EDITORIAL COMMENT

Cor Pulmonale Revisited*

Lewis J. Rubin, MD

La Jolla, California

I remember first being introduced to the term *cor pulmonale* in medical school, which was used to describe right heart failure due to chronic lung disease, and I still have a mental picture of the typical patient as a former heavy smoker, dyspneic at rest, and cyanotic with neck vein distention and lower extremity edema. However, even early catheterization studies of the normal and diseased human pulmonary circulation emphasized that chronic cor pulmonale was characterized not by right ventricular failure but by pulmonary hypertension and right ventricular hypertrophy and/or dilation (1,2).

Subsequent studies by Burrows et al. (3) and Kessler et al. (4) showed that, while the degree of pulmonary hypertension in cor pulmonale due to chronic obstructive pulmonary disease (COPD) is modest, survival is poor and correlates more strongly with the presence of an elevated pulmonary vascular resistance than with the degree of airflow obstruction. Despite being the second most frequent cause of pulmonary hypertension worldwide (left-sided heart failure is the most frequent), the management of cor pulmonale has changed little over the past 30 years, with the primary treatment objectives of optimizing lung function and maintaining oxygen saturation above 90% (5).

In this issue of the *Journal*, Hilde et al. (6) report a study that challenges us to reconsider the definition of cor pulmonale even further. They studied 98 subjects with stable, moderate to severe COPD using both hemodynamic and echocardiographic methods and compared the echocardiographic findings with those of a matched healthy control group. They divided their COPD cohort into 2 groups: those who met the current definition of pulmonary hypertension (a resting mean pulmonary artery pressure >25 mm Hg) and those who did not. While the group with pulmonary hypertension had the most advanced hemodynamic and echocardiographic changes, the group without pulmonary hypertension also manifested echocardiographic abnormalities, including

increased right ventricular wall thickness and altered right ventricular systolic function. The degree of these abnormalities was midway between the parameters of the healthy controls and those observed in the pulmonary hypertension cohort, suggesting that cor pulmonale is, in fact, a continuum of right heart disease that begins long before resting pulmonary hypertension is present.

What accounts for these abnormalities in right heart structure and function in the absence of pulmonary hypertension? Although hypoxemia is the major cause of pulmonary vasoconstriction and remodeling in severe chronic respiratory disease, a substantial proportion of the subjects in the present study had right heart abnormalities in the absence of hypoxemia, at least at rest. Chronic lung disease is also characterized by widespread destruction of the lung parenchyma with accompanying loss of vascular surface area, but this is unlikely the explanation for the observed findings in the absence of either end-stage lung disease or pulmonary hypertension. Finally, hypercarbia also induces pulmonary vasoconstriction and potentiates the vasoconstrictor effects of hypoxia, but pCO_2 levels were generally within the normal range in their patients.

The explanation for these abnormalities in the absence of either severe lung disease or pulmonary hypertension likely lies in the circulatory events that are not captured during a routine right heart catheterization. The normal pulmonary circulation has the capacity to accommodate multiples of resting cardiac output with little or no change in pressure due to vasodilation of existing vessels and recruitment of unused vasculature. Accordingly, pulmonary artery pressure at rest remains normal until 50% of the vascular surface area has been obliterated by diffuse lung disease (7). In the interval between normality and resting pulmonary hypertension in the setting of lung disease, it is likely that incipient pulmonary vascular disease is present and evolving. This may be unmasked by exercise, where the pulmonary circulation no longer has the capacity to adapt, and pressure increases along with increasing blood flow. Coupled with dynamic hyperinflation during exercise, which results in vascular compression as alveolar pressure exceeds intramural vascular pressure, it is likely that the right ventricle at this stage of lung disease is faced with increased afterload throughout much of the time course of daily physical activity. Finally, nocturnal hypoxemia, which is common in chronic lung disease (8), would further contribute to altered vascular compliance and impaired right ventricular function.

The study by Hilde et al. (6) highlights the importance of early recognition of pulmonary vascular disease, because interventions at an earlier stage may reverse the process or slow its progression. Pulmonary hypertension is currently defined as a mean pulmonary artery pressure >25 mm Hg at rest, but recent studies demonstrating increases in pulmonary arterial pressure and other abnormalities in cardiopulmonary function with exercise in symptomatic patients with normal resting pulmonary artery pressures (9,10), as well as the demonstration in the present study of echocardiographic

right heart abnormalities in patients with a mean pulmonary artery pressure <25 mm Hg but above the normal value of ~15 mm Hg, suggest that it may be time to revisit the hemodynamic definition of pulmonary hypertension. At the very least, the observations of Hilde et al. (6) warrant a revised definition of chronic cor pulmonale to "altered structure and/or function of the right ventricle in the setting of chronic lung disease." It is time to replace the mental image of the patient with cor pulmonale from the end-stage "blue-bloater" to a younger patient with only moderate airflow obstruction and to translate the findings of Hilde et al. (6) to more aggressive efforts directed at preventing and treating this important cardiopulmonary condition.

Reprint requests and correspondence: Dr. Lewis J. Rubin, 5550 Caminito Genio, La Jolla, California 92037. E-mail: ljrubin@ucsd.edu.

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