Bronchoscopic Lung Volume Reduction
To the Heart of the Matter

Chronic obstructive pulmonary disease (COPD) is a complex inflammatory disorder characterized by progressive and irreversible airflow limitation (1). It is associated with a number of comorbidities, in particular, heart failure, and they share risk factors, notably exposure to cigarette smoke and ageing (2). Furthermore, it is appreciated that patients with coexisting COPD and heart failure experience disproportionately worse outcomes: the suggested pathophysiological mechanisms underlying their association, although not fully understood, include systemic inflammation, COPD exacerbations, pulmonary hypertension, and lung hyperinflation (3, 4).

Severe emphysema with hyperinflation is the end stage of the COPD spectrum with substantial loss of terminal bronchioles and destruction of the elastic scaffold maintaining patency of airways and facilitating passive recoil (5). The respiratory pump is mechanically disadvantaged by splinting of the diaphragm, malalignment of the thoracic cage, and chest wall asynchrony (6). Intrathoracic pressure is increased and the vasculature is compressed, which, in addition to parenchymal loss, contributes to pulmonary hypertension (7). The increased intrathoracic pressure also impedes venous return, and the cardiac chamber sizes are reduced (8, 9), leading to impaired left ventricular filling and reduced cardiac output.

Lung volume reduction (LVR) via surgical or minimally invasive bronchoscopic approaches offers a means of restoring some normality to the intrathoracic mechanics and has been shown to compare favorably with standard of care in patients with severe emphysema and hyperinflation (10). After close to 20 years of research, the endobronchial valve (EBV) is now a guideline recommended pulmonary volume reduction (BRV) with one-way valves monitored with transthoracic echocardiography have reported improvements in cardiac indices, including right ventricular function (19, 20), which, moreover, correlated with the reductions in lobar volumes (20). Few of the participants, however, had confirmed pulmonary hypertension.

Problems inherent with the traditional tools investigating cardiac function include poor acoustic windowing in hyperinflated chests (echocardiography), invasiveness (thermodilution), and surrogate physiological measurements (cardiopulmonary exercise testing). Cardiac magnetic resonance (CMR) is a recent acquisition and noninvasive and affords information on cardiac structure and function with unparalleled image quality, accuracy, and reproducibility (21).

In this issue of the Journal, van der Molen and colleagues (pp. 704–711) report their investigation of cardiac function using CMR to evaluate cardiac preload (the primary endpoint), represented by the right ventricle end-diastolic volume index (RVEDVI; with an effect size of 5 ml/m² chosen) and additional secondary endpoints (including cardiac output, myocardial contractility, and pulmonary artery pressures) in 24 subjects with severe emphysema and hyperinflation (without a history of cardiovascular disease) 1 day before and 8 weeks after BLVR using EBVs (22). Abnormally low cardiac chamber sizes were measured at baseline. Eight weeks after valve implantation, all patients were observed to have achieved target lobe volume reduction, of whom 16 had developed complete radiological atelectasis. Improvements in airflow limitation, lung volumes, exercise capacity, and quality of life were accompanied by increases in RVEDVI (7.9 ml/m² ± 10.0; P = 0.001), left ventricular stroke volume (12.6 ml ± 18.3; P = 0.010), and cardiac output (0.9 L/min ± 1.5; P = 0.007) that were clinically meaningful. Enhanced ventricular contractility (as measured by ejection fraction and strain) was also observed. The LVR achieved in this study was greater than in an earlier pharmacological study using CMR (23) and accompanied by larger increases in cardiac preload, in agreement with the Frank-Starling relationship. Blood flow within the pulmonary artery was also augmented but there was no increase in pulmonary pressures (as is typically seen in patients without COPD undergoing lobectomy) and may reflect a counterbalancing effect between reduced vascular bed surface area (secondary to lobar atelectasis) and resurrection of compromised tissue with functional potential. Similar findings have been observed in patients who have undergone LVRS (18).

The authors are to be congratulated on undertaking a detailed CMR study that sheds light on the interaction between hyperinflation
and cardiac function and how successful BLVR can alter pulmonary hemodynamics. They do, however, acknowledge several limitations. Patients without a prior history of cardiovascular disease were recruited, and therefore the impact of BLVR in those individuals with cardiovascular dysfunction remains unclear. Second, the study was not supplemented with invthoracic pressure measurements (transoesophageal and transdiaphragmatic) or right heart catheter indices, which may have helped to clarify underlying mechanisms. The addition of quantitative computed tomography measuring pulmonary artery-to-aorta ratio and small vessel volume could prove informative. Lastly, the cohort was small and may be underpowered to detect changes in secondary outcome measures, which may also explain the absence of statistically significant associations between cardiac preload and the conventional metrics, notably lobar volume reduction.

Further studies using a combination of imaging (CMR) and physiological measurements are now needed to confirm the cardiovascular benefits conferred by BLVR with EBVs and establish hyperinflation as a modifiable risk factor for heart failure. 

Author disclosures are available with the text of this article at www.atsjournals.org.

Justin L. Garner, B.Sc., M.B. B.S., M.R.C.P., Ph.D.
Royal Brompton Hospital
London, United Kingdom

and
National Heart and Lung Institute
Imperial College London
London, United Kingdom

Pallav L. Shah, M.B. B.S., F.R.C.P., M.D., F.E.R.S.
Royal Brompton Hospital
London, United Kingdom

National Heart and Lung Institute
Imperial College London
London, United Kingdom

and
Chelsea and Westminster Hospital
London, United Kingdom

ORCID ID: 0000-0002-9052-4638 (P.L.S.).

References

1. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. Global Initiative for Chronic Obstructive Lung Disease; 2021.

2. Mannino DM, Thom D, Swensen A, Holguin F. Prevalence and outcomes of diabetes, hypertension and cardiovascular disease in COPD. Eur Respir J 2008;32:962–969.

3. Smith MC, Wrobel JP. Epidemiology and clinical impact of major comorbidities in patients with COPD. Int J Chron Obstruct Pulmon Dis 2014;9:571–888.

4. Rabe KF, Hurst JR, Suissa S. Cardiovascular disease and COPD: dangerous liaisons? Eur Respir Rev 2018;27:180057.

5. Kemp SV, Polkey MI, Shah PL. The epidemiology, etiology, clinical features, and natural history of emphysema. Thorac Surg Clin 2009; 19:149–158.

6. O'Donnell DE, Webb KA, Neder JA. Lung hyperinflation in COPD: applying physiology to clinical practice. COPD Research and Practice. 2015;1:4.

7. Zangiabadi A, De Pasquale CG, Sajkov D. Pulmonary hypertension and right heart dysfunction in chronic lung disease. BioMed Res Int 2014; 2014:739674.

8. Watz H, Waschki B, Meyer T, Kretschmar G, Kirsten A, Claussen M, et al. Decreasing cardiac chamber sizes and associated heart dysfunction in COPD: role of hyperinflation. Chest 2010;138:32–38.

9. Barr RG, Bluemke DA, Ahmed FS, Carr JJ, Enrigt PL, Hoffman EA, et al. Percent emphysema, airflow obstruction, and impaired left ventricular filling. N Engl J Med 2010;362:217–227.

10. Shah PL, Herth FJ, van Geffen WH, Deslee G, Siebos DJ. Lung volume reduction for emphysema. Lancet Respir Med 2017;5:147–156.

11. Kemp SV, Siebos DJ, Kik A, Komaszewska M, Carron K, Elk L, et al. A multicenter randomized controlled trial of Zephyr endobronchial valve treatment in heterogeneous emphysema (TRANSFORM). Am J Respir Crit Care Med 2017;196:1535–1543.

12. Criner GJ, Sue S, Wright S, Dransfield M, Rivas-Perez H, Wiese T, et al.; LIBERATE Study Group. A multicenter randomized controlled trial of zephyr endobronchial valve treatment in heterogeneous emphysema (LIBERATE). Am J Respir Crit Care Med 2018;198:1151–1164.

13. Garner JL, Biddiscombe MF, Meah S, Lewis A, Buttery SC, Hopkinson NS, et al. Endobronchial valve lung volume reduction and small airway function. Am J Respir Crit Care Med 2021;203:1576–1579.

14. Dransfield MT, Garner JL, Bhat SP, Siebos DJ, Klooster K, Scuruba FC; et al.; LIBERATE Study Group. Effect of zephyr endobronchial valves on dyspnea, activity levels, and quality of life at one year. Results from a randomized clinical trial. Ann Thorac Soc 2020;17:829–838.

15. Hopkinson NS, Kemp SV, Toma TP, Hansell DM, Geddes DM, Shah PL, et al. Atelectasis and survival after bronchoscopic lung volume reduction for COPD. Eur Respir J 2011;37:1346–1351.

16. Garner J, Kemp SV, Toma TP, Hansell DM, Polkey MI, Shah PL, et al. Survival after endobronchial valve placement for emphysema: a 10-year follow-up study. Am J Respir Crit Care Med 2016;194:519–521.

17. van Geffen WH, Siebos DJ, Herth FJ, Kemp SV, Weder W, Shah PL. Surgical and endoscopic interventions that reduce lung volume for emphysema: a systemic review and meta-analysis. Lancet Respir Med 2019;7:313–324.

18. Criner GJ, Scharf SM, Falk JA, Gaughan JP, Stemborg AL, Patel NB, et al.; National Emphysema Treatment Trial Research Group. Effect of lung volume reduction surgery on resting pulmonary hemodynamics in severe emphysema. Am J Respir Crit Care Med 2007;176:253–260.

19. Pizarro C, Schueler R, Hammerstingl C, Tuleta I, Nickenig G, Skowasch D. Impact of endoscopic lung volume reduction on right ventricular myocardial function. PLoS One 2015;10:e0121377.

20. Fiorelli A, Cascone R, Natalone G, Peritore V, Vanni C, Poggi C, et al. Cardio-pulmonary changes after bronchoscopic lung volume reduction with endobronchial one-way valves. Lung 2020;198:565–573.

21. Hudsmith LE, Petersen SE, Francis JM, Robson MD, Neubauer S. Normal human left and right ventricular and left atrial dimensions using steady state free precession magnetic resonance imaging. J Cardiovasc Magn Reson 2005;7:779–782.

22. van der Molen MC, Hartman JE, van Vletteren LEGW, Kerstjens HAM, van Meile JP, Willems TP, et al. Reduction of lung hyperinflation improves cardiac preload, contractility, and output in emphysema: a clinical trial in patients who received endobronchial valves. Am J Respir Crit Care Med 2022;206:704–711.

23. Stone IS, Barnes NC, James WY, Midwinter D, Boubertakh R, Follows R, et al. Lung deflation and cardiovascular structure and function in chronic obstructive pulmonary disease. A randomized controlled trial. Am J Respir Crit Care Med 2016;193:717–726.

Copyright © 2022 by the American Thoracic Society