Bronchoscopic Procedures Tested in Emphysema

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SALT LAKE CITY — Pulmonologists are developing a variety of innovative bronchoscopic procedures to achieve nonsurgical lung volume reduction as treatment for advanced emphysema—and hoping to reinvent their specialty along the way.

The goal is to capitalize upon the functional and mortality benefits documented with lung volume reduction (LVR) surgery in a subset of participants in the NIH-sponsored National Emphysema Treatment Trial—but without the associated hefty perioperative mortality, major morbidity, and expense. If the bronchoscopic innovations prove successful, they could transform the field of respiratory medicine, much as percutaneous angioplasty and stenting have revolutionized cardiology, speakers predicted at the annual meeting of the American College of Chest Physicians.

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Planning is now underway for large, multicenter randomized trials of several novel investigational bronchoscopic LVR procedures that have successfully passed the pilot study phase of development.

Among them are insertion of one-way valves into pockets of diseased lung tissue, biologic tissue destruction with induction of scarring, and stent placement to create decompression of hyperinflated diseased lungs.

"I have this dream that you'll go into the recovery room and you'll be sweating with scrubs on and the cardiologist is going to come in and say, 'Wow, I had a tough case—I put three stents in,' and you'll say, 'Well, I had a tougher one—I put in seven valves,' or 'glued six subsegments,' or 'put in six stents.' Maybe we'll be able to induce physiologic changes and gain time for these patients," said Dr. Bartolome Celli, professor of medicine at Tufts University, Boston.

Dr. Daniel H. Sterman said that although LVR surgery didn't increase survival in the 180-patient National Emphysema Treatment Trial as a whole, it did improve survival, pulmonary functional capacity, and health status in the subset of participants with heterogenous, predominantly upper lobe emphysema and poor exercise capacity (N. Engl. J. Med. 2003;348:2059-73).

The price of surgical LVR, however, was steep: a 30-day mortality of about 5%, close to 50% major morbidity, and lengthy hospitalization. This has prompted intense research interest in developing procedures to reduce the volume of hyperinflated diseased lung without actually cutting out tissue, added Dr. Sterman, an interventional pulmonologist at the University of Pennsylvania, Philadelphia. He disclosed that he has been a consultant and a member of the scientific advisory committee for Spiration Inc.

He was lead investigator in a multicenter U.S. pilot study of Spiration Inc.'s Intrabronchial Valve (IBV), a one-way valve allowing air to escape from diseased portions of the lung, enabling the lungs to work more efficiently.

A total of 520 IBV valves were implanted in the upper lobes of 75 emphysema patients in the nonrandomized study, which typically involved an overnight hospital stay.

Of the 75 patients, 46 benefited, showing significantly improved general and disease-specific health status and reduced oxygen consumption with up to 1 year of follow-up. Complications in this subgroup were limited to one case of bronchospasm and one flare of chronic obstructive pulmonary disease (COPD).

Follow-up CT scans at 3 and 6 months showed significant reduction in the volume of the upper lobes of the responders, compared with their lower lobes, which increased in both volume and vascularity. This suggests the clinical benefits resulted at least in part from a redirection of ventilation and perfusion to the relatively spared lower lung segment, he explained.

Responders were younger than 75 years old, had fewer lung segments treated, and didn't have any valves placed in

the lingula. These findings will be incorporated into the upcoming large randomized trial.

Dr. Celli reported on 15 patients who have undergone a total of 21 biologic LVR treatment sessions involving instillation of a biodegradable agent.

"It has one advantage compared to the other good ideas out there: There's no foreign body left inside the individual," the physician noted.

The procedure, being developed by Aeris Therapeutics Inc., is definitely safe, said Dr. Celli, who has received research funding from the company. The only associated adverse events have been the minor sort common with flexible bronchoscopy. All patients were by protocol discharged the day after the procedure, but most could have gone home the same day, he said.

As for efficacy, early results look promising; but it will take many more patients and longer follow-up to know for sure, Dr. Celli added. The treatment concept involves identifying sick areas of lung, then instilling the biologic agent to induce atelectasis and shrink the volume so that much healthier but compressed lung tissue is allowed to expand.

A dose-response effect was apparent. The patients who have shown clinically meaningful improvements in vital capacity and exercise capacity were the ones who received the most extensive treatment: bilateral therapy targeting up to 10% of total lung volume. Future clinical trials may target 20%-30%.

The biologic procedure's safety lends itself to repeat sessions as additional areas of lung deteriorate. One appealing but as yet untested strategy: perform biologic LVR, measure lung function, then decide if the patient needs to come back in a few weeks for further LVR to optimize results.

The patient with the best response to treatment to date is swimming for exercise and still going strong 14 months after treatment. To physicians familiar with severe COPD, that's nothing short of miraculous, he said. But investigators haven't figured out why he's doing so well while some others who underwent extensive treatment didn't have major responses.

"We still have a long way to go," Dr. Celli emphasized.

Nonetheless, the future of nonsurgical interventions looks bright for patients with severe COPD, who traditionally have had few options other than the faint prospect of lung transplantation. Dr. Celli offered a final bit of advice to his fellow chest physicians: "Go learn bronchoscopy." ■