Pulmonary Diffusing Capacity in Left Ventricular Dysfunction*

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The purpose of this study was to determine whether there are any consistent spirometric or Dsb findings in patients with LV dysfunction characterized by a clinical diagnosis of CHF and an EF<40 percent. We performed spirometry and Dsb in 34 patients, and found that EF correlated only with Dsb. When we separated the patients into those with rales and those without, Dsb correlated strongly with EF only in those with rales. There was no correlation with other spirometric values. Mean Dsb percent predicted was significantly lower in patients with rales despite similar mean EF. Only two of 23 patients without rales had a reduced Dsb while only one of 11 with rales had a normal Dsb. We conclude that Dsb is a good predictor of clinically evident heart failure. When rales are absent, Dsb should be normal in patients with LV dysfunction; when present, Dsb will be diminished in proportion to the EF.

In patients with LV dysfunction, increased pulmonary blood volume may increase Dco through greater upper lung zone perfusion and capillary recruitment. This phenomenon was reported by Burgess in early mitral stenosis and in left-to-right shunts. He also noted a reduction in Dco in late mitral stenosis with the development of pulmonary hypertension. Similarly, we have noted that many patients with LV failure have Dsb values lower than expected. Interstitial edema and alveolar fluid may increase the distance between alveolar gas and red blood cells while peribronchiolar edema may reduce ventilation to lung units resulting in ventilation-perfusion mismatch. These factors may outweigh the greater pulmonary capillary volume and result in a decreased diffusing capacity in the absence of elevated pulmonary vascular resistance. We looked at spirometric measurements and Dsb in a prospective study of 34 patients clinically diagnosed to have CHF, who underwent extensive physiologic evaluation of their LV dysfunction with radionuclide ventriculography, to determine whether there are any consistent pulmonary function patterns in these patients.

Materials and Methods

Thirty-four patients (24 male, 10 female) with LV dysfunction underwent pulmonary function testing. We defined LV dysfunction as an EF less than 40 percent by first pass gated blood pool scan using technetium 99m. Thirty-one patients had hypertensive and/or ischemic cardiomyopathy and three had rheumatic valvular disease. As part of the study design, chest radiographs made within one week preceding pulmonary function testing were evaluated to rule out pneumonia, pleural effusion and overt pulmonary edema, and each patient's chest was auscultated immediately before performing spirometry and diffusing capacity tests. Eleven patients had audible bilateral rales but were not in respiratory distress or gross pulmonary edema while at the pulmonary function laboratory; 23 patients did not have rales.

Spirometry was performed with a Medical Graphics model 1070 computerized pneumotachograph-based system following ATS standards. Diffusing capacity was obtained utilizing the same equipment by single-breath method following ATS guidelines; TLC, and Dco/Va were derived from the same tests. This system utilizes a demand valve to supply the test gas and gas chromatography for analysis. Predicted values were obtained by this laboratory in a survey of the general population. Spirometric values were adjusted for black subjects. Values were considered abnormal if they were below the lower 95 percent confidence limit. All values for Dco and Dco/Va were corrected for hemoglobin and for smoking status (all the patients were ex-smokers).

Of the total of 34 patients, 13 were admitted to the Medical Service during a three-month interval with a diagnosis of CHF, while 21 were patients with known CHF under consideration for amiodarone therapy of arrhythmias who had not yet received this medication. All patients had radionuclide ventriculography performed fewer than two weeks before pulmonary function tests. Patients were excluded from the study if they had underlying lung disease, clinical or radiographic evidence of neoplasm, previous lung resection or a history of use of drugs which could result in pulmonary toxicity.

Statistical analysis was performed by using least-squares linear regression and Pearson's correlation coefficients to test the relation-

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ships between EF and Dsb percent predicted and EF and various spirometric values: FVC percent predicted, FEV1 percent predicted, FEV1/FVC, FEF25-75\% percent predicted, MET, and MVV percent predicted. Comparison of spirometric and Dco values between the group with and without rales was done using unpaired Student’s t test. Significance was assessed by means of the F ratio of multiple regression analysis of variance.

**RESULTS**

In the total of 34 patients, EF correlated only with Dsb percent predicted (r = 0.34; p<0.05) and not with FVC percent predicted, FEV1 percent predicted, FEV1/FVC, MET or MVV percent predicted. Patients were separated into those without rales (n = 23) and those with rales (n = 11). Patients admitted to the Medical Service for CHF were more likely to have rales (seven of 13) than those being evaluated for chronic arrhythmias (four of 21) and had lower Dco values (67 vs 77 percent predicted) even though they had the same EF (24 percent). There was no significant difference in age, sex, ethnic background, mean duration of LV failure, or mean EF between patients with rales and those without (Table 1).

Ejection fraction correlated strongly with Dsb percent predicted in patients with rales (r = 0.81, p<0.001), but not in those without rales. The mean Dsb in the patients with rales (Dsb percent predicted, mean ± SD = 53 ± 15 percent) was significantly lower than in those without rales (Dsb percent predicted, mean ± SD = 83 ± 9 percent). Only one patient of 11 with rales had a normal Dsb while 21 patients of 23 without rales had a normal Dsb.

Both TLC\textsubscript{ab}, and Dco/VA were significantly lower in patients with rales. There were statistically significant reductions in FEV1 and MVV and trends toward lower FVC, lower FEF25-75\% and higher MET in the patients with rales.

**DISCUSSION**

Previous literature suggests that Dsb remains relatively normal in patients with CHF, despite reductions in VC and flow rates. Light and George\textsuperscript{7} reported that mean Dsb percent predicted was 91.4 percent in a group of 28 patients with CHF while there were reductions in the mean FEV1, FVC and FEF25-75\%. These investigators repeated the measurements during a course of treatment with diuretics and found that the flow rates returned toward normal and the mean Dsb increased to greater than 90 percent predicted.

Other studies also have shown a relatively normal Dsb in patients with CHF\textsuperscript{9,11} although many suffer from a lack of statistical rigor in their conclusions. It has been suggested that the greater red blood cell volume in pulmonary capillaries found in patients with CHF compensates for any factors tending to reduce diffusion, eg, interstitial edema, alveolar fluid, and ventilation/perfusion mismatch.

We found that values for Dsb in patients with LV dysfunction but not in gross pulmonary edema fell into two groups defined by the presence or absence of rales, which are a clinical correlate of the severity of pulmonary congestion. For the entire study group, EF correlated weakly with Dsb percent predicted, but not at all with various spirometric measurements. The correlation between EF and Dsb percent predicted is highly significant in patients with heart failure who have rales. Patients with LV dysfunction and no rales have a near normal Dsb. Only two out of 23 patients without rales had a reduced Dsb. In patients with LV dysfunction and rales, the Dsb percent predicted is significantly lower than in patients without rales despite a similar mean EF. Only one out of 11 with rales had a normal Dsb.

Both TLC\textsubscript{ab}, and Dco/VA are significantly lower in the group with rales. The reduction in TLC\textsubscript{ab}, like the reduction in FEV1 and the trend toward a lower FVC and flows, reflects the greater congestion in the patients with rales. It is important to note that Dco/VA also is significantly lower in those with rales, consistent with a longer pathway for diffusion, while it is quite normal in CHF patients with similar EFs who do not have rales.
our EFs and our total sample size (34), we should have been able to identify as statistically significant a difference in EF of slightly less than 10 percent. The observed difference of 4 percent therefore is of no statistical significance, as well as of no clinical importance.

The presence of rales indicates interstitial and alveolar fluid formation. Rales are believed to result from the transudation of fluid into the interstitium and small airways, which then moves into the alveoli in patients with CHF of at least moderate severity. Our data suggest that this process outweighs any increase in blood volume and results in a fall in diffusing capacity. Studies have shown that rales are a poor predictor of a patient's EF. Rales, along with other signs of congestion, have a high specificity but low sensitivity for an EF<30 percent. Our results confirm these findings since there was no statistical difference in EF between the group with rales and the group without. However, we did not measure extravascular lung water to demonstrate an increased transudation of fluid into alveoli in patients with rales.

The discrepancy between Dsb results reported in previous studies and those of our study may be due to differences in the severity of LV dysfunction. Previous studies made no mention of the patients' EFs nor did they note whether the patients had rales at the time of testing. It is likely that the Dsb values had returned toward normal by the time of pulmonary function testing.

In acute pulmonary edema there is a marked excess of extravascular lung water. Very few data are available concerning Dsb in patients with clinical pulmonary edema of any etiology. Frand et al studied 16 patients with acute noncardiogenic pulmonary edema. They compared diffusing capacities in heroin addicts to those in patients with heroin-induced pulmonary edema as determined by clinical and radiographic findings. They found that patients in noncardiogenic pulmonary edema had a reduced Dsb as compared with that of the control addicts. Said and associates studied gas exchange in anesthetized dogs during acute pulmonary edema and found that the diffusing capacity was reduced to 60.6 percent of baseline values, on average.

Our study, as many previous investigations, showed a reduction in FEV₁ in patients with CHF. All of our patients had a previous smoking history which may account for part of the decrease in FEV₁ and FEF25-75%, but not for the difference between the groups with and without rales. Increased airway resistance also may be due to compression of peripheral airways by distended pulmonary arterioles in the peripheral bronchovascular sheaths and to fluid in the airways. The FEV₁ was significantly lower in the patients with rales. The increase in MET, a measurement which is inversely related to flow, approached statistical significance (p<0.1) while reduction in FEV₂5-75% in patients with rales was not significant, perhaps because of the well-known inherent variability of this measurement.

Diffusing capacity appears to be a better predictor of clinically evident CHF than the EF derived from gated blood pool scans. This study suggests that the auscultation of rales reflects the presence of interstitial edema or fluid-filled alveoli, or both, which leads to the reduction in diffusing capacity. When no rales are present, the diffusing capacity is likely to be normal in patients with LV dysfunction.

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