Should buttresses and sealants be used to manage pulmonary parenchymal air leaks?

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Although the vast majority of air leaks after pulmonary resection are of no major significance and resolve spontaneously after a day or so, some air leaks will persist. These prolonged air leaks, and the initial air leaks that lead to them, have drawn substantial attention for a variety of reasons. First, air leaks are associated with (and may cause) other cardiopulmonary complications, thereby increasing the overall morbidity associated with pulmonary resection. Second, even in the absence of associated complications, an air leak that lasts after a patient is otherwise ready for discharge may prolong hospital stay, creating a substantial economic impact.

Both industry and independent investigators have proposed a variety of solutions to the problem of air leaks. We and other coauthors recently reviewed the postoperative techniques that might be used to reduce the duration of air leaks and made suggestions regarding the use of these techniques.¹ A number of equally controversial intraoperative products and maneuvers have been advocated to prevent or ameliorate air leaks. These potential solutions include a variety of glues and sealants designed to be applied to areas of leakage, buttressing materials for staple lines, and finally some traditional surgical techniques. Multiple studies, including quite a few randomized clinical trials, have been published in recent years to evaluate these products and techniques.

Several issues, however, complicate the thought process when deciding whether to use these products and techniques. First, the data that have accumulated regarding their effectiveness are often conflicting. Results that statistically favor the use of a product may not demonstrate a sufficient magnitude of benefit for clinical relevance. Second, the data suffer from broader problems, such as the frequent failure to report on the outcome variable of most concern to surgeons—the incidence of prolonged or complicated air leak—and the general failure to focus study on high-risk groups (eg, patients with emphysema). Finally, although

commercial products to manage air leak add substantially to the cost of an operation, few studies have reported on their cost-effectiveness. Certainly, use of an expensive product with marginal evidence of its effectiveness is in no one's best interest.

As a result of the controversy in this area, we embarked on a review of the available literature. We sought to identify, read, and evaluate all publications that address the 2 most commonly used techniques in intraoperative air leak management: sealants and buttresses. This commentary and our management suggestions (Table 1) are based on that review and, to a lesser extent, on our personal experience.

We specifically focus here on air leaks arising from the lung parenchyma—not bronchial dehiscence, for which management is generally quite different. We define air leak as any leakage of air from the lung that is detected as a result of bubbles in a chest drainage system, progressive subcutaneous emphysema, or an expanding pneumothorax.

BACKGROUND

Clinical Impact of Air Leaks

Several studies have demonstrated an association between postoperative air leak and increased complications after lobectomy. Brunelli and colleagues² found that patients with prolonged air leak had a dramatically greater rate of empyema. Varela and associates³ found that prolonged air leak was associated with greater pulmonary morbidity, including atelectasis, pneumonia, and empyema. Okereke and colleagues⁴ found that any air leak at all was associated with more complications, as did DeCamp and coworkers⁵ for patients after lung volume reduction surgery (LVRS).

It has also been clearly demonstrated in multiple studies that air leak increases both hospital stay and cost. Every study in the routine lung resection population reporting hospital stay or cost as a function of air leak has found a clear association.^{2-4,6,7} These studies have found that air leak prolongs hospital stay by between 4 and 13.1 days. In a study of post-LVRS patients,⁵ mean hospital stay with air leak was 11.8 days, versus 7.6 days without air leak ($P = .0005$).

Preoperative Risk Factors for Air Leaks

The most consistently identified risk factor for air leak is chronic obstructive pulmonary disease (COPD). Many pulmonary function test parameters that reflect severity of COPD are associated with air leak, including reduced forced expiratory volume in 1 second (FEV₁),^{6,8,9} both FEV₁ and ratio of FEV₁ to forced vital capacity less than 70%.¹⁰ and ratio of FEV₁ to forced vital capacity less than 50%.¹¹

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Abbreviations and Acronyms

COPD = chronic obstructive pulmonary disease

FEV₁ = forced expiratory volume in 1 second

LVRS = lung volume reduction surgery

Patients undergoing LVRS for severe emphysema are especially susceptible to air leak,⁵ as are those undergoing other types of resection with FEV₁ less than 35% of the predicted value.¹² It is our opinion that patients with COPD with predominant emphysema (bullous disease, fragile lung tissue) are at greater risk for prolonged air leak than are those with predominant chronic bronchitis.

Other risk factors convincingly associated with air leak include the presence of adhesions,⁸ upper lobectomy and bilobectomy versus other lobectomies,⁸ lobectomy versus lesser resections,⁹ and steroid use greater than 10 mg daily for longer than 1 month.⁹ The incidence of air leak is likely surgeon dependent,⁴ and larger air leaks clearly carry a greater risk of becoming prolonged air leaks.⁹ In the post-LVRS population,⁵ risk factors for air leaks were found to be similar to those after standard pulmonary resection, including severity of emphysema, adhesions, and steroid use (inhaled). In the quite different population of intubated patients undergoing lung biopsy for adult respiratory distress syndrome, the only multivariate predictor of air leak was peak airway pressure. The risk of air leak was reduced by 42% for every 5-cm H₂O reduction in peak airway pressure.¹³

THE EVIDENCE FOR STAPLE LINE BUTTRESSES

In the belief that many air leaks occur at and immediately adjacent to the holes created by staples in lung tissue, Cooper and colleagues¹⁴ first reported the use of bovine pericardium to buttress staple lines during LVRS. Subsequently, this technique has been extended to relatively less emphysematous patients undergoing pulmonary resection.¹⁵ Several other materials have also been used as buttresses, including parietal pleura, polydioxane ribbon, polytetrafluoroethylene felt, expanded polytetrafluoroethylene, and collagen patches. Nonabsorbable materials carry the risk of inducing granulomatous inflammation and bacterial colonization, which has led to rare cases of metalloptysis, largely with bovine pericardium.¹⁶⁻¹⁸

Four randomized studies have compared buttressed to nonbuttressed stapling: 2 in the post-LVRS setting^{19,20} and 2 among unselected patients after lobectomy.^{21,22} We briefly review these reports.

Pulmonary Resection in Patients Without Severe Emphysema

In studies of patients undergoing routine lobectomy (FEV₁ 70%–80% predicted), Venuta and associates²²

(n = 30) demonstrated decreased air leak and shorter hospital stay with pericardial buttressing, whereas Miller and co-workers²¹ (n = 80) demonstrated reduced duration of air leak ($P = .02$) but no significant difference in hospital stay ($P = .24$). The trial of Venuta and associates²² was very small and lacked the ideal control group with unbuttressed gastrointestinal anastomosis stapler use. Although both studies implied that buttressing slightly reduced duration of air leak, the larger and better-controlled trial did not identify a clear-cut benefit of in terms of either hospital stay or chest tube duration. Buttressing staple lines does add as much as several hundred dollars to procedural costs. In light of the increased costs and unclear benefits, we believe that buttressing staple lines is not recommended for the routine case of a patient with less than moderate emphysema.

Pulmonary Resection in Patients With Severe Emphysema

Management of air leak is particularly challenging in patients after LVRS. Although analysis of the National Emphysema Treatment Trial data identified no benefit to buttressing staple lines,⁵ this analysis was not randomized on the basis of buttressing. Other groups, with randomized study designs, have observed a benefit to reinforcing the staple line in patients undergoing LVRS for emphysema.

Two randomized trials in this high-risk population have demonstrated a benefit from buttressing staple lines with bovine pericardium.^{19,20} A 2-center study by Hazelrigg and colleagues¹⁹ involving 123 patients undergoing unilateral thoroscopic LVRS showed significant decreases both in the duration of postoperative air leak, chest drainage and in hospital stay.¹⁹ Patients with buttressing had chest drains removed 2.5 days sooner and were discharged from the hospital 2.8 days sooner. Total hospital charges were similar, because costs for the pericardial sleeves offset the savings in hospital time.

A 3-center study by Stammberger and associates²⁰ evaluating bilateral thoroscopic LVRS (n = 65) showed significant decreases in the incidence of initial air leak (77% vs 39%), median duration of air leak (0 vs 4 days, $P < .001$), and median drainage time (5 vs 7.5 days, $P = .045$). Hospital stay was slightly but not statistically significantly shorter in the group with buttressing (9.5 vs 12.0 days, $P = .14$).

In conclusion, the evidence from limited randomized studies suggests that using buttresses on staple lines in patients with emphysema undergoing nonanatomic pulmonary resections, such as LVRS, reduces both the incidence and the duration of air leak. This permits the earlier removal of chest drains and likely shortens hospital stay. It is not clear, however, that complicated, prolonged air leaks are reduced by these buttresses, and no cost benefit of using buttressed staple lines has been demonstrated, even in this high-risk population. A decrease in the costs of the buttresses could ultimately provide a cost advantage.

TABLE 1. Suggestions for intraoperative use of buttresses and sealants

Class	Recommendation	Level of evidence
Use of staple line buttresses		
I	In performing lung volume reduction surgery, buttressing staple lines is recommended to prevent postoperative air leaks.	B
Ila	In performing anatomic pulmonary resections in patients with severe emphysema (forced expiratory volume in 1 second $\leq 50\%$ predicted or gross parenchymal destruction), it is reasonable to buttress staple lines, but the benefit remains unproven.	B
III	In performing pulmonary resection in patients with less than severe emphysema, buttressing staple lines to prevent postoperative air leaks is not well established and, given the increased costs of therapy, should be avoided.	B
Use of topical sealants		
Iib	Although incompletely evaluated in high-risk subgroups, the use of topical sealants has not consistently translated into a shorter chest tube duration or stay. Because the overall benefit of these materials has not been demonstrated, they should not be used on a routine basis.	A

Classification of recommendations and quality of evidence are according to Sackett and colleagues⁴³ and the American College of Cardiology and American Heart Association Task Force for Practice Guidelines.⁴⁴

There are not sufficient data to provide a strong recommendation regarding the use of staple line buttresses when performing *anatomic* lobectomy or segmentectomy, even in patients with severe emphysema. We believe, however, that the benefit of buttressing staple lines in patients with severe emphysema likely translates to situations in which a surgeon is stapling incomplete interlobar fissures or intersegmental planes during lobectomy or segmentectomy.

THE EVIDENCE FOR TOPICAL SEALANTS

A variety of sealants have been developed in an effort to solve the problem of air leak. These topical sealants are designed to be applied over staple lines and other lung surfaces with violation of the visceral pleura. Surgical sealants appear, from the many studies that have described their application, to be successful in reducing the percentage of patients with a visible air leak at the conclusion of an operation. Studies have not, however, consistently shown that sealants substantially reduce (1) duration of air leak, (2) time to removal of chest drains, or (3) hospital stay (Table 2).

Belda-Sanchís and colleagues²³ and Tambiah and colleagues²⁴ performed comprehensive reviews of the literature

evaluating sealants during pulmonary resection in patients with lung cancer. Typically, standard closure techniques plus a sealant were compared with the same intervention without a sealant. The 2010 report from Belda-Sanchís and colleagues²³ identified 12 randomized, controlled trials with a total of 1097 patients.²⁵⁻³⁶ The 2007 review by Tambiah and colleagues²⁴ added 1 more study to that analysis.³⁷ Several additional studies³⁸⁻⁴² have been published in this area since these 2 reviews.

These studies have described a variety of types of sealants, ranging from fibrin- and thrombin-based products to synthetic polymers and from sprays to gelatinous solutions to moistened patches. There is a broad range in quality and methodology among these trials. For example, in most cases there was no standard definition of air leak, and no attempt was made to quantify the *degree* of air leak in the perioperative period. In 3 trials, patients were randomly assigned to treatment after checking for the presence of intraoperative air leak, whereas in 9 trials glue was applied regardless of the presence of air leak. These studies also present few data that address costs.

Although 11 trials found that a significantly lower percentage of patients had air leak at the conclusion of the operation when sealants were used,^{25-27,29-33,36,37,40} most of these trials did not demonstrate any reduction in the time of chest drainage. The limiting factor in removing chest drains in these patients was often the volume of fluid drainage, rather than the presence of air leak. There were 4 exceptions to this general result.^{27,37,41,42} Similarly, although there was a trend in most of the publications toward a shortened hospital stay in the sealant group, only 3 studies demonstrate a significant reduction in hospital stay^{25,37,42}: 1 with a polymeric sealant (U.S. Patent No. 5583114),²⁵ 1 with TachoSil (Nycomed International Management GmbH, Zurich, Switzerland),⁴² and 1 with BioGlue (CryoLife Inc, Kennesaw, Ga).³⁷

Among patients with a postoperative air leak, regardless of whether a surgical sealant had been used, there were reductions in mean air leak duration in 4 of the trials.^{25,27,32,40} Interestingly, in Fabian and associates' trial,²⁷ the incidence of *prolonged* air leak heavily favored sealants (2% vs 16%, $P = .015$). This important outcome measure was not, however, reported for most trials.

None of the previously mentioned randomized studies included subgroup analysis to evaluate the effectiveness of sealants for air leaks of varying sizes. Similarly, none of the studies were targeted at the patients at highest risk for complicated or prolonged air leaks—those with advanced emphysema—nor did any report results for subgroups of patients with substantial emphysema. There are therefore insufficient data available to determine whether there are specific subgroups of patients who would more clearly benefit from the use of sealants. One small, randomized study of sealants in patients with severe emphysema—but in the

TABLE 2. Randomized, controlled trials evaluating surgical sealants for intraoperative air leaks

Reference	Sealant	No.	Comparisons (treatment vs control)			
			With postoperative air leaks (%)	Mean air leak duration (d)	Mean chest drain duration (d)	Mean hospital stay (d)
Allen et al ²⁵	U.S. Patent No. 5583114 (novel polymeric sealant)	148	77% vs 16%	[2 vs 2]	[6.8 vs 6.2]	6 vs 7
Belboul et al ²⁶	Vivostat (autologous fibrin sealant)	40	20% vs 60%	NA	[1 vs 3]	[4 vs 4.5]
Fabian et al ²⁷	Fibrin glue	100	34% vs 68%	1.1 vs 3.1	3.5 vs 5	[4.6 vs 4.9]
Fleisher et al ²⁸	Fibrin glue	28	NA	[3.2 vs 3.3]	[6.1 vs 5.9]	[9.8 vs 11.5]
Lang et al ²⁹	TachoComb (fleece-bound sealant)	189	34% vs 37%	[1.7 vs 2]	NA	NA
Macchiarini et al ³⁰	Focal, Inc (fibrin glue)	26	0% vs 82%	[1.9 vs 2.4]	[6.1 vs 6.4]	[13 vs 14]
Moser et al ⁴¹	Vivostat (fibrin glue)	25 (bilateral)	NA	NA	2.8 vs 5.9	NA
Mouritzen et al ³¹	Fibrin glue	114	39% vs 66%	[4 vs 5]	[3 vs 4]	[9 vs 10]
Porte et al ³²	Advaseal (polymeric sealant)	120	Data not provided*	1.4 vs 2.6	NA	[9.2 vs 8.6]
Tansley et al ³⁷	BioGlue	52	53 vs 96%	1 vs 4	4 vs 5	6 vs 7
Wain et al ³³	Focal Seal (polyethylene glycol-based gel)	172	8% vs 71%	1.3 vs 2.2	[4.5 vs 5.2]	[7.4 vs 10.1]
Wong and Goldstraw ³⁴	Tisseal (fibrin glue)	66	NA	[5 vs 4]	[6 vs 6]	[8 vs 9]
Wurtz et al ³⁵	Fibrin glue	50	*	NA	NA	[11.4 vs 13]
Wurtz et al ³⁶	Fibrin glue	50	*	NA	NA	[9.9 vs 10.6]
Anegg et al ⁴²	Tachosil (fleece-bound sealing)	173	NA	Data not provided*	5.1 vs 6.3	6.2 vs 7.7
D'Andrilli et al ⁴⁰	Polymeric sealant	203	15% vs 41%	3.5 vs 4.2	NA	[5.7 vs 6.2]

Unbracketed values indicate significant difference ($P < .05$); bracketed values indicate difference not reaching significance. NA, Not available (not assessed or published). Vivostat is manufactured by Vivostat A/S, Allerød, Denmark; TachoComb is manufactured by Nycomed International Management GmbH, Zurich, Switzerland; Focal Inc, Lexington, Mass; Advaseal is manufactured by Ethicon Inc, Johnson & Johnson Medical, Somerville, NJ; BioGlue is manufactured by CryoLife Inc, Kennesaw, Ga; Focal Seal is manufactured by Focal Inc; Tisseal is manufactured by Baxter Healthcare Corp, Deerfield, Ill; and Tachosil is manufactured by Nycomed International Management GmbH. *Significant improvement reported (but raw data not provided) for treated group versus untreated group.

setting of LVRS—has been published. In this study of 25 patients undergoing bilateral thoracoscopic LVRS, autologous fibrin sealant was applied to the staple line on 1 side of the chest only.⁴¹ Both the incidence of prolonged air leak and mean duration of drainage were significantly reduced on the sealant side (4.5% and 2.8 days vs 31.8% and 5.9 days, respectively).

There have been recent reports that a particular type of sealant combined with electrocautery dissection of fissures may be superior to the use of stapler devices. A randomized trial of 60 patients with COPD ($FEV_1 \leq 65\%$) reported that collagen patches coated with human fibrinogen and thrombin (TachoSil) after electrocautery dissection reduced duration of chest tube drainage (3.5 vs 5.9 days, $P = .0021$) and hospital stay (5.9 vs 7.5 days, $P = .01$) relative to stapling.³⁹ In another study with 40 randomly assigned patients, there was a reduction in the duration of air leak in the electrocautery plus patch group (1.7 vs 4.5 days, $P = .003$). This relatively new concept of using electrocautery dissection plus sealants might even provide a cost benefit, because it would eliminate the significant costs associated with stapling devices.

To summarize the sealant data, most sealants appear to reduce the percentage of patients with a visible air leak present at the end of an operation. The vast majority of these sealants, however, do not appear to alter duration of air leak or

duration of chest tube drainage to a clinically significant degree (and, for the most part, not even to a statistically significant degree). Only 4 of 16 randomized studies showed significantly shortened hospital stays in the sealant group, and only 2 studies clearly showed the reduced air leak and chest tube durations that one might expect to result in this shortened hospital stay. Many of the studies have not report on whether the sealants reduced complicated or prolonged air leak, the outcome variable that is perhaps most important. Finally, only a single study of a liquid sealant applied the product to the group at highest risk, those with substantial emphysema. That study showed a benefit for its sealant (autologous fibrin), giving us a hint that perhaps sealants—like buttresses—might be appropriately applied to selected patients with substantial emphysema.

In light of these inconclusive results across sealant studies and the significantly increased costs that would be incurred by using sealants indiscriminately, it would seem appropriate to use sealants only very selectively at this point. Although our “gut feeling” is that patients with at least moderately severe emphysema undergoing lobectomy may well benefit from the use of sealants on large leaks, such a recommendation has not been securely established by the data.

There remains, then, a substantial need for randomized studies that either evaluate sealants in patients undergoing

lobectomy who have at least moderate emphysema or are large enough for stratification of results on the basis of degree of emphysema. Similarly, studies large enough for stratification on the basis of the size of the intraoperative air leak would represent substantial contributions, as would more studies that look at prolonged air leak as a primary outcome measure. The most recent data in support of managing incomplete fissures with cautery plus collagen fleece-bound sealants instead of staplers are promising, but the issue requires further study.

OTHER WELL-SUPPORTED TECHNIQUES

Although a full discussion is beyond the length limitations of this commentary, it must be mentioned that there are 2 traditional techniques of reducing air leaks that have support from prospective, randomized studies in the literature. These include creation of an apical pleural tent after upper lobectomy or upper bilobectomy (2 randomized trials with positive results)^{45,46} and creation of pneumoperitoneum after lower bilobectomy (1 randomized trial with positive results).⁴⁷ These techniques are safe and highly effective, and they have essentially zero cost. They are probably underutilized by surgeons.

CONCLUSIONS

The use of many of the intraoperative techniques that are available to prevent or reduce air leaks has been driven by aggressive marketing by industry of commercially available sealants and staple line buttresses. The appeal of these sealants and buttresses lies in their ease and speed of use. Their costs are sufficiently high, however, that they should be used only if they provide clear clinical benefits.

Buttresses have been shown in randomized trials to reduce the incidence and duration of air leak and to reduce the time that tube drainage is required in patients with severe emphysema undergoing nonanatomic resections. Although the data are not clear for patients with severe emphysema undergoing anatomic lobectomy and segmentectomy, we believe that it is reasonable to use staple-line buttresses in these patients as well.

With regard to liquid sealants, most studies have reported neither statistically nor clinically significant improvements in hospital stay or time to removal of chest tube. Although one might think it logical that sealants would demonstrate clearer benefits in patients with substantial emphysema, this may not be the case, and only a single small study (albeit with positive results) has looked at this subgroup of patients. Also needed are studies that are large enough for stratification on the basis of the size of the initial intraoperative air leaks, more studies that look at prolonged or complicated air leak as an outcome measure, and more studies that evaluate costs. We believe that on the basis of current data, sealants should not be used routinely, and hospitals and insurers may be justified in questioning their use on cost/benefit

grounds. The more traditional and relatively cost-free techniques—pleural tenting and pneumoperitoneum—are probably underutilized for high-risk patients.

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