Mean total lung capacity and residual volume decreased by 22% and 39%, respectively, and Pao₂ increased by 6 mm Hg. There was a significant decrease in the number of patients using oxygen postoperatively. Six-minute walk distances were improved, as was quality of life indicators. A great deal of attention was devoted to these findings in the lay press, and with increasing public demand, numerous centers began performing the surgery. Results differed among the techniques and surgical centers, and a number of ethical and scientific discussions ensued as to whether a prospective, randomized, controlled trial was needed to evaluate LVRS. In December of 1995 Medicare, the primary payer for most LVRS, ceased paying for the procedure until such a trial was undertaken. That trial, recently completed, was the National Emphysema Treatment Trial (NETT). The following discussion will focus on results from the NETT, which is the largest randomized, controlled trial of LVRS undertaken to date and has by far the longest follow-up.

**National Emphysema Treatment Trial**

The NETT is a randomized, controlled trial of maximal medical therapy, including pulmonary rehabilitation versus the same therapy plus LVRS. The study was undertaken because of disagreement in the medical community as to the risks, benefits, and long-term outcomes of LVRS. The NETT’s primary end points were mortality and exercise capacity measured with a maximal cycle ergometer exercise test. Secondary end points included quality of life, pulmonary function, 6-min walk distance. The investigators also attempted to determine predictors for both positive and negative outcomes following surgery. The
NETT represents a unique cooperation between several government agencies, including the National Heart Lung and Blood Institute, the Centers for Medicare and Medicaid Services (CMS), and the Agency for Healthcare Research and Quality. The study was designed over a 1-year period in 1997 and the first patients were randomized in 1998. The study involved 17 centers across the United States, a coordinating center at Johns Hopkins School of Medicine, and a data-safety monitoring board that frequently assessed outcome data, looking for significantly positive or negative results that might result in early study termination. The study was completed in December 2002 and results were published recently. Of the 3,777 patients evaluated for entry into the trial, 1,218 were enrolled: 610 in the medical arm of the study and 608 into the surgical arm. At selected centers patients were further randomized to receive LVRS via either video-assisted thoracotomy or median sternotomy. Results from the latter comparison are not yet available.

Prior to completion of the NETT, the data-safety monitoring board identified a subset of patients (high-risk group) who had a very high mortality rate and little likelihood of benefiting from LVRS. Patients with an FEV₁ < 20% of predicted and either a low diffusion capacity for carbon monoxide (< 20% of predicted) or homogeneous emphysema on CT had a 30-day mortality rate of 16%. High-risk subjects were excluded from further randomization. Excluding the high-risk group, there was no difference in mortality between the medical and surgical groups at a mean of 29 months of follow-up. The surgical group patients, however, were more likely to have improved exercise performance and quality of life. Further analysis of the results (using prognostic factors that were identified in large part prior to the initiation of the trial and before full analysis of the data) revealed 2 factors that predicted different responses to LVRS: (1) upper-lobe (versus non-upper-lobe) distribution of emphysema (identified with predetermined criteria by radiologists), and (2) low (versus high) exercise capacity. Exercise capacity was determined after initial pulmonary rehabilitation. Low exercise capacity was < 25 watts for women and < 40 watts for men. Figure 1 shows the overall results of the study, including these 4 subgroups and their responses to LVRS.

In summary, the NETT has identified 1 group of patients with whom LVRS has a high likelihood of benefiting mortality, quality of life, and exercise (upper-lobe disease/low exercise capacity), 2 groups that have a higher likelihood of mortality following LVRS and little likelihood of quality of life or exercise improvement (high-risk group and non-upper-lobe disease/high exercise capacity), and 2 groups that have little likelihood of survival benefit but a significant chance of improved quality of life and exercise capacity (upper-lobe disease/high exercise capacity and non-upper-lobe disease/low exercise capacity). Currently the CMS is reviewing these data and intends to produce a coverage decision for LVRS soon.

Alongside the primary outcome trial, a cost-effectiveness trial was performed that utilized costs determined from CMS billing. Quality of life was measured using the Quality of Well-Being Scale, and cost-effectiveness was calculated in quality-adjusted life years. Overall, the procedure was relatively expensive, with a cost per quality-adjusted life year of $190,000. Table 2 compares the cost per quality-adjusted life year with LVRS and other cardiothoracic surgeries.
**Bronchoscopic Lung-Volume-Reduction Surgery**

Recently, because of the clear morbidity and mortality of lung-volume-reduction surgery, investigation has been undertaken to establish the feasibility of bronchoscopic lung-volume-reduction surgery. In this procedure agents or devices that block segmental or subsegmental bronchi are placed in the airway. In theory, lung tissue distal to the endobronchial blockade collapses because air is being removed due to diffusion of gas from alveoli into the pulmonary capillary circulation and cannot be re-freshed. Initial studies in animals show that this is possible, and that in approximately 50–60% of the bronchoscopically obstructed airways, collapse and volume reduction is seen (Fig. 2). Some improvement in spirometry values has also been seen. Reported complications in these patients were pneumothoraces in two of 8 patients. The future of this less invasive procedure remains to be determined.

**Lung Transplantation**

The first human single-lung transplant for advanced emphysema was performed in 1970. It was not until the late 1980s that more widespread attempts at lung transplantation were undertaken. Currently COPD is the most common indication for lung transplantation.

Individuals with COPD who are candidates for lung transplantation are those who are predicted to have a survival of ≤ 2 years. Natural history data for COPD are imprecise, but generally accepted criteria include FEV₁ ≤ 25–30% of predicted or when there is a rapid decline in lung function, substantial hypoxemia, hypercapnia, and secondary pulmonary hypertension despite maximal medical therapy. Table 3 shows generally accepted inclusion and exclusion criteria for lung transplantation. Candidates for single-lung transplant should be < 65 years old and for double-lung transplant < 60 years old. The candidate should be free of other important co-morbidities. Optimal candidates should be motivated, have adequate social support to deal with the rigorous pre- and post-transplant activities, and have undergone a comprehensive preoperative pulmonary rehabilitation program. The patient’s preoperative weight should ideally be between 70 and 130% of predicted, and pre-transplant osteoporosis (a common finding among COPD patients) must be aggressively corrected to reduce the risk of postoperative fractures. Patients who are mechanically ventilated do poorly and are generally not considered candidates for lung transplantation. Candidacy for those who have undergone previous thoracic surgeries must be reviewed on a case-by-case basis. Previous talc instillation or pleurectomy are relative contraindications because of the risk of operative bleeding. Oral steroid therapy prior to transplant should be no greater than the equivalent of 20 mg of prednisone daily, as greater amounts impair postoperative healing.

Both unilateral and bilateral transplantation are possible for COPD patients. Exercise functional capacity after transplantation is not significantly different between those who undergo unilateral versus bilateral lung transplantation.

![Fig. 2. Computed tomograms of a patient who underwent bronchoscopic lung-volume-reduction surgery to the right upper lobe. A: Before surgery. B: One week after surgery. C: Four weeks after surgery. Black arrows point to major fissure. White arrows point to areas of collapse and volume reduction. (From Reference 41, with permission.)](image-url)
Unilateral transplantation has been the preferred procedure because it allows for 2 recipients from a single donor. However, more recent data suggest that there may be a reduced incidence of primary graft failure and perhaps better overall outcomes after bilateral transplantation in younger emphysema patients. Patients with COPD and associated purulent lung disease (bronchiectasis or marked daily sputum production) must undergo bilateral transplantation because of the risk of infection of the allograft by secretions from the native lung. Unilateral transplantation is a simpler procedure, performed via lateral thoracotomy incision. The bilateral procedure is performed either via median sternotomy or via a subcostal “clam shell” incision. About 20% of patients undergoing bilateral transplantation will require cardiopulmonary bypass.

Consideration of benefits of lung transplantation requires a careful assessment of the risks of this major surgery as well as complications of post-transplant immunosuppression and rejection versus the potential for dramatic gains in pulmonary function.

The survival rate for patients undergoing lung transplantation for COPD appears to be somewhat better than for patients with other lung diseases. Reports of survival differ, but it appears that 1-year survival is approximately 90%, 2-year survival 65–90%, and 5-year survival is as low as 41–53%. Most early deaths following lung transplant are related to infectious processes. Late mortality is related to obliterative bronchiolitis, a process thought to be a form of chronic rejection. Whether lung transplantation provides a survival benefit to COPD patients remains unclear.

In summary, it appears that lung transplantation can provide symptomatic and functional improvement for those with severe emphysema who qualify and are motivated to undergo this difficult procedure. Whether lung transplantation offers a survival benefit remains unclear.

Lung Transplantation Versus Lung Volume Reduction Surgery

Lung transplantation and LVRS are procedures that may be used in very similar patients. The relationship between the 2 procedures and the reasons for selecting one over the other are very important questions and are being carefully assessed with the recently released data from the NETT. Schulman has quite reasonably pointed out that there are essentially 5 ways in which LVRS and lung transplantation...
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Table 4. A Proposed Algorithm for Selecting Patients for LVRS Versus Lung Transplantation in COPD Patients

<table>
<thead>
<tr>
<th>Lung Transplantation</th>
<th>LVRS</th>
<th>LVRS or Lung Transplantation, or LVRS Followed by Lung Transplantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purulent obstructive disease</td>
<td>Age &gt; 65 years with upper-lobe emphysema and low exercise capacity</td>
<td>Age &lt; 65 years and meets criteria for both lung transplantation and LVRS</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>Age &gt; 65 years with upper-lobe disease and high exercise capacity</td>
<td></td>
</tr>
<tr>
<td>&gt; 1/4 cup phlegm/d</td>
<td>Age &gt; 65 years with non-upper-lobe disease and low exercise capacity</td>
<td></td>
</tr>
<tr>
<td>Associated pulmonary-artery hypertension and/or right heart failure</td>
<td>Age &lt; 65 years with FEV₁ 30–45% of predicted but disabling symptoms despite maximal medical therapy</td>
<td></td>
</tr>
<tr>
<td>Absence of hyperinflation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TLC &lt; 100% of predicted or RV &lt; 150% of predicted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV₁ &lt; 20% of predicted with either homogeneous emphysema or DLCO &lt; 20% of predicted (NETT high-risk subgroup)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-upper-lobe emphysema with low exercise capacity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaCO₂ &gt; 55 mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaO₂ &lt; 50 mm Hg</td>
<td></td>
<td></td>
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<tr>
<td>6-minute walk distance &lt; 300 m</td>
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</tbody>
</table>

LVRS = lung-volume-reduction surgery
COPD = chronic obstructive pulmonary disease
TLC = total lung capacity
RV = residual volume
FEV₁ = forced expiratory volume in the first second
DLCO = diffusing capacity of the lung for carbon monoxide
NETT = National Emphysema Treatment Trial

Summary

Surgical procedures for COPD have been tested since the early 1900s. Unfortunately, most of them were found not to benefit patients. Lung transplantation has been widely available for over a decade and is a generally accepted treatment for patients with very advanced COPD and who are expected to survive less than 2 years. LVRS now also appears to be an effective therapy for patients with emphysema. Recent results from the NETT have delineated patients for whom LVRS may be more and less effective. Newer, less invasive techniques for LVRS are being developed, and results from trials of these therapies should be available within the next several years.

REFERENCES


Discussion

Fahy: Besides oxygen and surgery, pulmonary rehabilitation also improves survival.

Hansen-Flaschen: A little perspective here, Josh. We were severely criticized for pursuing this research [NETT] as a randomized trial and for being very inclusive with regard to exclusion and inclusion criteria. With the perspective of results and a little passage of time, do you think we did the right thing?

REFERENCE


Benditt: That’s a very good question. One thing I learned is that if you are inclusive in a randomized controlled trial, and you’re going to try to do subgroup analysis, you are setting yourself up for criticism on the first day the data are released, because you are doing post hoc analysis.

If, on the other hand, you use very narrow criteria that are likely to result in a positive outcome, you haven’t really contributed much to the knowledge about the procedure. If I step back and say, “I really want to help patients here and I know who’s going to do well and who’s going to do poorly,” I think being more inclusive is better; that is my view as a clinician. The journal reviewers were quite critical about the subgroup analysis. They have a point, but they’re looking at it from a different perspective.

REFERENCE

1. [The OBEST study has not been published yet, but a description of the study is available at http://www.ctsnet.org/doc/2375.]

Benditt: I know OBEST combined their data with a similar study that was going on in Canada. I have not seen the results yet, but I know it’s somewhere in process. There were 2 other, shorter-term randomized trials: one by [Gerald] Criner and one by Duncan Geddes, in London. The OBEST trial is longer, although it also allowed patients to cross over earlier on. That report should be published shortly.

REFERENCES


Stoller: There was another randomized trial of LVRS, the Overholt-Blue Cross Emphysema Surgery Trial (OBEST), which was an interesting partnership between private insurance companies and academic medicine. Although I was involved with it early on, I had to opt out because of my subsequent involvement in NETT, and I lost track of OBEST’s status. I wonder if you know about it?

Stoller: Say something about LVRS in alpha-1 antitrypsin (AAT) deficiency. I’m aware of 2 smaller studies and I know this is being analyzed.
**Benditt:** Yes it is. There are data. In the NETT it was a very small fraction of patients who had AAT deficiency, so I’m not sure we’re going to be able to say a lot about AAT deficiency. But most of the AAT deficiency patients did not fall into the upper-lobedisease group, so they might fall into one of the 2 groups that had improvement in exercise and quality of life but not survival, but I’m not sure of that because I haven’t seen the data. A number of groups have reported that AAT deficiency patients don’t do well, but I can’t tell you from our data yet. That will certainly be looked at.

**Stoller:** As you set the stage for bronchoscopic LVRS, what are your thoughts with regard to the design challenges that John [Hansen-Flaschen] alluded to about randomized trials. Should the comparator for bronchoscopic LVRS be surgical LVRS or one of the emerging techniques such as Ed Ingenito’s fibrin glue, or plugs, or one of the other approaches? Or should it simply be optimal medical therapy?

**REFERENCE**


**Benditt:** I believe, looking at the history of the Food and Drug Administra-tion, which has to approve devices like those that would be used, that they will compare it with the existing ac-cepted technology. I don’t think they will require a placebo control or non-treatment control. I’m not sure about that, but it’s my impression that these novel techniques would be compared to surgery, not to no treatment. I haven’t heard any final decisions on that. I do know there was a meeting of a number of these groups and compa-nies looking at this with the Food and Drug Administration, but I don’t know the outcome of that.

**Hill:** This is one decision that I don’t envy the Centers for Medicare and Medicaid Services having to make, because almost any decision they make is going to be criticized and will raise a lot of other issues, such as who should be doing the surgery. The NETT cen-ters were specialized study centers se-l ected because of their expertise. Do you think Medicare is going to cover LVRS everywhere, or are they going to restrict it to certain centers? Also, how are the criteria going to be spelled out for widespread use? Are we going to have specific criteria for upper-lobe predominance and low-exercise ca-pacity? How are these determinations going to be made?

**Benditt:** I would not like to be on the panel that’s looking at this, because, for one, exercise ability, if it were a patient-selection criterion, would be very difficult. You can imagine that somebody might dodge the system, saying, “Hmm, yeah, that was about 19 watts, I think. That looks good.” And get the patient to exercise less well than he could, since that’s what the patient needs to qualify. I would have a hard time including an exercise measure as a selection crite-rion.

In the past Medicare has not gotten into choosing patients, but has instead let the physician decide about surger-ies. I don’t know if that will be the case. Regarding who will do the sur-gery, you could use the model of lung transplantation, for which they use specialized centers, or you could just let it get out there. There’s a big problem because a lot of senators from small states that do not have such centers want this kind of thing for their pa-tients and they don’t want them to have to travel to Seattle from eastern Montan-a. So there’s a lot of pressure to get community hospitals doing this. I think there’s a lot of arm wrestling going on right now between very powerful people. I will be fascinated to see what they come up with. I cannot predict in any way what it will be. I have no idea.

**Enright:** My question is for Neil MacIntyre, to get him warmed up for his upcoming talk. This is the first time that diffusing capacity [of the lung for carbon monoxide, $D_{LCO}$] measure-ments have become very important, and, unfortunately, down in the range of 20% of predicted, where the noise of measurement is equal to the signal. I haven’t seen the data from the LVRS trial yet, but if patients’ predicted $D_{LCO}$ is about 30 mL/min/mm Hg, then 20% is around 6 mL/min/mm Hg. That’s around the noise of measurement from visit-to-visit. Can pulmonary function testing in-struments accurately measure $D_{LCO}$ below 6 mL/mm/mm Hg.

**MacIntyre:** I think you bring up what Josh [Benditt] was talking about—the risk of coming up with a cut point, be it an exercise test, $D_{LCO}$ or an FEV₁. You could make the same argument there. It raises the issue of how on one day the patient is at 21% of predicted and he can get LVRS and the next day he’s at 19% of predicted and he can’t.

I sort of agree with Josh; if I were Medicare, I’m not sure I would put any number on it. Instead I would de-scribe it as “severe limitations in air-flow and severe $D_{LCO}$ defect” but not put specific numbers on those limi-tations and defects. I think that would put it in the hands of the physician and the patient to make a decision to-gether, rather than drawing a proverbial “line in the sand.” This is an issue for many other procedures too.

**Enright:** I think we should pressure the medical equipment community to improve their $D_{LCO}$ accuracy for pa-tients with very low $D_{LCO}$ values.

**MacIntyre:** Well, you’re on the American Thoracic Society profi-ciency committee, and that has been a
Gay: I’ll just make a prediction about the Centers for Medicare and Medicaid Services’ decision about LVRS coverage criteria. Their basic, boilerplate approach is, “We don’t have to get it right for everybody; if we get it right 90% of the time, we did very well.” So they might decide on thresholds for exercise capacity and the like, with a standard deviation that gets 90% of the people included in the NETT study. That would be my guess.

Pierson: Although it wasn’t explicitly stated, I think the NETT did a wonderful service for pulmonary rehab. By requiring all participating centers to put their patients through rehab, my understanding is that it caused some of those centers to get involved with rehab for the very first time ever. And, as was mentioned yesterday, there were some patients who dropped out of the study because they felt so much improved after their rehab that they didn’t want to go on with the surgery. Thus I think that if nothing else, the NETT study has raised awareness of the value of rehab to patients in ways that probably couldn’t have been done before.

My question (another comment, actually) goes back to your very first slide, which listed the different surgical procedures that have been done for COPD over the years. There’s another one that you didn’t include on the list: glomectomy, or bilateral carotid body resection, for the relief of dyspnea. Originally introduced almost 50 years ago to treat severe asthma, this procedure was subsequently popularized by Benjamin Winter and others as a therapy for dyspnea in COPD. There was a lot of controversy about this operation during the 1970s, because glomectomy reduced the patients’ hypoxic drive and there was concern that patients who had undergone the procedure would die of hypoxia during exacerbations. It was eventually abandoned, although controversy continued in the literature until the 1990s.

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1. Overholt RH. Resection of carotid body (cervical glomectomy) for asthma. JAMA. 1962;180:809–812.

Benditt: Yes, there have been many surgeries, such as glomectomy, thrown on the scrap heap of COPD therapy. They did a lot of surgeries related to the autonomic nervous system’s sensing of oxygen; even for asthma they were doing similar surgeries. I think the fact that the patients felt symptom relief points to the importance of having a control arm in those kinds of trials, and also that it’s hard to prevent a placebo effect in surgical trials, which is why, in part, we looked at mortality, which obviously could not be affected by the placebo effect.