Low $D_{LCO}$ predicts all-cause hospital admissions in patients with reduced left ventricular ejection fraction or diastolic dysfunction

To the Editor:

The diffusing capacity of the lung for carbon monoxide ($D_{LCO}$) can be decreased in many disease states, including COPD and interstitial lung disease [1, 2]. Low $D_{LCO}$ can also be seen in those with clinically relevant congestive heart failure (CHF) due to its deleterious consequences on lung volumes, perfusion and gas exchange efficiency [3, 4]. Pulmonary function testing results are frequently available in patients with CHF. $D_{LCO}$ measurements have previously been shown to impact exercise capacity in CHF patients with either reduced or preserved left ventricular ejection fraction (LVEF) [5–7]. Impaired $D_{LCO}$ has also been suggested as a potential predictor of negative clinical outcomes in CHF [8]. We, therefore, aimed to determine if patients with reduced LVEF or isolated diastolic dysfunction on echocardiography and a low $D_{LCO}$ are at a higher risk of hospital admissions than their counterparts with a preserved $D_{LCO}$. Confirmation of this hypothesis would support the need for closer monitoring of CHF patients who also present with a reduced $D_{LCO}$.

We performed a retrospective review at Montfort Hospital (Ottawa, ON, Canada), a large urban academic centre, to identify all patients who underwent echocardiography (1 January 2016 to 30 June 2017) and pulmonary function testing, including $D_{LCO}$ measurements by single-breath carbon monoxide uptake. We charted all-cause hospital admissions between 1 January 2016 and 31 December 2018 for all subjects. LVEF was determined by the biplane Simpson method and the American Society of Echocardiography guidelines were used for the evaluation of left ventricular diastolic function [9]. $D_{LCO}$ % predicted results were determined for each patient using the 2017 Global Lung Function Initiative reference values [10]. A reduced $D_{LCO}$ was defined as a result below the lower limit of normal.

A total of 363 individuals underwent both echocardiography and $D_{LCO}$ measurements; 128 (35.3%) had at least one admission to the hospital. 131 patients had evidence of cardiac dysfunction (40% with a decreased LVEF versus 60% with isolated diastolic dysfunction). 66 of these subjects (50.4%) had a reduced $D_{LCO}$ (33 from both the reduced LVEF and isolated diastolic dysfunction groups). Cigarette smoking status was similar in those with a low or preserved $D_{LCO}$, with 26% and 29%, respectively, reporting being lifelong nonsmokers. ANOVA revealed that $D_{LCO}$ had an independent relationship with all-cause hospital admissions ($p<0.01$). Indeed, patients with cardiac dysfunction and a low $D_{LCO}$ were admitted to the hospital more frequently than those with a preserved $D_{LCO}$ (mean of 1.29 versus 0.45 admissions, $p<0.01$). Subjects with a moderate or severe decrease of $D_{LCO}$ ($\leq 60\%$ predicted) were at an even higher risk of hospitalisation (mean of 1.64 admissions, $p<0.01$) compared with those with only a mild decrease (mean of 0.87 admissions) (table 1). No significant difference was seen amongst patients with a low $D_{LCO}$ when comparing individuals with a reduced LVEF versus isolated diastolic dysfunction ($p=0.25$). The mean±SD predicted $D_{LCO}$ in these two groups was 54±15% and 55±15%, respectively.

A low $D_{LCO}$ should be valued as a predictor of all-cause hospital admissions in patients with reduced LVEF or isolated diastolic dysfunction. The severity of the impairment seen on $D_{LCO}$ testing also appears to affect the risk of hospitalisation. https://bit.ly/3e4r8bH

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impaired ventricular function become more relevant. A reduced underlying mechanisms, these abnormalities are expected to worsen as the extracardiac manifestations of mismatch is an important determinant of a low ventilation distribution abnormalities could have also influenced our results [11 with preserved D

hospitalisations in those with a reduced LVEF or isolated diastolic dysfunction. There was a nearly threefold increase in mean worsening ventricular function on our main outcome. The confounding effects of anaemia should also be considered as well as the deleterious effects of recent smoking.

What are the implications of our results? First and foremost, our data provide novel support to the notion that patients with impaired systolic and/or diastolic function and a reduced D_lco should be flagged as being at a higher risk of admission to the hospital. Secondly, they set the stage for prospective studies looking at changes in D_lco as the treatment of the underlying cardiac dysfunction is optimised. If so, it is conceivable that a higher D_lco over time could be associated with a lower risk of hospitalisation, particularly when there is a direct cause-effect relationship between ventricular function and a low D_lco. Thirdly, the advent of reliable point-of-care D_lco measurement systems raises the perspective that easily accessible results could play an unexplored role in the longitudinal follow-up of these patients. Finally, the added value of the diffusion coefficient (K_co=D_lco/alveolar volume) in those with preserved D_lco also merits investigation since a low D_lco but normal D_lco indicates impaired gas exchange efficiency, which might be related to abnormal pulmonary perfusion due to cardiovascular disease [15].

Our analysis does have some inherent limitations given that it is a retrospective review from objective testing results. Despite the fact that a reduced D_lco remained a strong predictor of hospitalisations even when removing subjects with airflow limitation or a FEV1 <80% predicted, we cannot rule out that a low D_lco may have been negatively influenced by other concomitant pathologies, including pulmonary disease. The relatively small number of events also precluded further investigating the potential effects of worsening ventricular function on our main outcome. The confounding effects of anaemia should also be considered as well as the deleterious effects of recent smoking.
In conclusion, $D_{LCO}$ measurements provide meaningful clinical information to help predict hospital admissions in patients with CHF. As pulmonary function testing is frequently available in these patients, our data indicate that those with a reduced $D_{LCO}$ should be monitored more closely in an attempt to reduce the burden of repeated hospital admissions.

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