

Cost-effectiveness of bronchial thermoplasty for severe asthmatic patients in Japan

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Abstract: Bronchial thermoplasty (BT) is an interventional endoscopic treatment for severe bronchial asthma. Some studies have shown the clinical efficacy of this intervention, but its cost-effectiveness is unclear. The aim of this study was to evaluate the cost-effectiveness of BT. We collected data from the medical records of 16 Japanese patients who were treated with BT between February 2015 and April 2017, and compared asthma-related medical expenses between the year preceding and the year following BT. Four patients were Global Initiative for Asthma (GINA) treatment step 4, and 12 were step 5. In 8 patients who had a successful response to BT, the annual asthma-related medical expenses decreased because of a reduction in hospitalization and emergency outpatient visits due to asthma attacks, and termination of the use of biologics. Most patients in the non-responder group had increased asthma-related medical costs postoperatively. The main reason for the increase in medical costs was the add-on treatment of biologics. BT was cost-effective in the responder group. If its effects continue for more than 10 years, BT will be a cost-effective treatment. Medical costs will be reduced if those who respond to BT can be identified prior to commencement of treatment.

Keywords: intractable asthma, refractory asthma, bronchial asthma

Introduction

Bronchial thermoplasty (BT) treatment applies thermal energy to smooth muscle of the airway that has been thickened by severe asthma, resulting in a reduction in thickening (1). BT has been available in Japan since February 2015 and is covered by medical insurance for patients with severe asthma aged > 18 years in whom asthma symptoms cannot be controlled despite the use of high-dose inhaled corticosteroids (ICSs) and long-acting β_2 agonists (LABAs) (2). Patients with severe asthma often do not respond to maximal pharmacological treatments with inhaled therapy or even long-term oral corticosteroids (3). Several biologics have recently been developed to reduce comorbidity due to systemic steroid use in these patients. However, biologics remain expensive and long-term use is usually inevitable (Table 1). These patients often require emergency room visits and hospitalization due to exacerbation of asthma several times a year. Such frequent exacerbations increase the patient's medical expenses, which is a heavy burden on the medical economy (4). Although several previous studies have reported that BT improved asthma-related quality of life and frequency of exacerbation, the cost

effectiveness of BT is unclear (5). We examined whether BT is an economically useful treatment for severe asthmatic patients in Japan.

Materials and Methods

The study was approved by the Institutional Review Board of the National Center for Global Health and Medicine (NCGM-G-001801-00). Written informed consent was obtained from each participant and the study was conducted according to the principles expressed in the Declaration of Helsinki. Included in the study were 19 patients with severe asthma who underwent BT at our hospital between February 2015 and April 2017. We retrospectively recorded the number of asthma medications, the number of exacerbations, and asthma-related medical expenses incurred in the year prior to and in the year following BT, and compared the pre- and post-treatment expenses. After excluding 2 patients who discontinued treatment after the second of 3 BT treatments and 1 who dropped out during the follow-up period, a total of 16 patients were included in the study. Medical expenses were calculated by aggregating the Japanese prices of asthma-related drugs.

Table 1. Biologics for bronchial asthma available in Japan

biologics	omalizumab	mepolizumab	benralizumab	dupilumab
injection interval	2 or 4 weeks	4 weeks	8 weeks	2 weeks
maintenance dose	75-600 mg	100 mg	30 mg	300 mg
cost per 4 weeks (JPY)	23,556-371,376	178,937	179,023	166,304

Medical expenses for emergency admission due to exacerbation of asthma were estimated at approximately 1,300 Japanese yen (JPY) including bronchodilator nebulizers, systemic steroid use for 5 days, and the examination fee calculated by the medical fee points decided by Ministry of Health Labor and Welfare in Japan. Medical expenses for hospitalization due to exacerbation of asthma were calculated as 143,150 JPY for a 7-day hospitalization, according to the Japanese Diagnosis Procedure Combination system of 2018. The medical cost of a course of 3 BT treatment sessions in Japan is approximately 1,300,000 JPY according to the medical fee points decided by Ministry of Health Labor and Welfare and Japanese Diagnosis Procedure Combination system of 2018. We classified the patients as responders (defined as patients who had a reduction in the number of exacerbations and the amount of asthma-related medication, or an improvement of the asthma symptoms after BT treatment; responder group) or as non-responders (non-responder group). Estimated cost-effectiveness was calculated as the difference of medical costs (one year) \times 10 (years) minus BT treatment cost.

Results

Sixteen patients with severe asthma received BT treatment between February 2015 and April 2017 (Figure 1). The median age was 51.5 years and the sex ratio was 1:1. The ratio of smokers vs. never smokers was 3:1 and the median number of exacerbations during the preoperative year was 4.5. The GINA treatment step was step 4 in 4 cases and step 5 in 12 cases. The median eosinophil count was 67/ μ L and the median total-IgE was 154 U/mL. Many of the patients had received preoperative pharmacotherapy such as high dose ICSs and LABAs in addition to long-acting muscarinic antagonists (LAMAs), leukotriene receptor antagonists (LTRAs), and theophylline. Oral steroids were administered in 6 patients and omalizumab in 7 patients (Table 2).

Table 3 lists the asthma-related medical expenses in the year preceding and following BT for responders and non-responders. The total annual asthma-related medical expenses for all 16 patients decreased by a total of about 686,273 JPY after BT. Eight patients had fewer asthma attacks after BT and were classified as responders, and 8 who did not have a reduction in the number of asthma attacks after BT were classified as non-responders. In the responder group, the number of asthma exacerbations

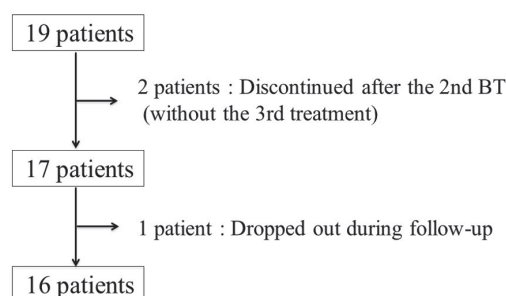


Figure 1. Overview of the study selection process. Patients who underwent BT treatment between February 2015 and April 2017.

Table 2. Patient characteristics

Characteristic	Median (range)
Age (y)	51.5 (33-77)
Gender (male/female), <i>n</i>	8/8
Smoking (never/ex), <i>n</i>	12/4
Exacerbations per year, <i>n</i>	1.5 (0-24)
Exacerbations requiring hospitalization, days	0 (0-27)
GINA step (4/5), <i>n</i>	4/12
Eosinophil, / μ L	67 (0-616)
Total IgE, U/mL	154 (29-2,318)
Medications	Median (range)
Short-acting β 2 agonist	8 (50%)
Long-acting β 2 agonist	16 (100%)
Inhaled corticosteroids	16 (100%)
Long-acting muscarinic antagonist	14 (88%)
Leukotriene receptor antagonist	15 (94%)
Theophylline	12 (75%)
Oral corticosteroids	6 (38%)
Omalizumab	7 (44%)

per year decreased from a median value of 4 times (range, 0-12) to 0 (range, 0-11), and the annual asthma-related medical costs decreased by a median value of 243,713 JPY (range, 77,341-603,099 JPY). Annual asthma-related medical expenses decreased in all responders because of a decrease in the number of hospitalization and emergency outpatient visits due to asthma attacks, and termination of the use of biologics. Of the non-responders, 4 had unchanged symptoms and 4 patients had worsening symptoms after the BT procedure. There was no change in the number of asthma exacerbations in this group and some patients increased the dose of asthma medications or introduction of biologics after the BT treatment. Accordingly, the annual asthma-related medical costs increased by a median value of 157,534

Table 3. Asthma-related medical expenses one year prior to and following BT

Group	No.	Sex	Age (y)	Preoperative medical expenses (JPY)	Postoperative medical expenses (JPY)	Difference (JPY)	Main reason of change of medical expenses	Estimated cost-effectiveness of BT for 10 years (JPY)	
Responders	1	M	67	4,353,018	4,159,702	193,316	No hospitalization	633,160	
	2	F	71	1,173,150	570,051	603,099	Withdrawal of biologics	4,730,990	
	3	F	65	846,508	381,754	464,754	No hospitalization	3,347,540	
	4	M	55	848,567	505,355	343,212	No need for frequent SABA inhalation	2,132,120	
	5	M	62	556,261	478,920	77,341	No need for intravenous steroid administration	-526,590	
	6	M	48	414,241	317,694	96,548	Reduction of ER visits	-334,520	
	7	F	77	1,144,055	1,065,650	78,405	Disappearance of asthma attacks	-515,950	
	8	M	46	646,140	352,031	294,109	No need for oral steroids	1,641,090	
			Sub total	9,981,940	7,831,157	2,150,783		11,107,840	
Non-responders	9	F	33	3,798,768	3,756,726	42,042	Frequent asthma attack	-879,580	
	10	F	43	326,941	316,631	10,310	Symptoms unchanged	-1,196,900	
	11	M	36	2,859,716	3,017,250	-157,534	New biologics use	-2,875,340	
	12	F	69	224,402	565,945	-341,543	Frequent asthma attack	-4,715,430	
	13	M	47	5,278,305	2,799,666	2,478,639	Switching biologics	23,486,390	
	14	M	68	381,846	2,599,006	-2,217,160	New biologics use	-23,471,600	
	15	F	35	2,936,701	2,935,568	1,133	New biologics use	-1,288,670	
	16	F	40	652,241	1,932,638	-1,280,397	New biologics use	-14,103,970	
				Sub total	16,458,920	17,923,430	-1,464,510		-25,045,100
				Total	26,440,860	25,754,587	686,273		-13,937,260

JPY (range, -2,478,639 to 2,217,160 JPY). The main reason for the increase in medical costs was add-on biologic treatments such as omalizumab or mepolizumab. The medical cost decreased significantly in 1 patient, but this was due to a change in biologic from omalizumab to mepolizumab, but there was no significant improvement in symptoms.

The cost-effectiveness of BT was estimated in Table 3 if the effect of BT continues for 10 years. The cost-effectiveness of BT was not observed in the total 16 patients. However, the average cost-effectiveness of BT was observed in BT responders (1,388,479 JPY for 10 years per person).

Discussion

There are 2 types of medical costs: direct costs (hospital consultation costs, drug prices, hospitalization costs) and indirect costs (social costs arising from taking leave from work, *e.g.*, due to asthma attacks). In this study, we investigated and compared only the direct costs; however, we consider that the remission of asthma in the responder group after BT retreatment also reduced the indirect costs, and that if the direct and indirect costs were combined, the treatment would be even more cost-effective. In a previous study that examined the cost-effectiveness of standard therapy, BT, and omalizumab over 5 years in patients with moderate to severe asthma in Canada, BT was cost-effective in > 60% of patients (6). A study of the cost-effectiveness of BT and high-dose combination therapy in patients with severe persistent asthma in the USA using quality-adjusted life year (QALY)/incremental cost-effectiveness ratio (ICER)

found that BT was cost-effective in about 66% of patients (7). In another study in the USA, BT was estimated to be cost-effective in patients with severe uncontrolled asthma who had a high risk of exacerbation (8). In contrast, a study that examined the cost-effectiveness of patients with severe asthma in Singapore who received standard therapy alone or standard therapy plus BT showed that BT was not cost-effective (9). It is important to note that the results of these previous studies differ slightly because the costs of BT and emergency outpatient consultation differ among these countries. In addition, there is selection bias in patients who received BT, (*e.g.*, severity) in clinical practice in each country. In the present study, 5 patients (31%) had markedly increased asthma-related medical expenses following BT, caused mainly by the introduction of new biologics to treat the unchanged symptoms. The factors that are predictors of response to BT are not yet known. The identification of responders prior to BT treatment would enable a further reduction in medical costs.

A recent study of 192 patients enrolled in Asthma Intervention Research (AIR), AIR2, or Research in Severe Asthma (RISA) trials demonstrated that a reduction in severe exacerbation continued for more than 10 years after BT treatment (median, 12.1 years; range, 10.6-15.8 years) (10). Based on the estimated annual reduction in asthma-related medical expenses shown in Table 3, we would expect savings to exceed direct BT treatment costs (approximately 1.3 million JPY) within 10 years after BT in 5 of the responders. So far, there is evidence only that the effects of BT will last for 10 years (10); however, if the therapeutic effects continue for more than 10 years, further cost-effectiveness of BT can

be expected.

A recent previous study reported that baseline Asthma Control Questionnaire (ACQ) score and exacerbation frequency were a predictor of BT responders (11). In our study, the median number of asthma exacerbations in the responder group during the preoperative year was 4 times (0-12) and the median number of asthma exacerbations in the non-responder group was 0 times. Our results supported the previous study that the number of preoperative asthma exacerbations is one of the factors for predicting BT responders.

There are several limitations in this study. First, the number of patients is small, the study design is retrospective, and it was conducted at a single center. Second, the preoperative annual medical expenses were estimated according to the number of asthma exacerbations. The actual direct expenses for each patient may differ slightly from the estimated expenses. A large prospective multi-center study is required to further elucidate the cost-effectiveness of BT.

In conclusion, in terms of the calculated asthma-related medical expenses after treatment, BT therapy was cost-effective in responders. Identification of BT responders will further increase the cost-effectiveness of BT.

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