Evolving Technology

Clinical application of airway bypass with paclitaxel-eluting stents: Early results

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Objective: To assess the safety and early clinical results of a multicenter evaluation of airway bypass with paclitaxel-eluting stents for selected patients with severe emphysema.

Methods: Airway bypass was performed with a fiberoptic bronchoscope in three steps: identification of a blood vessel–free location with a Doppler probe at the level of segmental bronchi, fenestration of the bronchial wall, and placement of a paclitaxel-eluting stent to expand and maintain the new passage between the airway and adjacent lung tissue. All adverse events were recorded, as well as 1- and 6-month pulmonary function tests and dyspnea index.

Results: Thirty-five patients received the airway bypass procedure with a median of 8 stents implanted per patient. At 1-month follow-up, statistically significant differences in residual volume, total lung capacity, forced vital capacity, forced expiratory volume, modified Medical Research Council scale, 6-minute walk, and St George's Respiratory Questionnaire were observed. At the 6-month follow-up, statistically significant improvements in residual volume and dyspnea were demonstrated. One death occurred after bleeding during the procedure. Retrospective analysis revealed that the degree of pretreatment hyperinflation may be an important indicator of which patients achieve the best short- and long-term results.

Conclusions: The airway bypass procedure reduces hyperinflation and improves pulmonary function and dyspnea in selected patients with severe emphysema. Duration of benefit appears to correlate with the degree of pretreatment hyperinflation. These preliminary clinical results support further evaluation of the procedure.

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Research supported by Broncus Technologies, Inc. Mountain View, Calif.

Read at the Eighty-sixth Annual Meeting of The American Association for Thoracic Surgery, Philadelphia, Pa, April 29–May 3, 2006.

Received for publication April 27, 2006; revisions received April 1, 2007; accepted for publication May 11, 2007.

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J Thorac Cardiovasc Surg 2007;134:974-81

0022-5223/$32.00

doi:10.1016/j.jtcvs.2007.05.040

The irreversible destruction of lung parenchyma in emphysema is characterized by progressive air space enlargement within the lung and is associated with marked enhancement of collateral ventilation. The concept of collateral ventilation was first introduced by Van Allen, Lindskog, and Richter[1] in 1930. Collateral ventilation is inconsequential in normal human lungs; however, in emphysematous lungs it can be essential for ventilation distribution beyond the obstructed airways.[2] In emphysema, the resistance of the airways can exceed collateral resistance, forcing air to flow preferentially through collateral pathways, which may ultimately promote the redistribution of ventilation within the lungs.[3] Revisiting this concept in 1978, Macklem[4] proposed its potential clinical applicability for reducing gas trapping by venting the hyperinflated emphysematous lungs through spiracles—the creation of artificial passages from the lung surface to the outside of the chest. A recent revision of this lung deflation concept proposed bronchial fenestration for venting the emphysematous air spaces into the main airway, coining the term "airway bypass."[5] Airway bypass is the process of creating extra-anatomic passages between the collaterally ventilated pulmonary parenchyma and larger airways, allowing trapped gas to exit from the lung. This decrease in gas trapping reduces hyperinflation, allowing better chest wall and diaphragmatic excursion and therefore improving dyspnea. The feasibility of airway bypass was first tested experimentally on ex vivo explanted native lungs obtained from patients with emphysema undergoing lung transplantation.[6] This study demonstrated an improvement in the forced expiratory volumes in 1 and 5 seconds (FEV_1 and FEV_5), thus suggesting airway bypass as a potential therapeutic option for patients with marked hyperinflation and severe pulmonary destruction. These early clinical feasibility and safety studies in human lungs[5,7] recognized, but did not address, the need to develop the technology to improve long-term passage patency. Other laboratory research studied the value of combining stents with pharmaceuticals to inhibit tissue growth around the stent.[7] This, in turn, resulted in the development of the paclitaxel-eluting stent, which significantly prolonged stent patency in animals.[8] On the basis of these advances, the current research was undertaken to assess the safety and short-term clinical results of the airway bypass procedure using paclitaxel-eluting stents. It evaluates the applicability of the procedure to a multicenter study while suggesting an optimum target group for future clinical studies.

Abbreviations and Acronyms

COPD	= chronic obstructive pulmonary disease
FEV_1, FEV_5	= forced expiratory volumes in 1 and 5 seconds
FVC	= forced vital capacity
6MW	= 6-minute walk
mMRC	= modified Medical Research Council
NETT	= National Emphysema Treatment Trial
RV	= residual volume
SGRQ	= St George's Respiratory Questionnaire
TLC	= total lung capacity

Patients and Methods

Patients with emphysema were enrolled in the study according to the following major criteria: computed tomographic scan evidence of bilateral emphysema; post-bronchodilator residual volume (RV) 220% or more of predicted; post-bronchodilator total lung capacity (TLC) 133% or more of predicted; post-bronchodilator FEV_1 40% or less of predicted or FEV_1 of less than1 L; dyspnea scoring of 2 or more according to the modified Medical Research Council (mMRC) scale; arterial oxygen tension of 45 mm Hg or more on room air; and subjects who signed an informed consent form, were compliant, judged not suitable for other interventions, and considered fit to undergo a procedure under general anesthesia. Major exclusion criteria were the following: inability to walk more than 140 m at level in 6 minutes after pulmonary rehabilitation; presence of pulmonary hypertension (peak systolic pressure of >45 mm Hg or mean pressure of >35 mm Hg) as documented by 2-dimensional echocardiogram or right heart catheterization; any previous pulmonary resection; coronary artery disease with angina; history of myocardial infarction within 6 months or stroke less than 1 year before the procedure; insulin-dependent diabetes; unequivocal lung cancer or the presence of suspicious pulmonary nodule/infiltrate; large bullae; ventilator dependence; alpha-1 antitrypsin deficiency; coagulation disorder; steroid therapy of 20 mg prednisone or more per day; unequivocal and symptomatic bronchiectasis; and 3 or more respiratory infections requiring hospitalization within the past 12 months. Subjects who met the criteria underwent a pulmonary rehabilitation program of 16 to 20 sessions over 6 to 10 weeks, ending no greater than 6 weeks before the procedure. Rehabilitation resumed after the procedure for up to 8 weeks and was then encouraged but not required. Within 24 to 48 hours before the procedure, all subjects underwent a chest computed tomographic scan, spirometry, body plethysmography, and dyspnea scoring (baseline measurements). Subjects received intravenous antibiotics starting on arrival at the operating room. The airway bypass procedure was performed with the patient under general anesthesia with orotracheal intubation and controlled mechanical ventilation. The Exhale Emphysema Treatment System (Broncus Technologies, Inc, Mountain View, Calif) has 4 components: (1) the Exhale Doppler Probe, which is a catheter with a 1.4-mm ultrasonic Doppler transducer at the distal tip; (2) the Exhale Doppler Processing Unit, which amplifies the sounds of the Doppler probe; (3) the Exhale Transbronchial Dilation Needle, which is a combination 25-gauge needle and 2.5-mm dilation balloon catheter for passage creation and dilation; and (4) the Exhale Drug-Eluting Stent (3.3-mm inner diameter, 5.3-mm outer diameter, 2 mm in length) with paclitaxel embedded within the silicone layer mounted on a delivery balloon catheter (Figure 1). All these catheters were designed to pass through the 2 mm or larger working channel of a flexible bronchoscope. The system uses a standard, commercially available inflation syringe to inflate

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