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Bronchial Thermoplasty in the Treatment of Asthma: A Literature Review

Authors:

Katarzyna Torbacka [KT]- corresponding author

5 Military Clinical Hospital with Polyclinic SPZOZ, Wrocławska 1/3, 30-901 Kraków

ORCID: https://orcid.org/0009-0002-7208-3725

E-mail: katorbacka@gmail.com

Zuzanna Wróbel [ZW]

The West Hospital in Grodzisk Mazowiecki, Daleka 11, 05-825 Grodzisk Mazowiecki

ORCID: https://orcid.org/0009-0005-7529-0641

E-mail: zuzannaw76@gmail.com

Katarzyna Rozkosz [KR]

Independent Public Health Care Center of the Ministry of the Interior and Administration in

Katowice named after sergeant Grzegorz Załoga, Wita Stwosza 39-41, 40-042 Katowice

ORCID: https://orcid.org/0009-0000-3610-1901

E-mail: km.rozkosz@gmail.com

Maja Torbacka [MT]

Jagiellonian University Collegium Medicum, Świętej Anny 12, 31-008 Kraków

ORCID: https://orcid.org/0009-0000-7139-2134

E-mail: majka.torbacka@op.pl

Joanna Kaczor [JK]

Independent Public Healthcare Institution in Myślenice, Szpitalna 2, 32-400 Myślenice

ORCID: https://orcid.org/0009-0002-1714-2630

E-mail: joanna.kaczor97@gmail.com

Natalia Wróbel [NW]

5 Military Clinical Hospital with Polyclinic SPZOZ, Wrocławska 1/3, 30-901 Kraków

ORCID: https://orcid.org/0009-0005-9236-9802

E-mail: natalia.wrobel2323@gmail.com

Aleksandra Sosin [AS]

Jagiellonian University Collegium Medicum, Świętej Anny 12, 31-008 Kraków

ORCID: https://orcid.org/0009-0008-0440-5431

E-mail: a.sosin@student.uj.edu.pl

Wojciech Bednarz [WB]

Independent Public Healthcare Institution of the Ministry of the Interior and Administration in

Kraków, Kronikarza Galla 25, 30-053 Kraków

ORCID: https://orcid.org/0009-0003-9522-6298

E-mail: wojciechbednarz2@gmail.com

Olga Jakubik [OJ]

Praski Hospital, Sp. z o.o., al. "Solidarności" 67, 03-401 Warszawa

ORCID: https://orcid.org/0009-0006-4378-7087

E-mail: o.jakubik.99@gmail.com

Patrycja Podlejska [PP]

Independent Public Health Care Center of the Ministry of the Interior and Administration in

Katowice named after sergeant Grzegorz Załoga, Wita Stwosza 39-41, 40-042 Katowice

ORCID: https://orcid.org/0009-0002-0074-9778

E-mail: patrycja.podlejska@gmail.com

ABSTRACT

Introduction and purpose

Asthma is a chronic inflammatory disorder affecting people worldwide. Although standard pharmacological

management is adequate for most asthma patients, bronchial thermoplasty may serve as a therapeutic alternative

in individuals with severe, uncontrolled asthma. The aim of this review is to summarize the knowledge of the

effects of bronchial thermoplasty on symptom control, quality of life, and airway remodeling, as well as the use

and effectiveness of this procedure in treating asthma.

Description of the state of knowledge

Bronchial thermoplasty (BT) is an endoscopic treatment method that can be used in patients with severe asthma,

whose condition has not been adequately controlled with recommended pharmacological treatment. This

procedure involves the application of radiofrequency energy to modify the airways' structure and decrease

airway smooth muscle mass. It is regarded as a safe and effective treatment option for long-term asthma

management.

Conclusion

After bronchial thermoplasty, improved symptom control and a reduction in the frequency of exacerbations were

observed, resulting from a decrease in airway smooth muscle mass and an expansion of airway volume. However,

this therapeutic strategy is recommended for individuals for whom other treatments have proven ineffective.

Keywords: bronchial thermoplasty; asthma; treatment.

3

Introduction and purpose

Asthma is a chronic, globally occurring respiratory disease that affects millions of people worldwide. The clinical course of bronchial asthma is characterized by symptoms such as wheezing, shortness of breath, chest tightness, and coughing with variable frequency and intensity. They are caused by reversible airflow restriction through the airways, increased airway smooth muscle layer (ASM) thickness, and other structural changes. There are several classifications of asthma, including those based on etiology into allergic and non-allergic asthma, phenotypes, and the type of airway inflammation. However, in everyday clinical practice, the classification of asthma according to the degree of control is of fundamental importance. Most patients maintain asthma control with treatment involving inhaled corticosteroids and bronchodilators and by treating comorbidities. However, certain patients fall into the group of people with severe asthma, meaning they do not respond to optimal therapy and experience frequent exacerbations and uncontrolled symptoms. In this group of patients, treatment with biological drugs and macrolides is used, but bronchial thermoplasty can also be considered, as it offers other mechanisms of action. [1,2].

Difficult asthma refers to a form of asthma that remains poorly controlled despite therapy at stage 4 or 5 or requires such treatment to sustain adequate symptom management and minimize the risk of exacerbations. Severe asthma, which is a subset of difficult asthma, persists as uncontrolled despite optimized, high-intensity treatment and addressing coexisting factors that could worsen the condition. Additionally, it may deteriorate when high medication doses are reduced. [2].

The purpose of this review is to evaluate the effect of bronchial thermoplasty (BT) on airway remodeling and its use in the treatment of severe asthma.

Materials and methods

The literature review was based on the most recent literature published between 2015 and 2025. PubMed and Google Scholar open databases were utilized in this study to search by keywords like bronchial thermoplasty, asthma, and treatment. In the end, 31 sources were cited.

Description of the state of knowledge

Bronchial thermoplasty (BT) is an endoscopic treatment for severe asthma, which involves the use of radiofrequency to remodel the airways and reduce the mass of the airway smooth muscle [3]. This procedure uses radiofrequency to ablate hypertrophic bronchial smooth muscle and reduce hyperactivity in bronchi that are 3-10 mm in diameter. A special bronchoscopic catheter is used during the procedure [4]. The electrode array is inserted and then expanded to contact the airway walls while being directly visualized through the working channel of a compatible flexible bronchoscope. The therapy involves treating the right lower lobe, the left lower lobe, and then both upper lobes [5]. This procedure is typically performed in three bronchoscopic procedures, which are performed 3–4 weeks apart [6]. During the procedure, the patient is under general anesthesia. Bronchial thermoplasty is considered an effective and safe therapeutic option in long-term treatment for patients with severe asthma and airflow limitation. However, early complications may occur after individual bronchoscopy sessions [7,8].

Impact of bronchial thermoplasty on symptom control and quality of life

The effects of treatment with bronchial thermoplasty are best seen through the improvement in the results of ACQ, ACT, and AQLQ questionnaires completed by the study participants before and after this procedure. Additionally, clinical improvement is indicated by a change in the number of exacerbations, modification of the dose of medications taken, change in the need for reliever medications, and assessment of lung function by spirometry and body plethysmography.

The Asthma Control Questionnaire (ACQ) is a symptom assessment questionnaire that contains 6 self-response questions and 1 question about FEV1% completed by clinic staff. Scores range between 0 (totally controlled) and 6 (severely uncontrolled) [9].

The Asthma Control Test (ACT) includes questions about the occurrence of shortness of breath and general asthma symptoms, the use of rescue medications, the impact of asthma on daily functioning, and a general self-assessment of asthma control.

The scores range from 5 (poor control of asthma) to 25 (complete control of asthma). An ACT score >19 shows well-controlled asthma [10].

The Asthma Quality of Life Questionnaire (AQLQ) consists of 32 questions in 4 categories: symptoms (11 questions), activity limitations (12 questions, of which 5 are individual), emotional functions (5 questions), and exposure to environmental factors (4

questions). Possible scores are 1–7 points for each question and a higher score indicates a better quality of life [11].

In a retrospective multicenter study in 2021 researchers conducted a review of subjects who underwent bronchial thermoplasty at four centers in India. They included 36 subjects who received 105 sessions of BT. All patients were classified as having severe asthma as they met the American Thoracic Society/European Respiratory Society criteria. Asthma control improved after the procedure which was evident from the results of the questionnaires before and after bronchial thermoplasty. In the Asthma Control Test (ACT), the score improved from: a mean of 10.3 before BT to: a mean of 20.5 after BT, ACQ from: a median of 3.91 before BT to: a median of 1.08 after BT, and Asthma Quality of Life Questionnaire Quality (AQLQ) from: mean 2.89 before BT to: mean 5.59 after BT. In addition, the number of asthma exacerbations was reduced after BT (median 3 per year before BT vs 0.5 per year after BT). FEV1 values did not change. Sixty-four percent of subjects who previously had inadequately controlled asthma reached asthma control and 50% of patients reduced their use of controller medication [4].

In another prospective, open-label, multicenter study from 2021, The Bronchial Thermoplasty Global Registry (BTGR) collected data on subjects who underwent BT from eighteen centers in Spain, Italy, Germany, Great Britain, the Netherlands, the Czech Republic, South Africa and Australia. One hundred fifty-seven adult patients who were treated with BT were included, and 153 had all three BT procedures. After thermoplasty, there was a decrease in the number of severe asthma exacerbations requiring systemic corticosteroids. 12 months before BT, 90.3% of patients had an exacerbation, and two years after BT only 56.1%, a reduction of 37.9%. Additionally, there was a decrease in the number of subjects who visited the ER due to asthma symptoms (53.8% vs 25.5%) and a decrease in the number of hospitalizations (42.9% vs 23.5 %). There was no change in FEV1 or forced vital capacity. There was a decrease in the average daily dose of inhaled corticosteroids, a decrease in the number of patients using oral corticosteroids (from 47.8% to 24.8%), and a decrease in the percentage of patients taking biologics (from 9.6% to 5.7%) after 2 years after BT. The ACT score improved from 11.18 to 15.54 and the AQLQ score from 3.26 at baseline to 4.39 after 2 years [12].

In the next study from 2023 in Australia researchers assessed the safety and effectiveness of BT 5 years after treatment in a cohort of patients with severe asthma. A total of 51 patients from two centers participated in a 5-year follow-up review. There was an improvement in the ACQ from a mean of 3.0 at baseline to 1.8 5 years later. There was a

decrease in the frequency of exacerbations requiring steroids from a mean of 3.8 to 1.0 exacerbations per year after 5 years and a reduction in the need for reliever medication by more than 50%. There were no changes in FEV1 in spirometry [13].

In a 2018 cohort study, researchers assessed the efficacy and safety of bronchial thermoplasty in 21 participants in clinical practice at a center in Spain. After the study, the ACT improved by an average of 7.1 points, and the number of severe exacerbations decreased by an average of 75% in most participants. Additionally, there was a 38% decrease in the number of hospitalizations per year. After treatment, the dose of inhaled corticosteroids was reduced by 430 µg of budesonide-equivalent, and the dose of prednisone-equivalent was reduced by 4 mg. There were no significant changes in lung function parameters [14].

In 2020, researchers in an observational cohort study analyzed the impact of BT on lung function using spirometry, body plethysmography, forced oscillation technique (FOT), and asthma questionnaires while also examining the relationship between pulmonary function parameters and the effectiveness of BT treatment. A total of 24 patients were evaluated in the study. There was an improvement in the AQLQ and ACQ questionnaire scores 6 months after BT, with AQLQ increasing from a mean of 4.15 to 4.90 and ACQ decreasing from a mean of 2.64 to 2.11. Pulmonary function parameters remained unchanged, while an increase in FEV1 was associated with improvements in AQLQ. In this study, patients who originally had higher respiratory resistance measured with FOT experienced smaller improvements in both questionnaires following BT compared to those with lower resistance. However, this relationship was not observed when airway resistance was assessed using conventional spirometry and body plethysmography [15].

In 2018, a prospective cohort of 32 consecutive patients with severe asthma who were referred for BT treatment at two Australian university hospitals was analyzed. Patients were assessed at three different time points: before therapy initiation, 6 weeks, and 6 months after completion of all procedures. After six months of BT treatment, the ACQ score showed a significant improvement, decreasing from an initial, mean value of 3.0 to 1.5. Additionally, daily salbutamol usage was reduced from a mean of 8.3 to 3.5 puffs per day. The number of exacerbations requiring oral corticosteroids declined from a mean of 2.5 in the six months before BT to a mean of 0.6 in the 6 months after BT. No changes in spirometric parameters were noted after the procedure. Additionally, lung function was assessed by body plethysmography and a noticeable reduction in gas trapping was noted, as residual volume (RV) decreased from a mean 146% of the predicted value in the beginning to 136% six

months after BT. Notable enhancements were also observed in total lung capacity (TLC) and functional residual capacity (FRC) [16].

Bronchial thermoplasty also improves the quality of life in overweight/obese people with uncontrolled severe asthma. In a 2023 retrospective and observational cohort study, researchers divided patients into 2 groups according to their body mass index and assessed AQLQ. Overweight/obese patients had greater improvement in these scores than normal-weight patients [17].

The effect of bronchial thermoplasty on airway remodeling

In patients with asthma, airway remodeling is characterized by epithelial cell hyperplasia, goblet cell metaplasia, subepithelial fibrosis, angiogenesis, an increase in airway smooth muscle (ASM) mass, thickening of the reticular basement membrane (RBM) and changes in extracellular matrix (ECM) proteins. These structural alterations are associated with the severity of asthma and the extent of airflow obstruction. After BT therapy, in addition to a reduction in the mass of airway smooth muscles, a decrease in the thickness of the reticular basement membrane and a change in the arrangement of the extracellular matrix was observed, with more tissue surface being occupied by collagen with a less dense organization of fibers [18,19].

Additionally, certain cytokines contribute to airway inflammation, including TGF- β , which plays a complex role in the development of severe asthma. This cytokine is produced by various cell types, such as epithelial cells, eosinophils, macrophages, fibroblasts, and helper T cells, and is involved in processes like epithelial transformation, subepithelial fibrosis, airway smooth muscle remodeling, microvascular alterations, mucus secretion, and the regulation of inflammatory cytokines, both through activation and suppression. In asthmatic airways, TGF- β 1 expression is significantly elevated. A notable decline in TGF- β 1 levels after BT suggests a potential role in reducing inflammation and fibrosis within the initial weeks following treatment [20].

The effect of bronchial thermoplasty on the reduction of ASM mass is demonstrated in the TASMA international multicenter randomized controlled trial. In this study 40 patients were randomized to either an immediate BT treatment group or a control group with a sixmonth delay before receiving BT. In the group that received immediate treatment, desmin-positive ASM mass was reduced by 53%, decreasing from 8.75% to 4.14%. In contrast, the delayed treatment group showed no significant change, with ASM mass measuring 7.08% at the time of randomization and 7.56% following six months of standard care. A comparable

pattern was observed for α -SMA-positive ASM mass. Although ACQ and AQLQ scores showed improvement, there was no correlation between baseline ASM mass, post-BT ASM mass, or changes in ASM mass and the enhancements in ACQ and/or AQLQ scores [21].

Long-lasting clinical efficacy was also shown in the 2024 study by confirming a sustained reduction in ASM mass of >50% 2.5 years after BT [22].

In a 2015 study, 17 patients underwent bronchial thermoplasty over 3 visits. Bronchial biopsies were then collected at three visits, and the samples were evaluated histologically and immunohistochemically. Bronchial thermoplasty led to a reduction in airway smooth muscle area, decreasing from a mean of 12.9% of the total biopsy area at the first visit to 4.6% at the second visit. Among the nine patients who had a third biopsy, the average airway smooth muscle area measured a mean of 5.3% at Visit 3. Additionally, it lowered subbasement membrane collagen type I deposition, which declined from a mean of 6.8 µm at visit 1 to 4.3 µm at visit 2. and remained at a mean of 4.4 µm in nine patients by visit 3. One year post-treatment, improvements were observed in inhaled corticosteroid dosage, the frequency of severe exacerbations, and asthma control. These results, however, cannot be sufficient to determine the correlation between clinical improvement and the analyzed histological parameters [23].

A complementary effect of BT is to reduce the number of nerve fibers in the submucosa and smooth muscle layers, which results in a weakening of the nervous reflexes that could otherwise lead to bronchospasm and this effect is associated with clinical improvement [24].

Influence of bronchial thermoplasty on respiratory resistance and airway volume

Bronchial thermoplasty also contributes to the expansion of airway volume, reduced airway resistance, and air trapping, complementing its primary effect of decreasing airway smooth muscle mass and improving symptoms following treatment [25,26].

In the 2020 research, lung plethysmography and computed tomography were used to assess the change in airway resistance and volume before and after BT therapy. After BT, there was an improvement in respiratory resistance, a decrease in residual volume, an increase in vital capacity, and no change in FEV1. Computed tomography showed an enlargement in airway volume [27].

Another study also demonstrated a significant reduction (28%) in total airway resistance determined by plethysmography after BT therapy [26].

In a separate study, a rise in total airway volume was observed twelve months after bronchial thermoplasty, which was associated with better symptom control [28].

Moreover, in a subsequent study using xenon ventilation computed tomography, it was observed that after BT, air trapping in the lungs decreased along with the alleviation of asthma symptoms, and enhancement in peripheral lung ventilation was noted in both treated and untreated areas [29].

Comparison between bronchial thermoplasty and biological therapy

Monoclonal antibodies and bronchial thermoplasty (BT) may be used as additional treatment options for asthma with uncontrolled symptoms despite maximal doses of inhaled corticosteroids and long-acting bronchodilators, that is severe asthma. In an observational cohort study conducted at a university hospital in Australia, patients with severe asthma were divided into two groups, one group treated with BT and the other with mepolizumab. After BT, the ACQ score decreased from an initial value of 3.3 to 1.7 and following mepolizumab treatment, the ACQ score improved from a baseline of 3.7 to 1.9, after 12 months of treatment. Additionally, similar results were observed in both groups in terms of a decrease in the frequency of exacerbations, a decline in the use of reliever medications, and a reduction in the doses of oral corticosteroids. These findings indicated that bronchial thermoplasty is equally effective as mepolizumab in the treatment of severe asthma [30].

However, another study that performed a systematic review of the literature based on randomized trials revealed differences in the patient populations in the analyzed studies. As a result, despite the positive treatment effects of BT compared to omalizumab, these findings should be approached with caution. [31].

Conclusion

Bronchial thermoplasty has been demonstrated to be an effective and safe treatment method for people with severe asthma. This procedure has been proven to reduce airway smooth muscle mass, lower airway resistance, and increase airway volume. These effects translate into improved symptom control, a lower frequency of exacerbations, and an overall enhancement in patients' quality of life, as evidenced by the results of the ACQ, ACT, and AQLQ questionnaires. However, this medical intervention is considered for patients with severe asthma whose symptoms remain uncontrolled despite optimized pharmacological management, including biologic therapy.

Disclosure:

Author's contribution:

Conceptualization: Katarzyna Torbacka, Zuzanna Wróbel

Methodology: Patrycja Podlejska, Natalia Wróbel

Software: Wojciech Bednarz, Katarzyna Rozkosz

Check: Katarzyna Torbacka, Aleksandra Sosin

Formal analysis: Olga Jakubik, Wojciech Bednarz

Investigation: Joanna Kaczor, Zuzanna Wróbel, Maja Torbacka

Resources: Olga Jakubik, Maja Torbacka, Wojciech Bednarz

Data curation: Natalia Wróbel, Katarzyna Rozkosz

Writing - rough preparation: Katarzyna Torbacka, Joanna Kaczor, Patrycja Podlejska

Writing - review and editing: Maja Torbacka, Zuzanna Wróbel

Visualization: Aleksandra Sosin, Olga Jakubik

Supervision: Katarzyna Rozkosz, Patrycja Podlejska

Project administration: Katarzyna Torbacka

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Declaration of generative AI and AI-assisted technologies in the writing process

In preparing this work, the authors used the ChatGPT tool, which helped them translate and improve the language and increase readability. After using this tool, the authors have reviewed and edited the content as needed and take full responsibility for the substantive content of the publication.

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