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Bronchial thermoplasty: A promising therapy, still in its infancy

Treating severe, refractory asthma is an ever-evolving challenge and a major source of frustration for patients and clinicians. Failure of inhaler treatment often results in debilitation of the patient and leads to long-term use of corticosteroids, with their insidious side effects.[1–3]

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Most asthma research continues to focus on inhibiting the cytokine cascade to reduce inflammation. However, inflammation is not the only pathophysiologic process underlying asthma.

Bronchial thermoplasty takes a novel approach and offers reason for some optimism.[4–6] The aim of this minimally invasive bronchoscopic procedure is to attenuate bronchoconstriction by reducing airway smooth muscle mass.

In this issue of the *Cleveland Clinic Journal of Medicine*, Dr. Thomas Gildea and colleagues[7] review the pathophysiology of asthma and the utility of decreasing airway smooth muscle via bronchial thermoplasty, its logistics, and the clinical trials that led to its approval by the US Food and Drug Administration (FDA) for the treatment of severe refractory asthma.

EVIDENCE FROM CLINICAL TRIALS

After studies in animals showed that bronchial thermoplasty was feasible, several randomized trials in humans—the Asthma Intervention Research (AIR) trial,[6] the Research in Severe Asthma (RISA) trial,[8] and the Asthma Intervention Research 2 (AIR2) trial[9]—found that the complication rates were acceptable, quality of life was improved, and health care utilization was reduced after the procedure during a 12- to 36-month period. These study results were essential in paving the way for FDA approval.

AIR2: A randomized controlled trial

The latest study to evaluate bronchial thermoplasty, the AIR2 trial,[9] was designed with a feature that is used relatively infrequently in trials of invasive procedures: a sham control. A sham procedure can be defined as one performed on control-group participants to ensure that they experience the same incidental effects of the procedure as do participants who actually undergo the procedure.[10]

Thus, the patients in the control group received the same medications before and after the procedure, they were taken to the procedure room, and the bronchoscope was actually inserted into their lungs—but thermoplasty was not performed. All of this was done in a double-blind manner: neither the patients nor the physicians caring for them before and after the procedure knew which group they were in.

The aim of this exercise was to reduce bias, namely, the placebo effect, and to reinforce results that depend on subjective symptoms, such as the Asthma Quality of Life Questionnaire (AQLQ) score. Clinical trials in severe asthma are notoriously marred by the placebo effect, resulting in spurious improvements in lung function and symptoms.

The AIR2 trial found a significant reduction in severe exacerbations and emergency

Long-term results with bronchial thermoplasty are not yet known, but studies are ongoing

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department visits, and a clinically meaningful improvement in AQLQ score from baseline at 6, 9, and 12 months in the bronchial thermoplasty group. However, 16 patients needed to be hospitalized after the procedure in the bronchial thermoplasty group, compared with two patients in the sham-procedure group.

The AIR2 trial, through the use of a sham-procedure control group, was able to minimize multiple forms of bias and thus provides the most reliable data for clinicians to extrapolate the good and the bad effects of bronchial thermoplasty.

THE PROCEDURE IS STILL IN ITS INFANCY

With any new therapy, we need to look at the benefits and complications not only in the short term but also the long term, ie, to determine whether the benefit is sustainable.

Long-term data on the benefits and side effects of bronchial thermoplasty have yet to be reported. However, radiofrequency ablation has been used in lung cancer therapy during the past decade, with favorable periprocedure complication profiles. Additionally, 5-year follow-up data have shown superior outcomes in stage I non-small-cell lung cancer survival rates with radiofrequency ablation compared with external-beam radiation.[11]

Ongoing studies will eventually provide insight on long-term outcomes of bronchial thermoplasty in asthma patients. Until such time, patients who have reached the limits of step-up therapy for severe refractory asthma should be informed that clinicians do not yet have a complete understanding of clinical benefits or sustainability of thermoplasty. Still, confidence in bronchial thermoplasty should be grounded in the simplicity of the procedure, the low short-term complication rates, and the long-term success of comparable medical procedures such as radiofrequency ablation in lung cancer, which utilizes similar technology.

Although this procedure is still in its infancy, the potential for long-term effectiveness in improving pulmonary function and quality of life in patients with severe asthma are undeniable. The body of data supporting its use will continue to evolve and hopefully point the way to better control of severe refractory asthma.

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