Airway Bypass Stents for Emphysema, Algorithm to Exclude Precapillary Pulmonary Hypertension, and Sildenafil for Pulmonary Hypertension in Heart Failure with Preserved Ejection Fraction

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Recommended Reading from the Temple University School of Medicine Fellows; Kathleen Brennan, Program Director


Reviewed by Matthew R. Lammi

In selected patients with emphysema, lung volume reduction surgery has been shown to improve exercise capacity, quality of life, and survival (2). Because of restrictive inclusion criteria and risk of surgery, there has been interest in bronchoscopic lung volume reduction as an alternative to lung volume reduction surgery. Creating airway bypass tracts (ABTs) attempts to bypass collapsed small airways, allowing air to escape on expiration. The Exhale Airway Stents for Emphysema (EASE) trial was the first randomized, double-blind, sham-controlled study of ABTs (1).

Patients were included if they had homogeneous emphysema with an FEV1 less than 50% predicted and an RV/TLC greater than 0.65. Of the 1,522 patients assessed for eligibility, 208 were randomized to ABT and 107 to sham bronchoscopry. All patients had bronchoscopy under general anesthesia; the intervention group had passages created in the airway and paclitaxel stents placed to maintain patency. Bayesian analysis did not show any superiority of ABT for the coprimary efficacy end point, which was met if the FVC increased by at least 12% and modified Medical Research Council (mMRC) score fell by 1 point from baseline at 6 months of follow-up. Mean FVC increased on Day 1 in the ABT group, but this returned to baseline by 3 months. Mean mMRC scores were significantly lower only at the 6-month time point in the intervention group.

This trial used a robust randomized, sham-controlled study design that included patients most likely to benefit from the treatment. There was no benefit in the coprimary end point, likely due to stent expectoration and low rates of stent patency (66% on Day 1 and 21% at 6 mo). Although there were no differences in composite safety end points or 6-month mortality between the groups, the risk of chronic obstructive pulmonary disease exacerbation or infection was almost twofold higher in the treatment group. This highlights the importance of noting individual safety end points that may be masked by reporting a composite end point alone. The EASE trial demonstrates that airway bypass tract formation with paclitaxel stents does not improve outcomes in patients with severe homogeneous emphysema. This is an interesting example of how theoretical benefit was attained through an intervention but was not sustained because of technical aspects of the procedure.

References

Bonderman D, et al. A Noninvasive Algorithm to Exclude Pre-capillary Pulmonary Hypertension. Eur Respir J (3)

Reviewed by Nicholas Panetta

Current international guidelines recommend right-heart catheterization (RHC) in symptomatic patients at risk for pulmonary hypertension (PH) with systolic pulmonary artery pressures greater than 36 mm Hg by transthoracic echocardiography (TTE) (4). TTE is frequently inaccurate in estimating pulmonary artery pressures and cannot distinguish precapillary PH from postcapillary PH (5). This study, through retrospective analysis, sought to identify a noninvasive diagnostic algorithm to identify or exclude precapillary PH, which was then validated prospectively.

Data, including TTE, 12-lead electrocardiography, serum N-terminal pro–brain natriuretic peptide (NT-proBNP), lung function tests, and RHC from 251 patients referred for suspicion of precapillary PH, were used to develop a noninvasive diagnostic decision tree algorithm. A prospective study of 121 patients then served as temporal validation of this diagnostic algorithm, which dichotomized patients as “precapillary PH excluded” and “precapillary PH likely.” A bootstrap approach was also used to provide internal validation. All patients subsequently underwent RHC. Precapillary PH was defined as a mean pulmonary artery pressure greater than 25 mm Hg at rest with a pulmonary capillary wedge pressure less than 15 mm Hg.
The noninvasive diagnostic algorithm initially stratified patients by the presence or absence of a right ventricular strain pattern on electrocardiography, and then by a serum NT-proBNP level below or above 80 pg/ml. Combining TTE with this diagnostic algorithm yielded a sensitivity of 100% and a specificity of 19.3% in the 121 prospectively studied patients.

The results of this study are tempered by the fact that it is based on data from a single center. Also, it is unclear how the cutoff point of 80 pg/ml for serum NT-proBNP was established as both groups in the retrospective analysis had significantly greater values.

This interesting, well-designed study should help clinicians with the decision of when to further proceed with RHC in the workup of their patients and when it can be safely withheld, with the knowledge that a case of true precapillary PH will not be missed. Further validation at other centers and among a wider range of patients would be needed before this could be adopted into regular practice, however.

References


Reviewed by Maria Elena Vega

The presence of pulmonary hypertension (PH) in patients with heart failure with preserved ejection fraction (HFpEF) is associated with increased morbidity and mortality (7). There is no specific therapy for PH due to left heart disease and most advances have focused on the treatment of patients with pulmonary arterial hypertension.

Guazzi and colleagues (6) conducted a 1-year, double-blind, placebo-controlled trial with the phosphodiesterase-5 inhibitor sildenafil in patients with PH and HFpEF. Forty-four patients were randomly assigned to placebo or sildenafil. At 6 and 12 months, sildenafil was associated with significant improvement in quality of life and sustained improvement in cardiopulmonary hemodynamics and lung function.

This was a small but comprehensive study and its results enhance our knowledge of the pathophysiological mechanisms associated with HFpEF and PH. Treatment with sildenafil induced reduction of pulmonary artery pressures, pulmonary arterial resistance, and pulmonary capillary wedge pressure (PCWP). In the placebo group, pulmonary arterial resistance increased over the course of 12 months with unchanged PCWP, suggesting remodeling rather than simply vasoconstriction. There was also an improvement in right-heart hemodynamics in the treatment group suggested by leftward shift of the right ventricular Frank-Starling relationship, increased tricuspid annular systolic excursion, right atrial and right ventricular end-diastolic pressures, and ejection rate. In addition, reduction in right atrial pressure and PCWP significantly correlated with improvement in the alveolar–capillary membrane conductance, suggesting that reduction in these pressures leads to an improvement in pulmonary lymphatic drainage.

Patients in both arms showed evidence of elevated systemic blood pressure and PCWP throughout the study. One may wonder whether the improvement in cardiopulmonary hemodynamics and quality of life could have also been achieved with more aggressive heart failure treatment. Although the results of this trial are promising and the primary end points of improvement in pulmonary hemodynamics and right ventricular performance are important, it will be crucial to verify these findings in a larger trial and to determine whether the use of sildenafil in patients with PH and HFpEF will translate into clinical benefit with acceptable safety profile and improved survival.

Author disclosures are available with the text of this article at www.atsjournals.org.

References
