Feasibility and safety of the airway bypass procedure for patients with emphysema

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Objective: We have proposed that direct passages created between pulmonary parenchyma and large airways (airway bypass) could take advantage of the extensive collateral ventilation present in emphysematous lungs to provide improvement in expiratory flow and respiratory mechanics. A critical step in the safe performance of these procedures is to create passages through the airway wall into lung parenchyma while avoiding injury to adjacent blood vessels.

Methods: The procedure consists of selection of a target site bronchoscopically, use of a Doppler catheter to detect and avoid peribronchial blood vessels, and creation of a passage through the airway wall with a cautery probe. To evaluate the safety of airway bypass, 10 patients were treated during prescheduled lobectomies for neoplasm. The procedure was done after thoracotomy and immediately before resection and was confined to airways in the lung identified for removal. Airway bypass was subsequently performed in 5 patients undergoing lung transplantation for emphysema just before lung excision to evaluate the procedure in emphysematous patients.

Results: Twenty-nine passages (1-5 per subject) were created in the patients undergoing lobectomy. Eighteen passages were created (3-4 per subject) in the patients undergoing transplantation. There were 2 instances of mild bleeding in the patients undergoing lobectomy and no bleeding in the patients undergoing transplantation. Both instances were treated with suction and topical application of epinephrine and resolved without incident.

Conclusion: The results of this study confirm that passages can be made safely through the airways of human subjects. These clinical results support further investigation of the efficacy of the airway bypass procedure in patients with emphysema.

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Collateral inspiration, later more appropriately defined as "collateral ventilation," was first observed by Van Allen and colleagues in 1930.[1] Collateral ventilation (ie, the ability of gas to move from one part of the lung to another through nonanatomic pathways) is present in the normal lung, but its importance in the distribution of ventilation is negligible because the resistance to air flow is higher in collateral channels than in the airway. Observations in postmortem emphysema-

tous human lungs[2] demonstrated, however, that the resistance to collateral air flow in the lungs of patients with emphysema is low in comparison with that in normal lungs. This finding was confirmed by Terry and coworkers[3] in emphysematous patients, and Macklem[4] noted that collateral ventilation not only improves our understanding of the pathophysiology of airway obstruction and gas distribution in the emphysematous lung but "may also have startling therapeutic implications."

Recently, a group of researchers from Washington University[5] has proposed that the creation of direct passages between the emphysematous pulmonary parenchyma and large airways (airway bypass) could take advantage of the extensive collateral ventilation present in emphysema to provide improvement in expiratory flow and respiratory mechanics. In an ex vivo study on 12 human emphysematous lungs, Lausberg and coworkers [5] demonstrated that the forced expiratory volume in 1 second increased from an average of 245 mL at baseline to an average of 447 mL after the creation of 3 passages and to an average of 666 mL after the creation of 5 passages.

These promising experimental results encourage further research to support investigation of the feasibility and safety of the airway bypass procedure in human subjects. A crucial step in the safe performance of this procedure is to create passages through the airway wall into the lung parenchyma while avoiding injury to adjacent blood vessels.

Methods

Our study was designed to evaluate the feasibility and safety of the creation of transbronchial passages (airway bypass) in human subjects. The study received approval from the institutional review board of both participating institutions. The airway bypass procedure was performed in airways in lungs to be removed after the chest was opened and full control of the pulmonary vessels and bronchus was obtained to prevent uncontrolled bleeding. Ten patients were selected among those scheduled for standard lobectomy for lung cancer and 5 among those undergoing double sequential lung transplantation for emphysema. Thirteen patients were men, and 2 were women (age range, 44-77 years; mean age, 63.5 years). After informed consent was obtained, the patients were anesthetized and intubated by means of an orotracheal tube, and the lung to be approached was obstructed with a bronchial blocker. After thoracotomy and preparation of the hilar elements to the lobe or lung to be resected, the bronchial blocker was deflated, and a 4.8-mm flexible bronchoscope with a 2.0-mm operating channel was advanced into the endotracheal tube. In the 5 patients undergoing transplantation, the 4.8-mm bronchoscope was introduced through a 41 double-lumen, left-sided endobronchial tube. The whole procedure was confined to the tissue identified for removal. A Doppler catheter (Broncus Technologies Inc) that permits detection and avoidance of peribronchial blood vessels was inserted into the operating channel of the bronchoscope, and a target site was selected by scanning the wall of the segmental or subsegmental bronchi Figure 1, *A*). Once the appropriate site was identified, the Doppler probe was withdrawn, and a radio frequency catheter (Broncus Technologies Inc) was advanced to create a passage through the bronchial wall into the lung parenchyma (airway bypass) (Figure 1, *B*). The radio frequency generator (Valley Lab Force FX) was set in the blend mode at 50 W. The same procedure was then similarly repeated as required. At the end of the airway bypass, the lung was reinflated underwater to check for parenchymal air leaks. Finally, the scheduled lobectomy or transplantation was carried out. No follow-up beyond surgical intervention was required for this study. Because accurate pathologic studies in previous animal experiments, including more than 100 transbronchial passages, showed no tissue damage, pathology was not carried out in this study (Figure 1).

Results

Twenty-nine airway bypasses (1-5 per lobe) were performed in the 10 patients undergoing lobectomy, and 18 airway bypasses were done (3-4 per lung) in the 5 patients undergoing transplantation (Tables 1 and 2). There were 2 instances of mild bleeding ($\leq$20 mL) in the patients undergoing lobectomy; one occurred in the right upper lobe and one in the right lower lobe. Both patients were treated with suction and topical application of epinephrine, and their symptoms resolved without any adverse effect on the tissue resection procedure. No bleeding occurred in patients undergoing transplantation. No sites of air leaks were detected. All patients tolerated the airway bypass well, and all lobectomy and transplant procedures proceeded as intended.

Discussion

Emphysema is defined as an irreversible increase in the size of air spaces distal to the terminal bronchioles.[6] This increase in size results from the destruction of pulmonary parenchyma (alveolar walls and interstitial tissue) and leads to a loss of elastic recoil and progressive dynamic hyperinflation of the lungs. Hyperinflation further decreases expiratory flow by compressing the small intraparenchymal airways and ultimately compromises respiratory mechanics, leading to respiratory failure. The results of lung volume reduction surgery demonstrate that the resection of areas of the lung in which hyperinflation is more severe yields an improvement in respiratory mechanics and increases expiratory flow in the residual lung.[7-9] On the basis of the concept of collateral ventilation, the group at Washington University[5] hypothesized that instead of resecting hyperinflated lung parenchyma, comparable results could be achieved by draining the air spaces, creating a direct passage between the lung and the airway. The concept of airway bypass was favorably applied in an experimental setting, in which a marked increase in forced expiratory volume in 1 second was observed.

Our study was designed as the first step in the clinical application of the airway bypass procedure. The first important point in carrying out this procedure is to safely create a passage connecting segmental or subsegmental

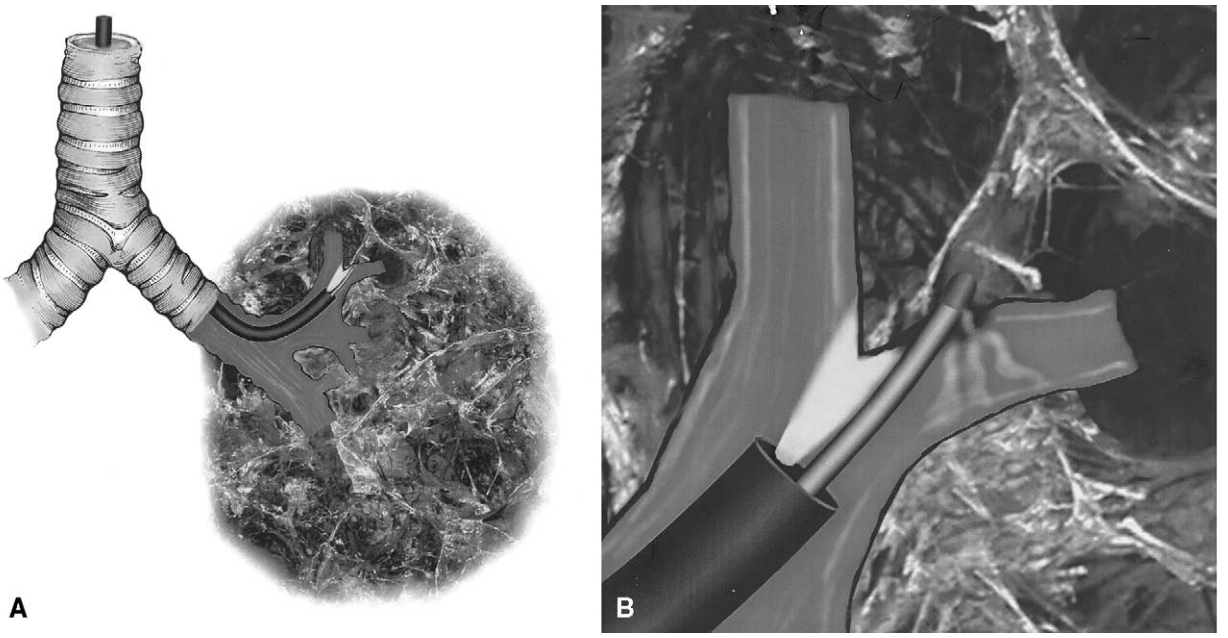

Figure 1. Airway bypass procedure. A, A Doppler catheter inserted bronchoscopically is used to scan the wall of a segmental bronchus. B, A passage between the bronchus and the pulmonary parenchyma is created with a cautery probe.

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TABLE 1. Airway bypass in patients undergoing lobectomy

Patient no.	Total no.	Lobe
1	2	LLL 1 LUL 1
2	2	RML 1 RLL 1*
3	1	RUL
4	4	LUL
5	3	RLL
6	4	RLL
7	3	RLL
8	4	RLL
9	1	RUL*
10	5	LUL

Mild bleeding is defined as less than 50 mL.
**LLL,* Left lower lobe; *LUL,* left upper lobe; *RML,* right middle lobe; *RLL,* right lower lobe; *RUL,* right upper lobe.

TABLE 2. Airway bypass in patients undergoing lung transplantation

Patient no.	Total no.	Lobe
1	3	LLL 1 LUL 1 Lingula 1
2	4	RUL 2 RLL 2
3	3	RUL 1 RLL 2
4	4	RUL 2 RLL 2
5	4	RUL 2 RLL 2

LLL, Left lower lobe; *LUL,* left upper lobe; *RUL,* right upper lobe; *RLL,* right lower lobe.

bronchi with the pulmonary parenchyma while avoiding injury to the peribronchial vessels. For this purpose, we have devised a Doppler catheter enabling detection of blood flow outside the bronchus by scanning the inner surface of the bronchial wall. This device was first used in experimental animals and proved effective in detecting pulmonary vessels. For use in human subjects, it is important that both the Doppler probe and cautery catheter can be introduced in the 2.0-mm operating channel of a 4.8-mm flexible bronchoscope, which can be easily manipulated through the endotracheal tube. The size of the bronchoscope was selected as a compromise between the width of the operating channel and the possibility to reach subsegmental bronchi, which are located more deeply in the pulmonary parenchyma and are less likely to be adjacent to pulmonary vessels. The mild bleeding seen in the 2 instances was likely due to bleeding from the parenchyma because a much larger amount of bleeding can occur if a pulmonary vessel is breached. In earlier animal research breaching of a pulmonary vessel resulted in bleeding of up to hundreds of milliliters and could result in the loss of the animal. Because the purpose of our study was specifically to ascertain that the creation of the passage was safe and no foreign material was

left in place, we believe the relatively short observation period was sufficient. We also believe from this study that the location of pulmonary vessels (which are the vessels heard by the Doppler catheter) are difficult to predict without using the Doppler catheter. There was little predictability of vessel location in these segmental and subsegmental airways, making use of this device vital in avoiding contact with major vessels lying adjacent to the airway walls. As far as the question of creating the passages in segmental or subsegmental bronchi is concerned, we believe this has little relevance because both segmental and subsegmental bronchi are equally surrounded by emphysematous lung tissue, as can be seen on high-resolution computed tomographic scans. Manipulation of the of the catheters was easy in the lower lobes, whereas in the upper lobes the procedure required some training because of the unfavorable angle of the bronchoscope and the need to withdraw the Doppler catheter and introduce the cautery probe while keeping the tip of the bronchoscope stationary. All considerations about the clinical effects of the airway bypass procedure are beyond the purpose of this study; namely the effect of secretions in the patency of the passages, the best way to keep the passages steadily open, and the clinical benefit of the procedure.

Our study proved that the airway bypass procedure is safely feasible in normal human subjects, as well as in patients with emphysema requiring lung transplantation. The Doppler device used to detect pulmonary vessels is effective, and the cautery probe enables safe creation of airway bypasses. These clinical results support further investigation of the efficacy of the airway bypass procedure in patients with emphysema. In particular, animal studies with long-term follow-up are ongoing to develop the ideal stent to keep the passages open.

References

1. Van Allen CM, Lindskog GE, Richter HT. Gaseous interchange between adjacent lung lobules. *Yale J Biol Med*. 1930;2:297-300.
2. Hogg JC, Macklem PT, Thurlbeck WM. The resistance of collateral channels in excised human lungs. *J Clin Invest*. 1969;48:421-31.
3. Terry PB, Traystman RJ, Newball HH, Batra G, Menkes HA. Collateral ventilation in man. *N Engl J Med*. 1978;298:10-5.
4. Macklem PT. Collateral ventilation [editorial]. *N Engl J Med*. 1978; 298:49-50.
5. Lausberg HF, Chino K, Patterson GA, Meyers BF, Toeniskoetter PD, Cooper JD. Bronchial fenestration improves expiratory flow in emphysematous human lungs. *Ann Thorac Surg*. 2003;75:393-8.
6. Snider G, Kleinerman J, Thurlbeck W, et al. The definition of emphysema. Report of a National Heart, Lung, and Blood Institute, Division of Lung Disease Workshop. *Am Rev Respir Dis*. 1985;132:182-5.
7. Cooper JD, Patterson GA, Sundaresan RS, Trulock EP, Yusen RD, Pohl MS, et al. Results of 150 consecutive bilateral lung volume reduction procedures in patients with severe emphysema. *J Thorac Cardiovasc Surg*. 1996;112:1319-30.
8. Sciurba FC, Rogers RM, Keenan RI, Slivka WA, Gorcsan J III, Ferson PF, et al. Improvement in pulmonary function and elastic recoil after lung reduction surgery for diffuse emphysema. *N Engl J Med*. 1996; 334:1095-9.
9. Cassart M, Hamacher J, Verbandt Y, Wildermuth S, Ritscher D, Russi EW, et al. Effects of lung volume reduction surgery for emphysema on diaphragm dimensions and configuration. *Am J Respir Crit Care Med*. 2001;163:1171-5.

Discussion

Dr Scott J. Swanson *(New York, NY).* This well-presented article discusses a novel concept first presented at this year's meeting of The Society of Thoracic Surgeons by Dr Lausberg of Dr Cooper's group that examines the feasibility of creating small passages from segmental or subsegmental airways into the parenchyma of the lung as a treatment for emphysema using a Doppler device for guidance and a radiofrequency catheter to create the passage. The idea is to provide nonanatomic routes into the lung to permit improved ventilation. At the prior presentation, this method was used ex vivo in human patients with emphysema undergoing transplantation and was shown to improve a surrogate forced expiratory volume in 1 second calculation by 78%. Today's article is an extension of that study and was performed in vivo at the time of either lobectomy for lung cancer or bilateral lung transplantation for emphysema. From 1 to 5 passages were created per patient. In the 10 patients undergoing lobectomy, there was a 20% incidence of mild bleeding, and in the 5 patients undergoing transplantation, this was not observed. The conclusion by the authors is that this procedure is safely feasible.

I would like to make 1 comment and ask 4 questions. It is a privilege to discuss an article by such a renowned group that has made many seminal contributions in advancing the treatment of patients with emphysema.

First, did the pathologists examine the lung specimens, and, if so, what did they see at the site of the neopassages? Was there hemorrhage, and how big were the channels?

Second, it is widely known and my colleagues from Boston have shown that obstruction to air flow in emphysema occurs in the very distal airways. How many of the passages in this experiment were in the segmental airways and how many were in the subsegmental airways, and why do you surmise that this might have an effect on the trapped ventilation that occurs much more distally?

Third, is it true to conclude that this is safe and feasible when the observation period after the procedure was minutes rather than hours or days? Are there plans to carry this out in an animal model to truly show safety before attempting this in human subjects?

Fourth, if stenting the passages is the plan to keep the channels patent, we know that stenting larger airways and the esophagus for benign lesions is fraught with problems from the radial traction and occlusion from secretions. How will these issues be addressed?

Dr Rendina. At the beginning of your discussion, you mentioned a 20% rate of bleeding considering the 2 episodes occurring in the 10 patients undergoing lobectomy. The denominator should, however, be considered the 47 passages created overall and not the 10 patients undergoing lobectomy, so that this rate drops to 4.2%. Regarding pathology, we had performed accurate pathologic studies in previous animal experiments, including more than 100 transbronchial passages, and we could demonstrate that the passages were about 1.5 mm in diameter, there was no bleeding around the site of the passage, and there was no necrosis of the

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