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ORIGINAL RESEARCH

Long Term Efficacy and Safety of Bronchoscopic Thermal Vapor Ablation in Patients with COPD: A Retrospective Study of 50 Patients

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Background: Bronchoscopic Thermal Vapor Ablation (BTVA) has demonstrated improvements in FEV1 and quality of life in clinical trials. However, the long-term benefits and overall efficacy of this procedure remain uncertain and are not yet fully established.

Methods: We conducted a retrospective observational study of all patients who underwent BTVA at Rabin Medical Center, Israel. The primary outcome was the change in FEV_1 from baseline. Secondary outcomes included other pulmonary function parameters and procedural adverse events.

Results: A total of 50 patients were included in the study. The mean FEV1 values at baseline, 6 months, and 12 months post-procedure (n=31) were 0.74±0.21 L, 0.93±0.32 L, and 0.85±0.25 L, respectively (overall P<0.001; pairwise comparisons: baseline to 6 months, P<0.001; baseline to 12 months, P=0.016). The mean FVC values at baseline, 6 months, and 12 months post-procedure (n=31) were 1.97±0.56 L, 2.27±0.71 L, and 2.14±0.68 L, respectively (overall P=0.003; pairwise comparisons: baseline to 6 months, P=0.002; baseline to 12 months, P=0.125). Post-procedural complications included pneumonia in 5 patients (11%), of whom 3 developed necrotizing pneumonia and subsequently died, resulting in a 6% post-procedural mortality rate in the entire cohort. Hemoptysis was reported in 1 patient (2%).

Conclusion: Bronchoscopic thermal vapor ablation is a minimally invasive bronchoscopic intervention for lung volume reduction. The procedure was associated with significant improvements in FEV_1 at 6 to 12 months and in FVC at 6 months, followed by a gradual decline over 12 to 24 months. Further research is warranted to optimize patient selection, enhance procedural safety, and assess long-term efficacy.

Plain Language Summary: COPD is a disease that damages lung tissue. The damaged areas become hyperinflated, compressing healthier parts of the lung and reducing their function. Bronchoscopic Thermal Vapor Ablation (BTVA) is a minimally invasive treatment that uses heated water vapor to target and shrink these damaged areas. During the procedure, a thin tube with a camera (bronchoscope) is inserted into the lungs to deliver vapor directly to diseased regions. The vapor causes controlled injury, leading to shrinkage of the targeted tissue and allowing healthier lung areas to expand and function more effectively. BTVA can be repeated by treating different regions over time, potentially maintaining its benefits.

In this study, we evaluated the effectiveness and safety of BTVA in patients with advanced COPD. Lung function improved significantly at 6 and 12 months compared to baseline. Between 12 and 24 months, the benefits gradually declined but remained above baseline.

Side effects were primarily pneumonia and temporary coughing up of blood, which resolved in most cases. However, three patients developed severe pneumonia and died, highlighting the need for further research.

In conclusion, BTVA improved lung function, but careful selection of treatment areas and energy levels is important to reduce complications and enhance safety.

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Introduction

Bronchoscopic Thermal Vapor Ablation (BTVA) is a bronchoscopic lung volume reduction (BLVR) technique designed for patients with Chronic Obstructive Pulmonary Disease (COPD). This approach employs thermal energy in the form of vapor to induce tissue inflammation, which is subsequently followed by fibrosis, resulting in a reduction in the volume of the treated lung segment or subsegment. BTVA was first introduced in 2009 as a novel method for managing hyperinflation in COPD patients.[1,2]

The initial clinical trial of BTVA was a single-arm study involving 44 patients, which demonstrated significant improvements in clinical outcomes with a low incidence of adverse events.[3] In 2016, the first and only multicenter randomized controlled trial with BTVA was published (STEP-UP trial), including 45 patients in the BTVA group and 24 controls. Results after six months showed an improvement of 14.7% in Forced Expiratory Volume in one second (FEV_1).[4] The 12-month follow-up showed a 9.2% improvement in FEV_1 compared to a decrease of 5.4% in the control group.[5]

Additional small trials have also been published, reporting good safety and variable clinical efficacy.[6,7] In 2023, Kontogianni et al presented real-life experience with BTVA and extended follow-up of 36 months at the European Respiratory Society (ERS) conference. This abstract included 204 patients from 10 clinical sites, encompassing a total of 314 BTVA procedures. Statistically significant improvements were observed in the St. George's Respiratory Questionnaire (SGRQ) and Residual Volume (RV) at 12 and 24 months, respectively. However, changes in FEV_1 and the 6-Minute Walk Test (6-MWT) did not achieve statistical significance.[8]

Although BTVA is a minimally invasive and potentially cost-effective procedure for BLVR, there is a paucity of clinical trial data, and its efficacy and safety remain inconclusive. Our aim in this study is to provide additional clinical and safety data regarding BTVA as a treatment option for patients with COPD.

Methods

This is a single-center, retrospective, observational study designed to evaluate the efficacy and safety of BTVA in patients with COPD. The study was conducted at Rabin Medical Center in Israel between March 2020 and December 2024.

Study Population

The study included all COPD patients who underwent BTVA at Rabin Medical Center and met the inclusion criteria, with no exclusion criteria applied.

Study Endpoints

The primary outcome was the change from baseline in FEV_1 (L) at 12 months. Secondary outcomes included changes from baseline in forced vit FVC (L), carbon monoxide diffusing capacity (DLCO, % predicted), residual volume (RV, L), and 6MWT distance (meters). Patients were included in the final 12-month analysis only if they had completed measurements at baseline, 6 months, and 12 months, and in the 24-month analysis only if they had completed measurements at baseline, 12 months, and 24 months.

Data Collection

Data collection for the 6-month, 12-month, and 24-month time points occurred within 4–8 months, 10–18 months, and 20–28 months, respectively, ensuring a minimum interval of 4 months between assessments. Pulmonary function tests were conducted using the ZAN 300 nSpire Health system. Lung volumes, including total lung capacity (TLC) and residual volume, were measured with a Pressure (Closed-Type) Plethysmograph. Diffusion capacity was assessed using the single-breath method with 0.3% carbon monoxide.

Procedure-related adverse events were documented from the date of the procedure until 1 month post-procedure, while hospital admissions and mortality were tracked throughout the follow-up period. Since post-procedural infiltrates are common, we defined pneumonia/pneumonitis only in cases where the patient was either not discharged within 24 hours or was readmitted due to clinical deterioration with compatible radiological findings. COPD exacerbation was defined as clinical deterioration without a radiological pattern consistent with pneumonia/pneumonitis.

The study complies with the Declaration of Helsinki and was approved by the Rabin Medical Center institutional ethical review board (IRB number: 0602-24-RMC).

Statistical Methods

Continuous variables were presented as mean ± standard deviation (SD) or median with interquartile range (IQR), as appropriate. Demographic and baseline characteristics were compared using the chi-square test or Mann–Whitney *U*-test, based on data distribution. The primary outcome was analyzed using a repeated measures general linear model, with results reported as estimated marginal means. Pairwise comparisons were adjusted for multiple testing using the Bonferroni correction. Only patients with complete data at all relevant time points were included in the repeated measures analysis. A two-sided P-value ≤0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 29.

Procedure Flow

The BTVA procedure was performed using the InterVapor® Bronchoscopic Thermal Vapor Ablation system. Prior to the procedure, an updated chest CT scan was analyzed by Uptake Medical® to develop a personalized treatment plan, which included assessing the severity of disease in each lung segment and selecting appropriate energy levels based on the patient's anatomy. The energy level was calibrated according to the duration, in seconds, of vapor release into each segment.[9] Once the targeted segments were identified, the procedure commenced. All procedures were conducted in the bronchoscopy suite under moderate sedation, utilizing midazolam (1 mg), fentanyl (50–100 mcg), and propofol (dosed according to procedure duration). The targeted lobe and subsegments were first identified, and the bronchoscope was positioned at the ostium of the segment or subsegment to be treated. The disposable InterVapor catheter was then placed into the segment, and the catheter balloon was inflated. Thermal energy was delivered to the segment, and this process was repeated for each targeted segment. Post-procedure, patients were monitored in recovery for 1–2 hours before being admitted to the internal medicine ward. Post-procedural care included prednisone at 40 mg daily for 7 days and ciprofloxacin 500 mg twice daily for 7 days. Patients without complications were discharged after 24 hours.

Results

A total of 50 patients from Rabin Medical Center were included in the study. The median follow-up time was 19 months (IQR 12–38). The mean age of the cohort was 65.7 ± 5.9 years, and 28 (65%) were male. Most patients were classified as GOLD stage 3–4 (96%), and the median BODE score was 7 (IQR 5.5–7.5) (Table 1).

Mean FEV_1 values at baseline, 6 months, and 12 months post-procedure (n = 31) were 0.74 ± 0.21 L, 0.93 ± 0.32 L, and 0.85 ± 0.25 L, respectively (overall P < 0.001). Pairwise comparisons between baseline and 6 months, and baseline and 12 months, yielded P-values of <0.001 and 0.016, respectively. Mean FVC values at baseline, 6 months, and 12 months (n = 31) were 1.97 ± 0.56 L, 2.27 ± 0.71 L, and 2.14 ± 0.68 L, respectively (overall P = 0.003). Pairwise comparison showed a significant improvement in FVC at 6 months compared to baseline (P = 0.002), while the difference between baseline and 12 months was not statistically significant (P = 0.125).

Mean residual volume (RV) values at baseline, 6 months, and 12 months (n = 18) were 4.89 ± 1.25 L, 4.66 ± 1.22 L, and 4.92 ± 1.20 L, respectively (overall P = 0.38). Six-minute walk distance (6MWD) data were available for 15 patients. Mean distances at baseline, 6 months, and 12 months were 288.7 ± 78.5 m, 323.0 ± 108.6 m, and 309.9 ± 127.2 m, respectively (overall P = 0.294). Pulmonary function test and 6MWD results are summarized in Table 2 and Figure 1.

An extended two-year follow-up was available for 20 patients, with 14 having documented pulmonary function test results at 24 months. For these 14 patients, mean FEV_1 values at baseline, 12 months, and 24 months were 0.67 ± 0.15 L,

Table 1 Baseline Clinical and Demographic Characteristics

Number of patients		50
Age[b]		65.74 (5.92)
Male gender (%)		29 (66%)
Baseline FEV1 L[a]		0.69 (0.56–0.91)
Baseline FEV1 %pred[a]		29 (22–34)
Baseline FVC L[a]		1.88 (1.41–2.52)
Baseline FVC %pred[a]		61 (50–70)
Baseline TLC L[a]		7.11 (5.98–9.06)
Baseline TLC %pred[a]		123 (111–141)
Baseline RV L[a]		5.46 (4.10–6.38)
Baseline RV %pred[a]		247 (190.5–273)
Baseline DLCO %pred[a]		30 (25.5–37.5)
GOLD stage	4	28 (56%)
	3	20 (40%)
	2	2 (4%)
	1	0
BODE score[a]		7 (5.5–8.5)
Supplemental Oxygen (%)		28 (56%)
Pack years[a]		57 (40–70)
DM (%)		7 (14%)
HTN (%)		17 (34%)
IHD (%)		14 (28%)
Follow up time, Months[a]		19 (12–38)

Notes: [a]Data presented in median and (IQR); [b]Data presented in mean and (SD).

Abbreviations: FEV1 %pred, forced expiratory volume in the first second percent predicted; DLCO %pred, carbon monoxide diffusing capacity percent predicted; Baseline TLC %pred, total lung capacity percent predicted; BODE score, BMI, obstruction, dyspnea, and exercise capacity; DM, diabetes mellitus; HTN, hypertension; IHD, ischemic heart disease; IQR, interquartile range.

0.81 ± 0.25 L, and 0.78 ± 0.22 L, respectively (overall P = 0.10). Pairwise comparisons between baseline and 12 months, and baseline and 24 months, yielded P-values of 0.099 and 0.114, respectively.

Mean FVC values at baseline, 12 months, and 24 months were 1.80 ± 0.52 L, 2.06 ± 0.71 L, and 1.97 ± 0.70 L, respectively (overall P = 0.043). Pairwise comparisons between baseline and 12 months, and baseline and 24 months, yielded P-values of 0.140 and 0.661, respectively (Figure 2).

Post-procedural complications included pneumonia in 5 patients (11%), hemoptysis in 1 patient (2%), and COPD exacerbation in 2 patients (4%). Overall, 7 patients died during the follow-up period. Three deaths were post-procedural,

Table 2 Clinical Outcomes in Patients Who Underwent Bronchoscopic Thermal Vapor Ablation at 6 and 12 Months Post-Procedure

	N*	Baseline	6 Months	12 Months	P value		
					Overall	Baseline vs 6 Months	Baseline vs 12 Months
FEV1	31	0.74 (0.21)	0.93 (0.32)	0.85 (0.25)	<0.001	<0.001	0.016
FVC	31	1.97 (0.56)	2.27 (0.71)	2.14 (0.68)	0.003	0.002	0.125
RV	18	4.89 (1.25)	4.66 (1.22)	4.92 (1.20)	0.389	1.0	1.0
6MWTD	15	288.67 (78.47)	323.00 (108.60)	309.87 (127.22)	0.294	0.697	1.0

Note: *The analysis included only patients with data in all time points.
Abbreviations: FEV1, forced expiratory volume in the first second; FVC, Forced vital capacity; RV, residual volume; 6MWTD, six-minute walk test distance.

resulting from necrotizing pneumonia that developed within 2 weeks post-procedure. Four additional patients died during follow-up from causes unrelated to the procedure at 2, 13, 15, and 18 months post-procedure (Table 3).

Discussion

The search for a safe and effective bronchoscopic lung volume reduction (BLVR) technique has been a focus of ongoing research for several years. To date, only endobronchial valves have demonstrated sufficient efficacy to gain FDA approval.[10] Nonetheless, the pursuit of simpler, faster, and more cost-effective methods remains a priority. In this retrospective study, we evaluated 50 patients who underwent BLVR using bronchial thermal vapor ablation (BTVA). We have presented two time points for analysis. The main analysis, a repeated-measures assessment at 12 months, included 31 patients and demonstrated significant improvements in FEV1 and FVC and no difference in RV and

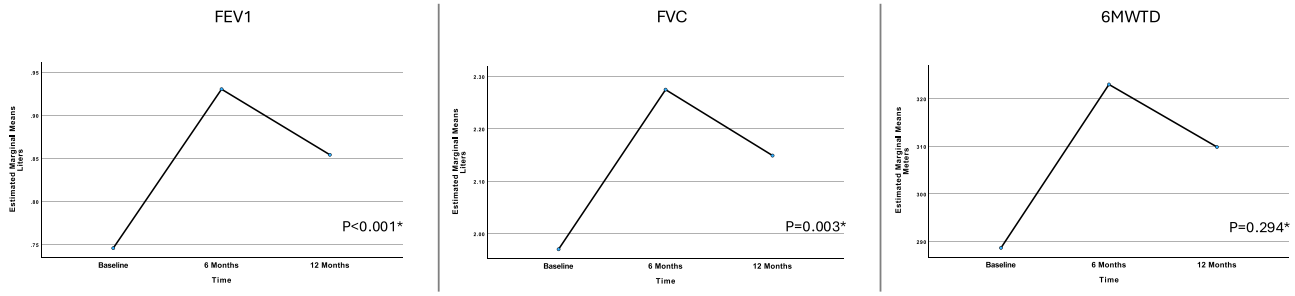

Figure 1 Repeated measures analysis of FEV1, FVC values and 6MWT distance at baseline and at 6- and 12-months post procedure (n=31, 31 and 15 respectively). *P values represent overall significance from repeated measures general linear model analysis.

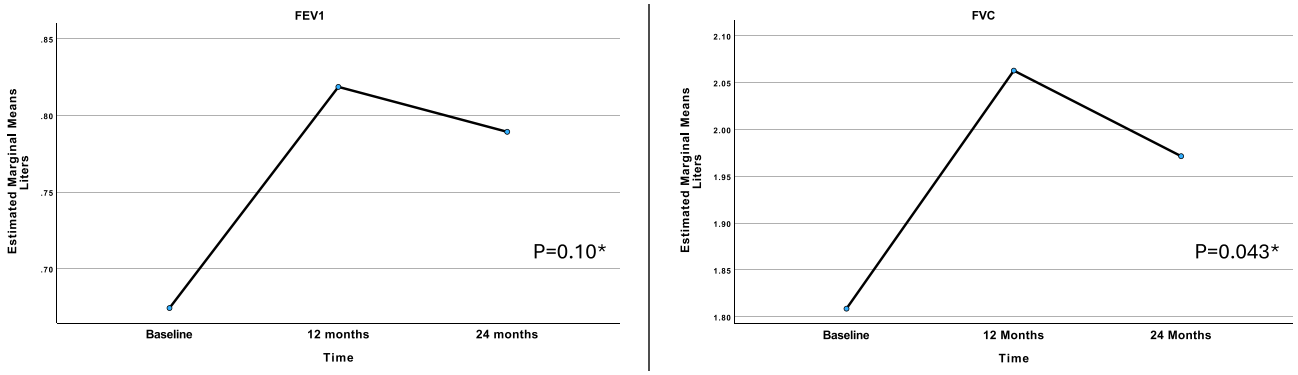

Figure 2 Extended follow-up: Repeated measures analysis of FEV1 and FVC values at baseline, 12 months, and 24 months post-procedure (n=14). *P values represent overall significance from repeated measures general linear model analysis.

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Table 3 Adverse Events and Overall Cohort Mortality

Adverse Event	Number of Events
Pneumonia	5 (10%)
Hemoptysis	1 (2%)
COPD exacerbation	2 (4%)
Procedure related mortality	3 (6%)
Overall mortality during FU	7 (14%)

Abbreviation: FU, Follow up.

6MWTD. The second analysis, a repeated-measures assessment at 24 months, included 14 patients. While this analysis did not reach statistical significance, it showed a similar trend with an initial improvement at 6–12 months followed by a gradual decline from 12 to 24 months.

These results align with real-world BTVA data, which show maximum effect at 6–12 months followed by a gradual decline until a return to baseline values at 24–36 months.[8] This pattern of initial improvement followed by gradual decline is consistent with other BLVR techniques, such as endobronchial coils and valves.[11–14] The gradual decline is likely due to the continued progression of the underlying disease, as BLVR does not alter the disease course but temporarily reduces lung overinflation, allowing previously compressed healthy lung tissue to expand. Compared to the steady decline seen in untreated patients, achieving an initial improvement—even with a gradual decline afterward—is a meaningful benefit.

What distinguishes BTVA from other BLVR methods is its potential for repeatability. The procedure is straightforward, brief, and allows for precise targeting of the most affected subsegments. As lung function and exercise capacity gradually decline after the initial benefit, the treatment can be repeated in different subsegments to restore some of the benefits, potentially extending the period of improved function. From our personal experience, three patients underwent repeated BTVA 1–2 years after the initial procedure with good results. However, open questions remain, as it has yet to be demonstrated in clinical trials whether sequential procedures continue to provide sustained benefits beyond the initial treatments.

Our study raises some safety concerns regarding BTVA due to three (6%) procedure-related deaths. Post-procedural pneumonia, COPD exacerbation, and mortality have been reported in previous trials. The STEP-UP trial reported three (9%) COPD exacerbations and eight (23%) cases of pneumonia in the BTVA group, with one mortality (3%).[4] Real-world data on BTVA reported 97 procedure-related serious adverse events (SAEs) in 314 BTVA procedures, including 26 COPD exacerbations, 30 pneumonias, and 6 cases of hemoptysis, although the number of deaths was not reported.[8] In our experience, after observing a higher rate of early SAEs, we made several modifications to our procedural approach in an attempt to improve safety. Specifically, we avoided treating the RB3 and LB3 segments, which appeared to carry a higher risk of post-procedural bleeding, and instead focused on treating RB1, RB2, LB1, and LB2. Additionally, we limited treatment to no more than two segments per side and discharged patients with a 10-day regimen of oral glucocorticoids and antibiotics. Following these adjustments, we observed a reduction in adverse events. However, it is important to emphasize that these measures were not part of the original study design and were applied in a limited number of cases. As such, these findings should be interpreted with caution until validated in prospective clinical trials.

Our study has several limitations. First, its retrospective design resulted in information bias, with incomplete data in some patients leading to dropout from a repeated-measures analysis, which requires complete data at all time points. Selection bias was likely minimized, as we included all cases of BTVA performed at our center. Second, the lack of a control group limits our ability to directly assess whether there is a significant improvement in lung function and exercise capacity attributable to BTVA. However, given the significant improvement observed in paired analyses compared to baseline and the typically progressive course of COPD, our results likely reflect a true improvement in

lung function following BTVA. Third, the cohort size is relatively small (50 patients). However, when compared to existing literature, this represents a moderate sample size for studies of this nature. Finally, the follow-up duration is limited. Only 31 patients reached the one-year follow-up mark, and 14 reached the 24-month follow-up, making it challenging to fully evaluate the long-term benefits of BTVA.

In conclusion, bronchoscopic thermal vapor ablation is a minimally invasive bronchoscopic intervention for lung volume reduction. In this retrospective study of 50 patients, the procedure was associated with significant improvements in FEV_1 at 6–12 months and in FVC at 6 months, with a gradual decline observed over 12–24 months. While re-treatment during this period may offer renewed benefit, this approach has not yet been evaluated in prospective trials. Further research is needed to refine patient selection, improve safety, and evaluate long-term outcomes.

Data Sharing Statement

The data supporting the findings of this study are available from the corresponding author, Dr. Barak Pertzov (BP), upon reasonable request.

Ethics Approval and Informed Consent

The study was approved by the Rabin Medical Center Institutional Ethical Review Board (IRB number: 0602-24-RMC). Since this was a retrospective study that collected anonymized data, the IRB committee determined that obtaining informed consent was unnecessary.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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