University of Groningen

Response to Endobronchial Valve Treatment in Emphysema Patients With Moderate Hyperinflation

Klooster, Karin; Hartman, Jorine E; van Dijk, Marlies; Koster, Theodoor David; Slebos, Dirk-Jan

Published in:
Journal of bronchology & interventional pulmonology

DOI:
[10.1097/LBR.0000000000000705](https://doi.org/10.1097/LBR.0000000000000705)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2021

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Klooster, K., Hartman, J. E., van Dijk, M., Koster, T. D., & Slebos, D-J. (2021). Response to Endobronchial Valve Treatment in Emphysema Patients With Moderate Hyperinflation. *Journal of bronchology & interventional pulmonology*, 28(1), e14-e17. <https://doi.org/10.1097/LBR.0000000000000705>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

silicone high tracheal stents.^{4,5} However, infection at the stitch site is a possible complication. Deploying a stent of adequate size is of utmost importance for preventing future stent migration. In our patient, stent removal under direct laryngoscopic guidance was also considered. This approach could be helpful, as it would have allowed removal under direct vision, followed by intubation with an endotracheal tube or rigid bronchoscope. However, the rigid bronchoscopic approach was considered safer to provide a conduit for removing the stent, preventing upper airway damage, and for handling any possible airway complications.

Manu Madan, MD
Avinash Jain, MD
Saurabh Mittal, MD, DM
Anant Mohan, MD, PhD
Karan Madan, MD, DM

Department of Pulmonary, Critical Care and Sleep Medicine, All India Institute of Medical Sciences (AIIMS), New Delhi, India

REFERENCES

1. Madan K, Dhoria S, Sehgal IS, et al. A multicenter experience with the placement of self-expanding metallic tracheobronchial Y stents. *J Bronchology Interv Pulmonol*. 2016; 23:29–38.
2. Madan K, Shrestha P, Garg R, et al. Bronchoscopic management of critical central airway obstruction by thyroid cancer: combination airway stenting using tracheal and inverted-Y carinal self-expanding metallic stents. *Lung India*. 2017;34: 202–205.
3. Amour J, Soummer A, Langeron O, et al. Emergency treatment of tracheobronchial stent migration. *Anesthesiology*. 2004;101:1230–1232.
4. Mehta RM, Singla A, Shah A, et al. The “hitch stitch”: an effective method of preventing migration in high tracheal stenosis. *Respiration*. 2017;93:106–111.
5. Dhoria S, Agarwal R. External fixation of a subglottic tracheal

silicone stent. *Ann Am Thorac Soc*. 2014;11:467–468.

6. Schmidt B, Massenkeil G, John M, et al. Temporary tracheobronchial stenting in malignant lymphoma. *Ann Thorac Surg*. 1999;67:1448–1450.

Response to Endobronchial Valve Treatment in Emphysema Patients With Moderate Hyperinflation

To the Editor:

The magnitude of hyperinflation in severe emphysema is very closely associated with poor survival outcomes.¹ Furthermore, severe hyperinflation in these patients is directly associated with worse patient-centered outcomes such as dyspnea and exercise limitation.²

In carefully selected chronic obstructive pulmonary disease patients with severe emphysema and hyperinflation, bronchoscopic lung volume reduction (BLVR) treatment using 1-way endobronchial valves has been shown to significantly improve pulmonary function, exercise tolerance, quality of life, and predictors of survival.^{3–8} Besides hyperinflation being the main patient limitation, the key factors for clinical benefit are a suitable treatment target lobe, absence of collateral ventilation and complete lobar occlusion.

The key question in lung volume reduction treatments is the amount of hyperinflation needed to achieve clinical

benefit after intervention. In prior randomized controlled trials investigating BLVR using valves, the mean baseline residual volume (RV) of the enrolled patients was between 210% and 275% of predicted.^{3–7,9} In these trials, the inclusion criteria for RV were equal to or greater than either 150%,^{7,9,10} 175%^{4,5} in patients with heterogenous emphysema or 200%⁶ in patients with homogenous emphysema. This indicates that on average these trials treated patients with very severe hyperinflation. The question arises if patients with less hyperinflation could also benefit from BLVR using valves. Previous studies showed that greater heterogeneity of emphysema between target lobe and adjacent lobe, and absence of collateral ventilation appear to identify patients with a greater likelihood of clinically important functional and physiological responses to endobronchial-valve therapy. Our hypotheses is that emphysema patients with moderate hyperinflation can also clinically benefit from endobronchial valve treatment, as measured by a reduction in RV, improved FEV₁, 6-minute walking distance, and quality of life.

To address this question, we performed a single-center retrospective analysis of patients with moderate hyperinflation, defined as a postbronchodilator RV measured with body plethysmography equal to or less than 175% of the predicted value. We included all patients with moderate hyperinflation who underwent BLVR with Zephyr endobronchial valves (PulmonX, Redwood City, CA) after Chartis assessment (PulmonX) in our center between 2010 and 2019. All patients provided written informed consent.

At baseline a quantitative high-resolution computed tomography (HRCT) analysis was

Disclosure: K.K. received travel reimbursement and speakers fee from PulmonX Inc. D.-J.S. received travel reimbursement and speakers fee from PulmonX Inc. and is adviser for CSA medical and Nuaira. The remaining authors have no conflict of interest or other disclosures.

DOI: 10.1097/LBR.0000000000000705

TABLE 1. Effectiveness Outcomes in Change From Baseline at 1 and 6 Months Follow-up (N = 12)

	Baseline	1-Month FU	6-Month FU
FEV₁			
Absolute value (L)	0.95 [0.53 to 1.78]	1.29 [0.82 to 1.94]	1.38 [0.74 to 1.91]
Relative change from baseline (%)		+21 [0 to +57]	+24 [+2 to +61]
MCID (+10%) responder rate		67%	91%
FVC			
Absolute value (L)	3.03 [1.55 to 4.67]	3.04 [2.01 to 4.51]	3.23 [1.94 to 4.73]
Relative change (%)		+5 [−6 to +35]	+7 [+1 to +47]
RV			
Absolute value (L)	3.46 [2.44 to 4.45]	2.82 [2.01 to 4.51]	2.80 [2.05 to 4.04]
Relative change from baseline (%)		−17 [−49 to +7]	−19 [−36 to +4]
MCID (−8.6%) responder rate		72%	63%
RV/TLC			
Absolute value (%)	51 [42 to 63]	45 [32 to 53]	46 [38 to 54]
Absolute change from baseline (%)		−8 [−33 to +6]	−15 [−26 to +4]
MCID (−4%) responder rate		63%	81%
SGRQ			
Points	59 [38 to 72]	36 [4 to 55]	40 [4 to 49]
Absolute change from baseline—points		−19 [−56 to +5]	−20 [−56 to +5]
MCID (−7 points) responder rate		83%	91%
6-minute walk distance			
Distance (m)	403 [285 to 518]		485 [335 to 586]
Absolute change from baseline (m)			+83 [−10 to +220]
MCID (+26 m) responder rate			55%

Values are presented in median [minimum to maximum]. To test for difference between baseline and follow-up a Wilcoxon Signed Ranks test was used. All outcomes were statistically significant compared with baseline ($P < 0.05$). The following thresholds were used; for FEV₁ we used the MCID threshold of +10%, for 6-minute walking distance +26 m,¹¹ for residual volume −8.6%,¹² and for SGRQ −7 points.¹³ Response rates were calculated by counting the number of patients for whom the change at 1 and at 6 months met or exceeded the minimal clinically important difference.

FEV₁ indicates forced expiratory volume in 1 second; FU, follow-up; FVC, forced vital capacity; MCID, minimal clinically important difference; RV, residual volume; SGRQ, Saint George Respiratory Questionnaire; TLC, total lung capacity.

performed (Thirion B.V., Nijmegen, the Netherlands). Furthermore, lung function measures, quality of life questionnaire (SGRQ) and 6-minute walk test (6MWT) were performed at baseline and at 1 and 6 months after treatment.

In total, 12 patients with a RV <175% predicted were treated in the University Medical Center Groningen, the Netherlands. Which is 3% of the total volume of patients treated with valves in our center. Six male, median [range] RV 161 [130 to 175] %predicted, age 68 [56 to 70] years, FEV₁ 41 [26 to 52] %predicted, 6-minute walk distance 403 [285 to 515] m, SGRQ total score 59 [38 to 72] points, HRCT %voxel density (−950 HU) in valve treatment target lobe 46% [35% to 78%], in ipsilateral lobe 29% [16% to

44%] and in contralateral lobes 33% [9% to 46%].

At 1 and 6 months after BLVR treatment all outcomes significantly improved and were clinically meaningful (Table 1). Three (25%) patients experienced a pneumothorax, which was managed with regular care and resolved. There were no other serious adverse events and no patients died.

Our analysis demonstrates that BLVR treatment with endobronchial valves in patients with moderate hyperinflation, defined as a RV equal to or less than 175% predicted, leads to statistically significant and clinically meaningful improvements in lung function, exercise tolerance, and quality of life.

In this cohort, despite the fact that median RV was only 161% [130% to 175%] predicted,

significant and clinically relevant outcomes were shown. We propose that the main driver of this response is having a very heterogeneous emphysema distribution in the treated lung, with still a well-preserved ipsilateral lobe—and often also a well-preserved contralateral lung. In this trial, the heterogeneity was pronounced to such an extent that “eyeballing” a clear destructed target lobe could be identified on the HRCT. Figure 1 shows a case example where both lower lobes “eyeballing” are more destructed, and quantitative analysis confirmed a 29% difference in %voxel density between the EBV target left lower lobe and the adjacent left upper lobe.

Lung volume reduction using either surgery or 1-way valves aims to reduce hyperinflation by

FIGURE 1. Example case. On sagittal high-resolution computed tomography scan reconstruction, the left lower lobe is a clear treatment target lobe with overexpansion. Destruction scores of the left lower lobe compared with the right lower lobe are high, and the lung tissue in both the ipsilateral left upper lobe and the right lung are pretty well preserved. Patient was treated with 4 Zephyr endobronchial valves. Pulmonary function test and St. George Questionnaires were performed at baseline, and 1 and 6 months after bronchoscopic lung volume reduction treatment. Six-minute walk test was performed at baseline and 6 months after treatment. HU indicates hounsfield units; LLL, left lower lobe; LUL, left upper lobe; ML, middle lobe; RLL, right lower lobe; RUL, right upper lobe.

“removing” the most hyperinflated portions of the lung, leaving the remaining lung room to expand and therefore function more efficiently, also by improved elastic recoil, allowing improved breathing mechanics and therefore function more efficiently and allow improved breathing mechanics.

Previous studies have shown that patients with heterogeneous emphysema on HRCT, thus having a clear treatment target lobe had better efficacy outcomes compared with patients with homogenous emphysema.^{3,6,10} BLVR treatment with valves can be effective in patients with homogenous emphysema, however the amount of hyperinflation needs to

be very severe.⁶ Therefore, patients with moderate hyperinflation and homogenous emphysema may not respond as well as the patients with heterogeneous emphysema who have a moderate hyperinflation included in this analysis.

Despite the fact that this analysis included only a small sample size and lacks a control group, the magnitude of benefit is very pronounced and replicates the efficacy benefit of the published randomized controlled trials.^{3–7} Future prospective trial data, with a larger population and longer follow-up period are needed to confirm our results.

In conclusion, the benefit of BLVR treatment with Zephyr

endobronchial valves is not limited to only patients with severe hyperinflation. BLVR in carefully selected patients with advanced emphysema and moderate hyperinflation improves lung function, exercise tolerance, and quality of life. However, it is of great importance that a very clear treatment target lobe is identified on HRCT.

Karin Klooster, PhD
Jorine E. Hartman, PhD
Marlies van Dijk, MD
Theodoor David Koster, MD
Dirk-Jan Slebos, MD, PhD
 Department of Pulmonary
 Diseases, University Medical Center
 Groningen, University of
 Groningen, Groningen
 The Netherlands

REFERENCES

1. Casanova C, Cote C, De Torres JP, et al. Inspiratory-to-total lung capacity ratio predicts mortality in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2005;171:591–597.
2. Cooper CB. The connection between chronic obstructive pulmonary disease symptoms and hyperinflation and its impact on exercise and function. *Am J Med*. 2006;119(10 suppl 1):21–31.
3. Klooster K, ten Hacken NHT, Hartman JE, et al. Endobronchial valves for emphysema without interlobar collateral ventilation. *N Engl J Med*. 2015;373:2325–2335.
4. Criner GJ, Sue R, Wright S, et al. A multicenter RCT of Zephyr(R) endobronchial valve treatment in heterogeneous emphysema (LIBERATE). *Am J Respir Crit Care Med*. 2018;198:1151–1164.
5. Kemp SV, Slebos DJ, Kirk A, et al. A multicenter, prospective, randomized, controlled trial of endobronchial valve treatment vs standard of care in heterogeneous emphysema (transform). *Am J Respir Crit Care Med*. 2017;196:1535–1543.
6. Valipour A, Slebos DJ, Herth F, et al. Endobronchial valve therapy in patients with homogeneous emphysema results from the IMPACT study. *Am J Respir Crit Care Med*. 2016;194:1073–1082.
7. Criner GJ, Delage A, Voelker K, et al. Improving lung function in severe heterogeneous Emphysema with the Spiration Valve System (EMPROVE) a multicenter, open-label randomized controlled clinical trial. *Am J Respir Crit Care Med*. 2019;200:1354–1362.
8. Klooster K, Hartman JE, Ten Hacken NHT, et al. Improved predictors of survival after endobronchial valve treatment in patients with severe emphysema. *Am J Respir Crit Care Med*. 2017;195:1272–1274.
9. Li S, Wang G, Wang C, et al. The REACH trial: a randomized controlled trial assessing the safety and effectiveness of the Spiration® valve system in the treatment of severe emphysema. *Respiration*. 2019;97:416–427.
10. Hartman JE, Vanfleteren LEGW, van Rikxoort EM, et al. Endobronchial valves for severe emphysema. *Eur Respir Rev*. 2019;28:180121.
11. Puhan MA, Chandra D, Mosenifar Z, et al. The minimal important difference of exercise tests in severe COPD. *Eur Respir Rev*. 2011;37:784–790.
12. Hartman JE, Ten Hacken NH, Klooster K, et al. Minimal important difference of target lobar volume reduction after endobronchial valve treatment for emphysema. *Eur Respir Rev*. 2012;40:1137–1141.
13. Welling JBA, Hartman JE, Ten Hacken NHT, et al. The minimal important difference for the St George's Respiratory Questionnaire in patients with severe COPD. *ERJ Express*. 2015;46:1598–1604.