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Medical Policy Manual

Topic: Bronchial Thermoplasty

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Section: Surgery

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION[1]

Bronchial thermoplasty is a newly-available potential treatment option for patients with severe persistent asthma. It consists of radiofrequency energy delivered to the distal airways with the aim of decreasing smooth muscle mass believed to be associated with airway inflammation.

Background

Asthma, a chronic lung disease, affects approximately 8% of adults and 9.5% of children in the U.S. and, in 2011, accounted for approximately 440,000 hospitalizations and 3,400 deaths.[2] Asthma symptoms include episodic shortness of breath that is generally associated with other symptoms such as wheezing, coughing, and chest tightness. Objective clinical features include bronchial hyper-responsiveness and airway inflammation, and reversible airflow obstruction (at least 12% improvement in forced expiratory volume in 1 second [FEV-1] post-bronchodilator, with a minimum of 200 mL improvement). However, there is substantial heterogeneity in the inflammatory features of patients who are diagnosed with asthma, and this biological diversity is responsible, at least in part, for the variable response to treatment in the asthma population.

Management of asthma consists of environmental control, patient education, management of comorbidities, and regular follow-up for all affected individuals, as well as a stepped approach to medication treatment. Guidelines from the National Heart, Lung and Blood Institute define six

pharmacologic steps; step 1 for intermittent asthma, and steps 2-6 for persistent asthma.[3] The preferred daily medications are:

Step 1: short-acting beta-agonists as needed
Step 2: low-dose inhaled corticosteroids (ICS)
Step 3: ICS and long-acting beta-agonists (LABA) or medium-dose ICS
Step 4: medium-dose ICS and LABA
Step 5: high-dose ICS and LABA
Step 6: high-dose ICS and LABA, and oral corticosteroids

Despite this multidimensional approach, many patients continue to experience considerable morbidity. In addition to ongoing efforts to optimally implement standard approaches to asthma treatment, new therapies are being developed. One new therapy is bronchial thermoplasty, the controlled delivery of radiofrequency energy to heat tissues in the distal airways. Bronchial thermoplasty is based on the premise that patients with asthma have an increased amount of smooth muscle in the airway and that contraction of this smooth muscle is a major cause of airway constriction. The thermal energy delivered via bronchial thermoplasty aims to reduce the amount of smooth muscle and thereby decrease muscle-mediated bronchoconstriction with the ultimate goal of reducing asthma-related morbidity. Bronchial thermoplasty is intended as a supplemental treatment for patients with severe persistent asthma (i.e., steps 5 and 6 in the stepwise approach to care).

Bronchial thermoplasty procedures are performed on an outpatient basis and last approximately one hour each. During the procedure, a standard flexible bronchoscope is placed through the patient's mouth or nose into the most distal targeted airway and a catheter is inserted into the working channel of the bronchoscope. After placement, the electrode array in the top of the catheter is expanded, and radiofrequency energy is delivered from a proprietary controller and used to heat tissue to 65°C over a 5 mm area. The positioning of the catheter and application of thermal energy is repeated several times in contiguous areas along the accessible length of the airway. At the end of the treatment session, the catheter and bronchoscope are removed. A course of treatment consists of three separate procedures in different regions of the lung scheduled about three weeks apart.

Regulatory Status

In April 2010, the Alair® Bronchial Thermoplasty System (Asthmatx, Inc, now part of Boston Scientific Corporation.) was approved by the US Food and Drug Administration (FDA) through the premarket approval process for use in adults with severe and persistent asthma whose symptoms are not adequately controlled with inhaled corticosteroids and LABAs.[4] Use of the treatment is contraindicated in patients with implantable devices and those with sensitivities to lidocaine, atropine or benzodiazepines. It should also not be used while patients are experiencing an asthma exacerbation, active respiratory infection, bleeding disorder, or within two weeks of making changes in their corticosteroid regimen. The same area of the lung should not be treated more than once with bronchial thermoplasty.

MEDICAL POLICY CRITERIA

Bronchial thermoplasty for the treatment of asthma is considered **investigational**.

SCIENTIFIC EVIDENCE[1]

Literature Appraisal

In order to evaluate the efficacy and safety of bronchial thermoplasty (BT) in the treatment of asthma, evidence from randomized controlled trials (RCTs) comparing BT with either medications or sham BT is required. In light of the high placebo effect suggested in the AIR2 study summarized below, a sham control group is preferable in studies of BT, particularly for subjective outcomes such as quality of life.

Systematic Reviews and Meta-analyses

- Wu et al. conducted a systematic review and meta-analysis of the 1-year data from the three RCTs currently published.[5] The RCTs were rated as good quality. Two of the RCTs included a medication control group; one included a sham procedure control group. The possible placebo effect that might impact quality-of-life reporting in the medication trials was not discussed in the article. The authors concluded that BT appears promising and well-tolerated, but additional long-term RCTs are needed for further evaluation of both efficacy and safety.

The meta-analysis of the pooled data reported the following findings:

Efficacy:

- The bronchial thermoplasty patients had a significantly greater mean improvement in asthma quality of life compared with the control groups (weighted mean difference [WMD]: 0.63, 95% CI: 0.10 to 1.15; p=0.02).
- The bronchial thermoplasty patients had a significantly greater improvement in the morning peak expiratory flow (PEF) compared with the control groups (WMD: 21.78, 95% CI: 8.06 to 35.50; p=0.002).

Exacerbations:

- During the treatment period, there was a significantly higher risk of hospitalization with bronchial thermoplasty than control (risk ratio [RR]: 3.78, 95% CI: 1.39 to 10.24; p=0.009).
- In the post-treatment period (end of treatment to the 12-month follow-up visit), there was no significant difference between groups in the risk of hospitalization between groups (RR: 1.15, 95% CI: 0.47 to 2.79; p value not reported).

Adverse events.
During the treatment period (beginning on the day of the first treatment session and lasting 6 weeks after the last session):

- There were more respiratory adverse events in the bronchial thermoplasty groups (1,113 events in 257 patients) compared with the control groups (369 events in 164 patients) (p value not reported).
- There were no patient deaths and no permanent disability in any study participant.

The article listed the following factors that limited the interpretation and validity of the analysis of the pooled data:

- Heterogeneity of patient characteristics, study methodology, and treatment protocols between the studies
- All three trials provided medications to all patients; thus, the independent effects of bronchial

thermotherapy cannot be determined
    - Small sample size due to the meta-analysis having been limited to the three RCTs
    - Lack of individual patient data and information for stratified analysis
    - The included trials were underpowered to detect some other important outcomes such as forced expiratory volume in one second (FEV-1), FEV-1 percent predicted, exacerbations, rescue medication use, and longer term (> one year) efficacy and safety.

- A recent 2014 Cochrane review of the 3 randomized BT trials showed no clinical or statistical difference in the asthma control scores [Asthma Quality of Life Questionnaire (AQLQ) or the Asthma Control Questionnaire (ACQ-which measures symptom control)].[6] Limitations of the analysis included a lack of sham intervention for the control groups in 2 of 3 of these studies, raising questions regarding placebo effect, as seen in the high rate of response in the single sham group. (AIR2 trial: 64% experienced a clinically significant increase in the AQLQ.). Two of the studies showed lower rates of exacerbation after 12 months with BT compared to medical treatment alone. BT patients had a greater risk of hospitalization for respiratory adverse events during the treatment period with an absolute increase from 2% to 8% (95% CI 3% to 23%) over the treatment period, suggesting 6 of every 100 participants treated with thermoplasty would require an additional hospitalization over the treatment period. The authors concluded additional data from clinical trials and registries was needed to, "better understanding of the mechanisms of action of bronchial thermoplasty, as well as its effect in different asthma phenotypes or in patients with worse lung function."

Randomized Controlled Trials (RCT)

Three RCTs evaluating the safety and efficacy of bronchial thermoplasty have been published. All of the RCTs were supported by Asthmatx, the manufacturer of the Alair system. The initial follow-up period for all three studies was one year. Reports with longer term data have also recently been published. The following is a summary of the findings in the three RCTs.

1. Research in Severe Asthma (RISA) trial

This study, published by Pavord and colleagues in 2007, was conducted at eight centers in the U.K., Brazil, and Canada, and was primarily intended to investigate the safety of BT.[7] Eligibility criteria included:

- age 18 or older; asthma diagnosis;
- uncontrolled symptoms despite treatment with high-dose inhaled corticosteroids (at least 750 µg fluticasone propionate per day or equivalent) and long-acting beta-agonists (LABAs) (at least 100 µg salmeterol per day or equivalent), with or without other medications including oral prednisone or leukotriene modifiers;
- forced expiratory volume in 1 second (FEV-1) at least 50% of predicted;
- demonstrated airway hyper-responsiveness by challenge with methacholine or reversible bronchoconstriction during the prior 12 months;
- abstinence from smoking for at least 1 year, and a past smoking history of less than 10 pack-years.

After a 2-week run-in period, 34 participants were randomly assigned to a control group (n=17) that received continued medical management alone or medical management plus treatment with the Alair Bronchial Thermoplasty System (n=17). The bronchial thermoplasty group received three procedures at least three weeks apart (weeks 0-6). During weeks 6-22 all participants remained on a stable dose of steroids, and then during weeks 22-36 an attempt was made to reduce the dose of oral corticosteroids (or

inhaled corticosteroids for patients not taking the oral medication). Between weeks 36 to 52, patients took the reduced dose of steroids.

The primary outcomes of the study were the rate of adverse events and serious adverse events (defined as any event that was fatal, required prolonged hospitalization, caused substantial immediate risk of death, resulted in permanent impairment, or required intervention to prevent permanent impairment). A total of 32 of the 34 participants (94%) completed the study. A limitation of the study is the lack of a sham intervention and consequently, an inability to blind patients to treatment group. In addition, the study was limited in its ability to accurately evaluate safety by a small sample size.

One-Year Outcomes

- *Adverse events (primary outcome for this study):* In the initial treatment period, four patients in the bronchial thermoplasty group experienced seven serious adverse events requiring hospitalization and none occurred in the control group. During the remainder of the study, three patients in the bronchial thermoplasty group experienced five serious adverse events, and one patient in the control group experienced four serious adverse events; all of these events required hospitalization. There were an additional five severe adverse events in two bronchial thermoplasty group patients and one event in a control group patient that were medically treated without hospitalization (the authors did not report whether these were the same patients who were hospitalized). No overall statistical analysis was done that compared serious adverse events in the two groups.

- *Efficacy variables (secondary outcome for this study):* The authors reported of the following efficacy variables at the end of the study at 52 weeks.

    - Bronchial thermoplasty patients had a significantly greater improvement in beta-agonist use than control patients (decrease of 26 puffs vs. 6 puffs per week, respectively, $p<0.05$)
    - There was no significant difference between groups in other efficacy variables including morning and evening peak expiratory flow (PEF), symptom scores, number of symptom-free days, improvement in FEV-1 predicted, and several quality of life measures.

The small sample size resulted in limited power to detect differences in the efficacy outcomes.

Extended Study

An unpublished FDA document with minutes from an advisory panel meeting reported that 14 of the 17 patients assigned to bronchial thermoplasty in the RISA trial had been followed through year 3, and follow-up will continue through year 5.[8] In the BT group, respiratory adverse events decreased from 8.4 per patient at year 1 to 0.9 at year 2 and 1.1 at year 3. Patients in the control group were not followed beyond one year.

2. Asthma Intervention Research (AIR) trial

Cox and colleagues published findings of the AIR trial in 2007, which was designed to evaluate symptom control and adverse events following bronchial thermoplasty. Patients were recruited from the same three countries as the RISA study plus Denmark.[9] The eligibility criteria included:

- age 18-65
- moderate to severe persistent asthma requiring daily therapy with inhaled corticosteroids (equivalent

to at least 200 µg beclomethasone) and LABAs (at least 100 µg salmeterol or equivalent).
- FEV-1 of 60%-85% predicted,
- airway hyper-responsiveness
- stable asthma in the six weeks before enrollment
- no current respiratory infection
- no more than two lower respiratory infections requiring treatment in the past year.
- worsening asthma control during a 2-week baseline test period during which time LABA were withheld.

A total of 112 individuals met eligibility following the baseline test phase and were randomly assigned to receive medical management with inhaled corticosteroids and LABAs (n=56), or the same medical management strategy plus bronchial thermoplasty three sessions approximately three weeks apart (n=56). After follow-up visits at 3, 6, and 12 months, there was a 2-week period of abstinence from LABAs, during which data on exacerbations were collected. Between data collection periods, patients could use all maintenance therapies.

The primary outcome was the difference between groups in change in rate of mild exacerbations from the baseline 2-week abstinence period. An exacerbation was defined as the occurrence on two consecutive days of a reduction in the morning peak expiratory flow of at least 20% below the average value (recorded during the week before the abstinence period), the need for more than three additional puffs of rescue medication compared to the week before the abstinence period, or nocturnal awakening caused by asthma symptoms. The study was powered to detect a difference between groups of eight mild exacerbations per person per year. Data were available at three months for 100 of 112 patients (89%) and at 12 months for 101 patients (90%); all patients were included in the safety analysis. A limitation of the study is the lack of a sham intervention and consequently, an inability to blind patients to treatment group.

One-Year Outcomes

- *Mild exacerbations:* The mean number of mild exacerbations per person per week in the bronchial thermoplasty group was 0.35 (standard deviation [SD] =0.32) during the baseline test period, and 0.18 (SD=0.31) per person per week at 12 months (a decrease of 0.17 per person per week). In the control group, the mean number of mild exacerbations per person per week was 0.28 (SD=0.31) at baseline and 0.31 (SD=0.46) at 12 months (an increase of 0.03 per person per week). Compared to the control group, the bronchial thermoplasty group had a significantly greater reduction in mild exacerbations at the 12-month follow-up (p=0.003). Overall, the average number of exacerbations during the 2-week data collection periods at 3, 6, and 12 months decreased in the bronchial thermoplasty group, a mean decrease of 0.16 (SD=0.37) per person per week but not in the control group, which had a mean increase of 0.04 (SD=0.29) mild exacerbations. This resulted in a mean difference of .2 mild exacerbations per week or about 10 per year.
- *Severe exacerbations:* In contrast, there was not a significant difference between the number of severe exacerbations at any time point, compared to baseline. However, the study may not have had sufficient statistical power for this outcome. At the 12-month follow-up, the mean number of severe exacerbations in the bronchial thermoplasty group was 0.01 (SD=0.08) per person per week compared to 0.07 (SD=0.18) at baseline. The number of severe exacerbations in the control group was 0.06 (SD=0.24) per person per week compared to 0.09 (SD=0.31) at baseline.
- *Adverse events:* The rate of adverse events was higher in the bronchial thermoplasty group during the active treatment period, but the proportion of adverse events was similar in the two groups in the post-treatment period. Post-treatment, three individuals in the bronchial thermoplasty group required

hospitalization and two patients in the control group required a total of three hospitalizations.

Five-Year Outcomes

In 2011, Thomson and colleagues published 5-year safety data from the AIR trial.[10] All study participants who completed the 1-year follow-up visit were invited to participate in the extension study; 45 of 52 (87%) in the bronchial thermoplasty group and 24 of 49 (49%) in the control group opted to participate. Follow-up was done on an annual basis. Patients in the control group were followed for two additional years and patients in the bronchial thermoplasty group were followed for five years. Twenty-one of 24 (88%) patients in the control group and 42 of 45 (93%) in the bronchial thermoplasty group completed the final follow-up.

Although the primary purpose of the Thomson study was to examine long-term safety of the Alair device, some efficacy data was reported for two measures of lung function, post-bronchodilator FEV1 and forced vital capacity (FVC). The group comparisons of safety and efficacy in this follow-up trial was limited by the differential rate of follow-up between the two groups, with a lower percent of patients in the control group agreeing to participate in the follow-up study. In addition, as previously stated, data were collected on both treatment groups only during the first two years of this extension study; thereafter, no further data was obtained from the control group.

- *Exacerbations:*
    - FEV1 and FVC remained stable in both groups during the Years 2 and 3 and in the bronchial thermoplasty group in Years 4 and 5. Exact numbers were not reported, but post-bronchodilator FEV1 did not go below 80% of predicted in either group.
    - In the first year (Year 2 of the study), the rate of hospitalizations was 3 of 45 (7%) in the bronchial thermoplasty group; there were no hospitalizations in the control group (p=0.55). In Year 3, the rate of hospitalizations in the bronchial thermoplasty group was again 3 of 45 (7%) and 1 of 21 (5%) patients in the control group was hospitalized (p=1.00).
    - Rates of emergency room visits in Year 2 were 3 (7%) and 3 (12.5%) in the bronchial thermoplasty and control groups respectively (p=0.41) and in Year 3 rates were 3 (5%) and 3 (5%), respectively (p=1.00). There was one hospitalization each year in the bronchial thermoplasty group in Years 4 and 5.

- *Adverse events:* In the extension study, unlike the initial follow-up period, respiratory adverse events with multiple symptoms were recorded as a single adverse event. This could give a misleading impression of the total number of adverse events or relative number in the two groups.
    - In Years 2 and 3, differences between groups for incidence of respiratory adverse events were not statistically significant. The incidence of respiratory adverse events during Year 2 was 24 of 45 (53%) in the bronchial thermoplasty group and 13 of 24 (54%) in the control group. During Year 3, incidence was 24 of 43 (56%) in the bronchial thermoplasty group and 12 of 21 (57%) in the control group.
    - In subsequent years, the incidence of respiratory adverse events in the bronchial thermoplasty group was similar to Years 2 and 3; rates were 23 of 43 (53%) in Year 4 and 22 of 42 (52%) in Year 5.
    - No instances of pneumothorax, intubation, mechanical ventilation, cardiac arrhythmias, or death were reported over the course of this extension study.

These 5-year safety data on a subset of the participants in the AIR trial do not suggest a high rate of delayed complications following bronchial thermoplasty.

3. Asthma Intervention Research 2 (AIR2) Trial

The AIR2 trial was a randomized, sham-controlled trial conducted at 30 sites in six countries including the U.S.; one- and two-year findings were published in 2010 and 2011 by Castro and colleagues.[11,12] Unlike the other two RCTs, the control condition was a sham intervention and the trial was double-blind; participants and outcome assessment was blinded, but the intervention team was unblinded. Eligibility criteria were similar to those in the AIR trial; key differences were that a higher initial dose of inhaled corticosteroids was required (equivalent to at least 1000 ug beclomethasone) and patients were required to have experienced at least two days of asthma symptoms during the 4-week baseline period and have a baseline score on the Asthma Quality of Life Questionnaire (AQLQ) of no more than 6.25. (The possible range of the AQLQ score is 1 to 7, with a higher number representing a better quality of life.) Also different from the AIR trial, patients were not required to experience symptom worsening during a period of abstinence from LABAs. Patients were stable on their asthma medication and continued their medication regimen during the study.

The primary outcome was the difference between groups in the change from baseline in the AQLQ score, with scores from the 6-, 9-, and 12-month follow-ups averaged (integrated AQLQ score). A related outcome was the proportion of patients who achieved a change in their AQLQ score of 0.5 or greater, generally considered the minimally important difference for this scale. Bayesian analysis was used. The target posterior probability of superiority (PPS) of bronchial thermoplasty over sham was 95%, except for the primary AQLQ endpoint; there the target was 96.4% to adjust for two interim looks at the data.

A total of 297 individuals were randomly assigned, 196 to a bronchial thermoplasty group and 101 to a sham control group. The intervention for all participants consisted of three bronchoscopy procedures, performed three weeks apart. The sham intervention was identical to the active treatment, except that no radiofrequency energy was delivered. Nine participants withdrew consent before beginning treatment, and 288 underwent bronchoscopy and were included in the intention to treat (ITT) population. One hundred and eight-five participants in the treatment group and 97 in the sham control group underwent the second bronchoscopy, and the same numbers of individuals had the third bronchoscopy; it is not clear whether these were exactly the same patients.

One-Year Outcomes[11]

A total of 278 out of the 297 enrolled patients (94%) completed the 12-month visit, 181 in the treatment group and 97 in the sham control group. Primary outcomes in the ITT population were as follows:

- The mean change in the integrated AQLQ score, the primary effectiveness outcome, was 1.35 (SD=1.10) in the bronchial thermoplasty group and 1.16 (SD=1.23) in the sham control group. Using Bayesian analysis, the posterior probability of superiority (PPS) was 96%. This did not surpass the target PPS of 96.4%.
- The percentage of patients achieving an AQLQ score change of 0.5 or greater (i.e., at least the minimal important difference) was 79% in the bronchial thermoplasty group and 64% in the control group. The posterior probability of superiority at 99.6% surpassed the target probability for secondary outcomes of 95%.
- Additional analysis of data from the active treatment group suggests that responders (defined as a change in AQLQ score of at least 0.5) were more likely to have a lower baseline score than nonresponders (mean of 4.1 vs. 5.1, respectively).

Several secondary outcomes favored bronchial thermoplasty over the sham control group. These included:

- Reduction in the proportion of patients reporting asthma worsening during follow-up (27.3% vs. 42.9%, respectively, posterior probability of superiority 99.7%)
- Reduction in the number of emergency department visits (0.07 vs. 0.43 visits per person per year, respectively, PPS=99.9%).
- Reduction in severe exacerbations of 0.47 per person per year in the bronchial thermoplasty group compared to 0.70 per person per year in the control group (the PPS was 95.5%).
- There was no significant difference between groups in other secondary efficacy outcomes including morning peak expiratory flow, number of symptom-free days, symptom score, and rescue medication use.

Regarding safety outcomes, during the treatment phase, there was a higher rate of respiratory adverse events in the active treatment group (85% of participants; mean of 1.0 event per bronchoscopy) compared to the sham group (76% of participants, mean of 0.7 events per bronchoscopy).

- A total of 16 patients (8.4%) in the active treatment group required 19 hospitalizations for respiratory symptoms during the treatment phase compared to two patients (2%) in the sham group who required one hospitalization each.
- However, during the post-treatment period, 70% of patients in the bronchial thermoplasty group and 80% of patients in the sham group reported adverse respiratory events. During this phase of the study, five patients (2.6%) in the bronchial thermoplasty group had a total of six hospitalizations for respiratory symptoms, and four patients (4.1%) in the sham group had 12 hospitalizations (one patient had nine hospitalizations).

In the AIR2 study, the sham group had a relatively high rate of response, e.g., 64% experienced a clinically significant increase in the AQLQ. Blinding appeared to be initially successful and remained so for the sham group. After the first bronchoscopy, participants in both groups were unable to correctly guess their treatment group after the first bronchoscopy. During subsequent assessments, this continued among patients in the sham group, whereas in the bronchial thermoplasty group, a larger proportion guessed correctly.

The high rate of response in the sham group of the AIR2 suggests a large placebo effect with novel asthma treatments, particularly for subjective outcomes such as quality of life. This calls into question conclusions about efficacy in the earlier trials that did not have a sham control. In the AIR2 trial, bronchial thermoplasty provided benefit in terms of quality of life and some, but not all, secondary outcomes. However, it is unclear which patients are most likely to respond. Data from this trial suggest that those with more severe asthma may experience the greatest improvement.

Two-Year Outcomes[12]

This study reported on the subset of subjects in the BT group who experienced exacerbations, adverse events, and healthcare utilization in the second year of the AIR2 trial. Patients in the sham control group were not included in the extension study because it was felt to be unethical to require patients with severe asthma to refrain from alternative treatment options beyond the first year of the study. A total of 166 of 190 (87%) individuals randomized to the bronchial thermoplasty group completed the two-year evaluation. The primary outcome was the proportion of BT subjects experiencing severe exacerbations

in Year 2 compared to Year 1. Other outcomes were severe exacerbation rates, proportions of subjects and rate of respiratory adverse events, emergency department visits and hospitalizations for respiratory symptoms, stability of pre- and post-bronchodilator FEV, and changes in maintenance asthma medications. No significant change was found in any of these measures. A limitation of this study included the lack of data from the sham control group and, thus, a non-inferiority model design was used.

Five-Year Outcomes[13]

Similar to the RISA trial, only BT treated patients (n=162 of 190) were followed up to 5 years. Authors reported that severe exacerbations and ED visits in each of the follow-up years (1 to 5) remained low compared to 12 months prior to BT treatment (average 5-year reduction in proportions: 44% for exacerbations and 78% for ED visits). In addition, respiratory adverse events and respiratory-related hospitalizations remained unchanged in years 2 through 5 compared with the first year after BT. Although several secondary outcomes favored BT therapy over sham, the primary outcome was the change in AQLQ score from baseline. AQLQ scores were not reported as part of the 5-year follow-up.

Clinical Practice Guidelines and Position Statements

European Respiratory Society and the American Thoracic Society (ERS/ATS)[14]

New 2014 ERS/ATS evidence-based guidelines indicated that bronchial thermoplasty may be considered as a potential treatment for severe asthma patients but only in the context of an IRB approved registry or clinical study. The committee indicated that, "This recommendation places a higher value on avoiding adverse effects and on increased use of resources, and on a lack of understanding of which patients may benefit, and a lower value on the uncertain improvement in symptoms and quality of life."

Global Initiative for Asthma® (GINA)[15]

In 2014, GINA updated their recommendations regarding BT treatment as part of asthma management and prevention. The group indicated that BT may be considered for some adult patients with severe asthma; however, this recommendation was solely based upon the ERS/ATS guidelines noted above. The GINA guidelines noted that the current evidence was limited and long term effects of BT therapy were unknown. In addition, the method for selecting the optimal patient who would most benefit from BT therapy was not indicated. Lastly, the GINA guidelines noted that, "(c)aution should be used in selecting patients for this procedure, as the number of studies is small, and people with chronic sinus disease, frequent chest infections or FEV < 60% predicted were excluded."

American College of Chest Physicians (ACCP)[16]

In 2014, the ACCP published a consensus statement in support of BT as a treatment option for patients with severe asthma; however, this recommendation is not based upon peer-reviewed evidence.

Summary

Current evidence regarding bronchial thermoplasty treatment in patients with severe, persistent asthma consists of three randomized controlled trials. While these studies have reported encouraging results, limitations in study design suggest a large placebo effect, particularly for subjective outcomes such as quality of life. In addition, all three studies indicated an increased risk for adverse events during the

bronchial thermoplasty treatment period. Therefore, bronchial thermoplasty is considered investigational as a treatment of asthma. Given the uncertainty about the impact of bronchial thermoplasty on net health outcomes, additional data from randomized trials using sham controls are needed.

REFERENCES

1. BlueCross BlueShield Association Medical Policy Reference Manual "Bronchial Thermoplasty." Policy No. 7.01.127
2. Centers for Disease Control and Prevention. Asthma FastStats fact sheet. [cited 08/08/2013]; Available from: http://www.cdc.gov/asthma/faststats.html
3. National Heart, Lung, and Blood Institute of the National Institutes of Health. National Asthma Education and Prevention Program (NAEPP) Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma (EPR-3). 2007. [cited 08/08/2013]; Available from: http://www.nhlbi.nih.gov/guidelines/asthma
4. Food and Drug Administration News Release. April 27, 2010. [cited 07/2010]; Available from: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm209909.htm
5. Wu, Q, Xing, Y, Zhou, X, Wang, D. Meta-analysis of the efficacy and safety of bronchial thermoplasty in patients with moderate-to-severe persistent asthma. *J Int Med Res*. 2011;39(1):10-22. PMID: 21672303
6. Torrego, A, Sola, I, Munoz, AM, et al. Bronchial thermoplasty for moderate or severe persistent asthma in adults. *Cochrane Database Syst Rev*. 2014;3:CD009910. PMID: 24585221
7. Pavord, ID, Cox, G, Thomson, NC, et al. Safety and efficacy of bronchial thermoplasty in symptomatic, severe asthma. *Am J Respir Crit Care Med*. 2007 Dec 15;176(12):1185-91. PMID: 17901415
8. Series, F, Series, I, Cormier, Y. Effects of enhancing slow-wave sleep by gamma-hydroxybutyrate on obstructive sleep apnea. *Am Rev Respir Dis*. 1992 Jun;145(6):1378-83. PMID: 1596007
9. Cox, G, Thomson, NC, Rubin, AS, et al. Asthma control during the year after bronchial thermoplasty. *N Engl J Med*. 2007 Mar 29;356(13):1327-37. PMID: 17392302
10. Thomson, NC, Rubin, AS, Niven, RM, et al. Long-term (5 year) safety of bronchial thermoplasty: Asthma Intervention Research (AIR) trial. *BMC Pulm Med*. 2011;11:8. PMID: 21314924
11. Castro, M, Rubin, AS, Laviolette, M, et al. Effectiveness and safety of bronchial thermoplasty in the treatment of severe asthma: a multicenter, randomized, double-blind, sham-controlled clinical trial. *Am J Respir Crit Care Med*. 2010 Jan 15;181(2):116-24. PMID: 19815809
12. Castro, M, Rubin, A, Laviolette, M, Hanania, NA, Armstrong, B, Cox, G. Persistence of effectiveness of bronchial thermoplasty in patients with severe asthma. *Ann Allergy Asthma Immunol*. 2011 Jul;107(1):65-70. PMID: 21704887
13. Wechsler, ME, Laviolette, M, Rubin, AS, et al. Bronchial thermoplasty: Long-term safety and effectiveness in patients with severe persistent asthma. *J Allergy Clin Immunol*. 2013 Dec;132(6):1295-302. PMID: 23998657
14. Chung, KF, Wenzel, SE, Brozek, JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2013. PMID: 24337046
15. Global Initiative for Asthma (GINA). The Global strategy for asthma management and prevention 2014. [cited 05/12/2014]; Available from: http://www.ginasthma.org/local/uploads/files/GINA_Report_2014.pdf
16. American College of Chest Physicians: Guidelines and Resources. Regulations and Reimbursement. 2014. [cited 05/12/2014]; Available from: http://www.chestnet.org/Guidelines-

and-Resources/Payment-Practice-and-Quality/Coding-Regulations-and-Reimbursement/Regulations-and-Reimbursement

CROSS REFERENCES

None

CODES	NUMBER	DESCRIPTION
CPT	31660	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with bronchial thermoplasty, 1 lobe
	31661	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with bronchial thermoplasty, 2 or more lobes
HCPCS	None	