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 treatment improving lung function and exercise capacity (11–13), quality of life (14), and survival (15, 16) in selected individuals, and LVR is key to attaining these clinically meaningful benefits (17). It is attractive to speculate whether the effects of LVR using EBVs can beneficially impact cardiovascular outcomes, which may further inform mechanistic rationale.

Historically, the reported effects of lung volume reduction surgery (LVRS) on pulmonary hemodynamics and right ventricle function, mainly from small single-center uncontrolled trials, have been inconsistent. A substudy of the NETT (National Emphysema Treatment Trial), a prospective randomized controlled trial comparing bilateral LVRS with standard of care using right heart catheterization, was intended to clarify the issue (18). Patients were excluded if their mean pulmonary artery pressure was ⩾35 mm Hg or their peak systolic pulmonary arterial pressure was ⩾45 mm Hg in keeping with moderate pulmonary hypertension at baseline. Of 110 eligible patients, only 55 patients had 6-month evaluable data (28 LVRS vs. 27 standard of care) revealing no significant effects on measured and calculated cardiac performance variables at rest. Several studies of subjects undergoing unilateral bronchoscopic lung volume reduction (BLVR) 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/m^2 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/m^2 ± 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

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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 intrathoracic 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. ■

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