Pulmonary Function in Patients With Reduced Left Ventricular Function*

Influence of Smoking and Cardiac Surgery

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Study objective: The impact of stable, chronic heart failure on baseline pulmonary function remains controversial. Confounding influences include previous coronary artery bypass or valve surgery (CABG), history of obesity, stability of disease, and smoking history.

Design: To control for some of the variables affecting pulmonary function in patients with chronic heart failure, we analyzed data in four patient groups, all with left ventricular (LV) dysfunction (LV ejection fraction [LVEF] ≤ 35%): (1) chronic heart failure, nonsmokers, no CABG (n = 78); (2) chronic heart failure, nonsmokers, CABG (n = 46); (3) chronic heart failure, smokers, no CABG (n = 40); and (4) chronic heart failure, smokers, CABG (n = 48). Comparisons were made with age- and gender-matched patients with a history of coronary disease but no LV dysfunction or smoking history (control subjects, n = 112) and to age-predicted norms.

Results: Relative to control subjects and percent-predicted values, all groups with chronic heart failure had reduced lung volumes (total lung capacity [TLC] and vital capacity [VC]) and expiratory flows (p < 0.05). CABG had no influence on lung volumes and expiratory flows in smokers, but resulted in a tendency toward a reduced TLC and VC in nonsmokers. Smokers with chronic heart failure had reduced expiratory flows compared to nonsmokers (p < 0.05), indicating an additive effect of smoking. Diffusion capacity of the lung for carbon monoxide (DlCO) was reduced in smokers and in subjects who underwent CABG, but not in patients with chronic heart failure alone. There was no relationship between LV size and pulmonary function in this population, although LV function (cardiac index and stroke volume) was weakly associated with lung volumes and DlCO.

Conclusions: We conclude that patients with chronic heart failure have primarily restrictive lung changes with smoking causing a further reduction in expiratory flows.

CHEST 2001; 120:1869–1876

Key words: expiratory airflow; heart failure; spirometry; vital capacity

Abbreviations: ACE = angiotensin-converting enzyme; BMI = body mass index; CABG = coronary artery bypass or valve surgery; CAD = coronary artery disease; DlCO = diffusing capacity of the lung for carbon monoxide; FEF = forced expiratory flow; FEF25 = forced expiratory flow at 25% of VC; FEF50 = forced expiratory flow at 50% of VC; FEF75 = forced expiratory flow at 75% of VC; LV = left ventricular; LVEF = left ventricular ejection fraction; MVV = maximal voluntary ventilation; PEF = peak expiratory flow; PFT = pulmonary function test; RV = residual volume; TLC = total lung capacity; VA = alveolar volume; VC = vital capacity

The lungs are linked in series with the cardiac pump, and they are not only influenced by mechanical alterations in pump function but likely by neurohumoral modulators and cytokines involved in the pathogenesis of heart failure.1–4 Multiple studies5–18 have been published describing pulmonary function-related changes in patients with chronic left ventricular (LV) dysfunction. These studies have varying conclusions concerning the influence of heart failure on resting pulmonary function, ranging from essentially normal values, to primarily restrictive changes, to combined restrictive and obstructive changes.6,9,10,14,19–22 There are many confounding influences in these previous studies that may influence pulmonary function independent of changes due to heart failure alone. These include changes due to normal aging, obesity, and environmental

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Groups
Most of these subjects were sent for PFTs for reasons that were of ischemia on an imaging study but with a normal LVEF history of documented CAD (previous inclusion into research studies, presurgical workup, as well as of LV dysfunction, and others to rule out asthma, screening for dyspnea that was believed to be out of proportion to the degree of LV dysfunction, and others to rule out asthma, screening for inclusion into research studies, presurgical workup, as well as smoking history. Control subjects included individuals with a history of documented coronary artery disease (CAD) precursor angioplasty, small or non-Q-wave myocardial infarction, evidence of ischemia on an imaging study) but with a normal LVEF (>50%) and no previous thoracic surgery or smoking history. Most of these subjects were sent for PFTs for reasons that were similar to the chronic heart failure population. To be included in the nonsmoking group, subjects had to have never smoked. For the smokers, a >5-pack-year history was set as the minimum criterion. Five groups were compared: (1) chronic heart failure, nonsmokers, no CABG; (2) chronic heart failure, nonsmokers, CABG; (3) chronic heart failure, smokers, no CABG; (4) chronic heart failure, smokers, CABG; and (5) control subjects. All subjects involved in the study signed releases allowing the use of clinical records for investigational purposes.

Materials and Methods

Subjects
A retrospective analysis was performed on data from heart failure patients obtained from databases maintained by the Cardiovascular Health Clinic (a preventive and rehabilitative cardiac clinic of the Mayo Clinic) and the Heart Failure Clinic at the Mayo Clinic, Rochester, from 1994 to 1998. Heart failure included patients with histories of dilated and ischemic pathologic conditions and with ejection fractions ≤35% with and without a history of CABG. A body mass index (BMI) of >35 kg/m² was also used to exclude morbidly obese subjects. Pulmonary function test (PFT) results for patients were obtained from the database of the Pulmonary Function Laboratory at Mayo for spirometry, plethysmographic total lung capacity (TLC), and diffusing capacity of the lung for carbon monoxide (Dlco). The PFTs were obtained within a 2-month period from the determination of LV ejection fraction (LVEF). Ejection fraction data were obtained primarily from echocardiography, but were also obtained by radionuclide angiography and first pass with Sestamibi. The reason PFTs had been ordered on the chronic heart failure patients varied considerably. Many had been ordered simply as a part of their clinical workup or follow-up, some for dyspnea that was believed to be out of proportion to the degree of LV dysfunction, and others to rule out asthma, screening for inclusion into research studies, presurgical workup, as well as smoking history. Control subjects included individuals with a history of documented coronary artery disease (CAD) precursor angioplasty, small or non-Q-wave myocardial infarction, evidence of ischemia on an imaging study) but with a normal LVEF (>50%) and no previous thoracic surgery or smoking history. Most of these subjects were sent for PFTs for reasons that were similar to the chronic heart failure population. To be included in the nonsmoking group, subjects had to have never smoked. For the smokers, a >5-pack-year history was set as the minimum criterion. Five groups were compared: (1) chronic heart failure, nonsmokers, no CABG; (2) chronic heart failure, nonsmokers, CABG; (3) chronic heart failure, smokers, no CABG; (4) chronic heart failure, smokers, CABG; and (5) control subjects. All subjects involved in the study signed releases allowing the use of clinical records for investigational purposes.

Measurements

Pulmonary function measurements included an assessment of lung volumes (TLC, vital capacity [VC], FVC, residual volume [RV], and FEF1), and an assessment of expiratory flows (peak expiratory flow [PEF], forced expiratory flow [FEF], FEF at 25% of VC [FEF25], FEF at 50% of VC [FEF50], and FEF at 75% of VC [FEF75], respectively). Also included was the mean flow between 25% and 75% of FVC. Subjects also performed maximal voluntary ventilation (MVV) maneuvers for 12 s and single-breath DLco. Spirometry and DLco data were collected in accordance with American Thoracic Society standards. From the flow and volume data, mean expiratory maximal flow-volume envelopes were plotted for visual comparison between the various groups. Significant differences between groups were obtained with analysis of variance (p < 0.05), and subsequent post hoc analyses were performed using t tests.

In all patients with chronic heart failure for whom echocardiograms were available (n = 119), measurements were made of cardiac dimensions (LV end-diastolic diameter, LV end-diastolic posterior wall thickness, left atrial diameter) and cardiac function (stroke volume, cardiac index, and right ventricular pressures) and were obtained for correlational relationships with pulmonary function measurements.

Results

Subject Characteristics

Mean characteristics of the five groups are shown in Table 1. No significant differences were observed among the groups for age, height, weight, or BMI. LVEF did not differ among the groups with chronic heart failure (averaging 23%), but as designed was significantly reduced relative to the CAD control subjects. Smoking history was not different between

<table>
<thead>
<tr>
<th>Groups†</th>
<th>Age, yr</th>
<th>Subjects, No./Female (Male/Female)</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>BMI, kg/m²</th>
<th>Smoking, Pack-yr</th>
<th>LVEF, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>63 ± 2</td>
<td>78/34 (48/30)</td>
<td>170 ± 1</td>
<td>81 ± 3</td>
<td>28.4 ± 0.85</td>
<td>0</td>
<td>23 ± 1 §</td>
</tr>
<tr>
<td>2</td>
<td>66 ± 2</td>
<td>46/25 (24/21)</td>
<td>171 ± 1</td>
<td>77 ± 2</td>
<td>27.9 ± 0.69</td>
<td>0</td>
<td>23 ± 1 §</td>
</tr>
<tr>
<td>3</td>
<td>67 ± 2</td>
<td>40/30 (24/16)</td>
<td>172 ± 2</td>
<td>79 ± 2</td>
<td>27.8 ± 0.79</td>
<td>46 ± 31</td>
<td>23 ± 1 §</td>
</tr>
<tr>
<td>4</td>
<td>67 ± 2</td>
<td>48/26 (24/24)</td>
<td>171 ± 1</td>
<td>81 ± 3</td>
<td>28.5 ± 0.54</td>
<td>54 ± 41</td>
<td>21 ± 1 §</td>
</tr>
<tr>
<td>5</td>
<td>65 ± 2</td>
<td>112/31 (64/48)</td>
<td>168 ± 2</td>
<td>82 ± 3</td>
<td>29.0 ± 0.43</td>
<td>0</td>
<td>61 ± 1</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SE.
†Group 1 = chronic heart failure, nonsmokers, no CABG; group 2 = chronic heart failure, nonsmokers, CABG; group 3 = chronic heart failure, smokers, no CABG; group 4 = chronic heart failure, smokers, CABG; group 5 = control subjects.
§Smokers (groups 3 and 4) different from nonsmokers (groups 1 and 2 (p < 0.05).
|Clinical Investigations|
Smokers with previous CABG vs smokers with no previous CABG (p > 0.05). There was a tendency for a greater number of female patients (percent) in the chronic heart failure nonsmokers and smokers with no previous CABG, as well as in the control group vs the other groups. There were no differences in medications in the groups with chronic heart failure, with the majority of patients receiving angiotensin-converting enzyme (ACE) inhibitors, diuretics, digoxin, and aspirin. Most CAD control subjects were receiving aspirin, statin, and variable additional medications, ranging from no additional medications to use of β-blockers, calcium-channel blockers, ACE inhibitors, and diuretics.

**Lung Volumes**

Mean lung volumes for each group are shown in Table 2. TLC, VC, FVC, and FEV\(_1\) were all significantly reduced in the groups with chronic heart failure relative to the control group (p < 0.05). Nonsmokers with a history of CABG tended to have the greatest reduction in TLC relative to control subjects and the other groups with chronic heart failure (p < 0.05). Smokers tended to have a greater reduction in VC, FVC, and FEV\(_1\)/FVC relative to nonsmokers and an elevated RV/TLC ratio (p < 0.05). The RV/TLC ratio did not differ between nonsmokers with chronic heart failure and the CAD control subjects.

**Expiratory Flows**

Table 3 lists average expiratory flows for each group. PEF was reduced slightly in the smokers with chronic heart failure relative to control subjects but not in nonsmokers with chronic heart failure. All other expiratory flows were reduced significantly in all groups with chronic heart failure, but were reduced to a greater extent in the smokers compared to nonsmokers (p < 0.05). No differences were observed between subjects who underwent previous CABG vs those who did not. Interestingly, MVV did not differ among groups with chronic heart failure, but was significantly reduced relative to the CAD control subjects (p < 0.05).

**Mean Maximal Flow-Volume Curve**

Figures 1–3 are mean expiratory flow-volume curves plotted relative to the percent-predicted TLC. Figure 1 emphasizes the changes observed in the patients with chronic heart failure alone with no history of smoking or previous CABG, relative to the CAD control subjects and predicted values. Figure 2 emphasizes the groups with chronic heart failure with previous CABG relative to the groups with chronic heart failure without previous CABG compared to predicted values. Figure 3 shows the influence of smoking on lung volumes and flow rates relative to the nonsmoking patients.

**DLCO and Alveolar Volume**

Mean values for DLCO and alveolar volume (VA) are shown in Table 4. No differences were noted in DLCO between the control group and groups with chronic heart failure alone; however, significantly lower values were observed in the patients with chronic heart failure with previous CABG and in patients with a smoking history (p < 0.05). VA and DLCO/VA also tended to be lower in patients with chronic heart failure and a history of CABG, as well as in patients with a history of smoking.

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**Table 2—Lung Volumes**

<table>
<thead>
<tr>
<th>Groups</th>
<th>TLC, L (% Predicted)</th>
<th>VC, L (% Predicted)</th>
<th>FVC, L (% Predicted)</th>
<th>FEV(_1), L (% Predicted)</th>
<th>FEV(_1)/FVC, %</th>
<th>RV/TLC, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.54 ± 0.17</td>
<td>3.30 ± 0.12</td>
<td>3.08 ± 0.12</td>
<td>2.31 ± 0.09</td>
<td>75 ± 1</td>
<td>40 ± 1</td>
</tr>
<tr>
<td></td>
<td>(92 ± 2)†</td>
<td>(84 ± 2)†</td>
<td>(79 ± 2)†</td>
<td>(75 ± 2)†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>5.39 ± 0.16</td>
<td>3.18 ± 0.11</td>
<td>3.03 ± 0.10</td>
<td>2.28 ± 0.09</td>
<td>75 ± 1</td>
<td>41 ± 1</td>
</tr>
<tr>
<td></td>
<td>(86 ± 3)†</td>
<td>(81 ± 2)†</td>
<td>(77 ± 2)†</td>
<td>(74 ± 2)†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>5.87 ± 0.17</td>
<td>3.22 ± 0.10</td>
<td>2.91 ± 0.08</td>
<td>2.02 ± 0.07</td>
<td>69 ± 2‡</td>
<td>45 ± 2‡</td>
</tr>
<tr>
<td></td>
<td>(92 ± 3)†</td>
<td>(78 ± 2)‡</td>
<td>(73 ± 2)‡</td>
<td>(65 ± 2)‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>5.66 ± 0.17</td>
<td>3.07 ± 0.10</td>
<td>2.85 ± 0.10</td>
<td>1.98 ± 0.09</td>
<td>69 ± 2‡</td>
<td>46 ± 2‡</td>
</tr>
<tr>
<td></td>
<td>(92 ± 2)†</td>
<td>(77 ± 3)‡</td>
<td>(73 ± 2)‡</td>
<td>(68 ± 3)‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>6.06 ± 0.16</td>
<td>3.75 ± 0.11</td>
<td>3.57 ± 0.11</td>
<td>2.72 ± 0.08</td>
<td>77 ± 1</td>
<td>40 ± 1</td>
</tr>
<tr>
<td></td>
<td>(100 ± 2)</td>
<td>(98 ± 2)</td>
<td>(93 ± 2)</td>
<td>(90 ± 2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SE. See Table 1 for group definitions. Predicted values for TLC from Miller et al\(^{54}\); FVC, VC, and FEV, from Knudson et al\(^{53}\); RV from Crapo et al.\(^{34}\)
†Heart failure patients (groups 1 to 4) different from control subjects (group 5) (p < 0.05).
‡Heart failure, nonsmokers with CABG (group 2) different from heart failure, nonsmokers, no CABG (group 1) (p < 0.05).
§Heart failure, smokers (groups 3 and 4) different from heart failure, nonsmokers, no CABG (group 1) (p < 0.05).
Relationship of LV Size and Function to Lung Volumes, Flow Rates, and DLCO

One hundred nineteen of a total of 203 patients with LV dysfunction had echocardiographic results. Weak correlations were observed among lung volumes, expiratory flows, DLCO, and several indexes of cardiac function; however, no significant relationships were observed between lung function and indexes of cardiac dimensions (p > 0.05). The most significant relationships observed between the lung volume measurements and cardiac function were the association of TLC, FVC, and FEV₁ (both absolute values and percent predicted) with stroke volume (r² range, 0.25 to 0.37, p < 0.01). We also noted weak but significant correlations between right ventricular pressures and cardiac index with percent-predicted TLC and FVC (r² range, 0.21 to 0.29, p < 0.05). DLCO absolute values and predicted values were weakly associated with stroke volume and ejection fraction (r² range, 0.22 to 0.26, p < 0.05). Although no significant relationships were observed between ejection fraction and lung volumes or expiratory flows, when the subjects were split into the highest and lowest ejection fractions (16 ± 1 vs 29 ± 1), the group with the lowest LVEFs demonstrated slightly lower lung volumes (percent-predicted TLC, FVC, and FEV₁), as well as a lower percent-predicted DLCO (p < 0.05).

**DISCUSSION**

We were interested in the changes in baseline pulmonary function induced by stable chronic heart

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**Table 3—Expiratory Flows**

<table>
<thead>
<tr>
<th>Groups</th>
<th>PEF, L/s ( % Predicted)</th>
<th>FEF₂₅, L/s ( % Predicted)</th>
<th>FEF₅₀, L/s ( % Predicted)</th>
<th>FEF₇₅, L/s ( % Predicted)</th>
<th>FEF₂₅₋₇₅, L/s ( % Predicted)</th>
<th>MVV, L/min ( % Predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.56 ± 0.31</td>
<td>5.41 ± 0.22</td>
<td>2.51 ± 0.15</td>
<td>0.72 ± 0.06</td>
<td>1.95 ± 0.12</td>
<td>89 ± 4</td>
</tr>
<tr>
<td>2</td>
<td>(94 ± 1)</td>
<td>(82 ± 3)†</td>
<td>(68 ± 4)†</td>
<td>(38 ± 4)†</td>
<td>(70 ± 4)†</td>
<td>(75 ± 3)†</td>
</tr>
<tr>
<td>3</td>
<td>7.96 ± 0.31</td>
<td>6.74 ± 0.35</td>
<td>2.67 ± 0.20</td>
<td>0.74 ± 0.06</td>
<td>2.03 ± 0.16</td>
<td>94 ± 4</td>
</tr>
<tr>
<td>4</td>
<td>7.28 ± 0.31</td>
<td>4.86 ± 0.31</td>
<td>1.97 ± 0.14</td>
<td>0.50 ± 0.03</td>
<td>1.42 ± 0.09</td>
<td>87 ± 4</td>
</tr>
<tr>
<td>5</td>
<td>7.06 ± 0.31</td>
<td>4.72 ± 0.25</td>
<td>2.05 ± 0.45</td>
<td>0.55 ± 0.05</td>
<td>1.54 ± 0.11</td>
<td>87 ± 5</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SE. See Table 1 for group definitions. Predicted values for PEF, FEF₂₅, FEF₅₀, and FEF₇₅, are from Knudson et al.53
†Heart failure patients (groups 1 to 4) different from control subjects (group 5) (p < 0.05).
‡Heart failure, smokers (groups 3 and 4) different from heart failure, nonsmokers (groups 1 and 2) (p < 0.05).
failure independent of smoking history, history of thoracic surgery, and morbid obesity. As summarized in Figure 4, we found that patients with chronic heart failure alone develop only mild restrictive changes in PFT results relative to control subjects and predictive values. Although these changes were significant, in most routine clinical laboratories the spirometric values would most likely be read as mildly restrictive or within the normal range (ie, within 2 SDs from the predicted values). Previous thoracic surgery (primarily coronary artery bypass surgery) tended to augment the observed restrictive changes, particularly in nonsmokers. For a given lung volume, expiratory flows were also reduced in the subjects with chronic heart failure alone, particularly at the lower lung volumes (FEF50 and FEF75); however, clear obstructive changes were most obvious in patients with a smoking history. Smoking history or previous CABG also resulted in lower DLCO values relative to patients with chronic heart failure and no previous smoking or CABG history.

**Previous Studies**

Multiple studies6,7,9,14,25 have examined pulmonary function changes in patients with a history of chronic heart failure; however, the majority of these studies did not distinguish clearly smokers from nonsmokers, a history of thoracic surgery, or significant obesity. In addition, the degree of stability or relationship between acute exacerbations in chronic heart failure symptoms has not always been clearly distinguished. It is clear that as symptoms resolve from an acute period of decompensation, pulmonary function improves10,26. VC has also been shown to vary in conjunction with NaCl loading and unloading over a 10-day period in patients with chronic heart failure, demonstrating that acute changes in fluid balance play a role in modulating pulmonary function changes.30 Most studies7,9,14 tend to show primarily restrictive rather than obstructive changes.

Obstructive changes tend to be mild and appear to be more prevalent during periods of decompensation, and tend to improve with diuresis presumably due to a reduction in extravascular lung water, and a general reduction in pulmonary and bronchial blood volumes.11,19,27 There may also be an enhanced degree of airway reactivity that diminishes with diuresis.28 The response to methacholine has been shown to increase in patients with chronic heart failure, demonstrating that acute changes in fluid balance play a role in modulating pulmonary function changes.25 Small improvements in expiratory flows are observed with anticholinergic and β-agonist drugs in patients with chronic heart failure.30,29

In patients in more stable condition, the degree of obstruction has been variable, but may relate to adequacy of treatment and smoking history as suggested by our findings.11 Variability in obstructive changes noted in the literature may also be due to the evolution of therapy with the current widespread use of ACE inhibitors vs past treatment. There also is a large degree of variability related to “aging” alone on pulmonary function and the observed obstructive changes.30

Obesity is increasing at a rapid rate in the United States and may contribute to some of the restrictive changes observed in other studies of patients with chronic heart failure.31 While the BMI was above ideal in our study, we were careful to exclude

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**Table 4 — DLCO and VA**

<table>
<thead>
<tr>
<th>Groups</th>
<th>DLCO, mL/min/mm Hg (% Predicted)</th>
<th>VA, L</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>22.3 ± 0.7 (90 ± 2)</td>
<td>5.23 ± 0.15</td>
</tr>
<tr>
<td>2</td>
<td>19.1 ± 0.6 (77 ± 2)†</td>
<td>5.06 ± 0.14</td>
</tr>
<tr>
<td>3</td>
<td>17.7 ± 0.6 (72 ± 3)‡</td>
<td>5.04 ± 0.13</td>
</tr>
<tr>
<td>4</td>
<td>18.0 ± 0.9 (74 ± 3)§</td>
<td>5.12 ± 0.16</td>
</tr>
<tr>
<td>5</td>
<td>24.3 ± 0.8 (102 ± 2)</td>
<td>5.46 ± 0.16</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SE. See Table 1 for group definitions. Predicted values are from Miller et al.52
†Heart failure patients (groups 1 to 4) different from control subjects (group 5) (p < 0.05).
‡Heart failure, no CABG (groups 1 and 3) different from heart failure, CABG (groups 2 and 4) (p < 0.05).
§Heart failure, smokers (groups 3 and 4) different from heart failure, nonsmokers (groups 1 and 2) (p < 0.05).
subjects with clear morbid obesity from the comparisons (BMI > 35 kg/m²). In most studies examining obesity, the fall in TLC and VC is similar to that observed in our patients with chronic heart failure alone. This is presumably due to the enhanced weight around the chest wall and abdomen and the resultant increased respiratory muscle load.

**Physiologic Mechanisms**

The cause of the restrictive changes in chronic heart failure remains unclear. We and others have found lung compliance to be reduced in patients with chronic heart failure in stable condition, consistent with the restrictive changes. Work by Hosenpud et al and Niset et al suggests that some of these changes (particularly the reduced VC) may be related to cardiac size. Since the heart and lung compete for space within the chest wall, an enlargement in cardiac size clearly could reduce VC and TLC. Enright et al found a relationship between LV posterior wall thickness in diastole and FVC in the Cardiovascular Health Study; however, the relationship was weak (regression coefficient = -0.246), and FVC only appeared to decline significantly in patients with the largest changes in LV size (i.e., highest deciles). Although we did not have cardiac dimensions in all of our subjects, in those that were available (119 of 203 subjects; 59% of patients with chronic heart failure), we found no relationships between these echocardiographic measurements and our measurements of lung function. Thus, within a group of patients with an ejection fraction < 35%, cardiac dimensions based on echocardiography do not appear to play a major role in the lung volume changes. A more accurate assessment may be to determine cardiac dimensions relative to chest wall size. Since chest wall size varies significantly for a given height and weight and general body habitus, cardiac dimensions alone would not necessarily predict alterations in lung function.

Since some of the restrictive changes observed in chronic heart failure resolve with fluid unloading, it has also been proposed that either an increase in pulmonary and/or bronchial blood volume or an increase in interstitial fluid accumulation likely accounts for some of these changes, even in patients with stable chronic heart failure. General muscle weakness and wasting, including the respiratory muscles, has also been well established in patients with chronic heart failure. Similar to our findings, several studies have noted a reduced MVV in patients with chronic heart failure, likely related to muscle weakness. This may result in a reduced ability to fully inspire, resulting in a reduced TLC and a reduced FVC. In addition, it has been proposed that chronic heart failure is associated with increased levels of circulating cytokines (such as tumor necrosis factor-α), which may induce changes in lung parenchyma, or that high left atrial pressures.

**Figure 4.** Summary of pulmonary changes related to chronic heart failure, smoking history, and previous CABG. Values are expressed relative to age-, gender-, and height-matched predicted values (see Tables 2–4 for predicted references).
may induce chronic remodeling of the pulmonary vasculature (smooth-muscle proliferation, intimal and medial thickening, and fibrinoid necrosis and arteritis) that could alter lung compliance and induce the observed mild restrictive changes.\textsuperscript{1,2,4,43}

Although we found an essentially normal resting DLCO in our group with chronic heart failure alone, most studies\textsuperscript{6,20,22,45} on patients with chronic heart failure have found DLCO to be reduced. Our data would suggest that patients with chronic heart failure and a smoking history clearly demonstrate a reduction in DLCO, and previous CABG may also contribute to a reduction. The fall in DLCO in our smokers is consistent with a loss of alveolar-capillary surface area commonly described.\textsuperscript{46} The mechanism for the reduced DLCO in postsurgical patients is unclear. Previous studies\textsuperscript{47,48} have reported declines in DLCO after cardiac surgery acutely that may persist for at least 2 weeks; however, most of our patients were many years postsurgery. Although speculative, this may reflect pathophysiologic changes in the pulmonary microcirculation initiated by cardiopulmonary bypass, as off-pump surgery eliminates potentially negative consequences of cardiopulmonary bypass, such as a systemic inflammatory response with coagulopathy and altered microvascular permeability.\textsuperscript{49}

The disparity in DLCO in our patients with chronic heart failure alone vs previous studies may also be related to the more recent use of ACE inhibitors as standard therapy in patients with chronic heart failure. Work by Guazzi et al\textsuperscript{50} suggested that treatment with enalapril increased DLCO toward normal in patients with LV dysfunction. Some recent data\textsuperscript{51} in our laboratory support the work of Guazzi et al.,\textsuperscript{50} as patients with chronic heart failure homozygous for the ACE deletion allele genotype (highest plasma ACE levels) tended to have lower DLCO values than those with the II genotype. This would suggest that the derangement in neurohumoral function that occurs with chronic heart failure might significantly alter normal function of the alveolar-capillary membrane.

\textbf{Potential Impact}

Do the changes in baseline spirometry contribute to the exertional dyspnea observed in this patient group? Although the changes in lung volumes and expiratory airflow are small, these changes may impact the sensation of dyspnea in these patients. We previously demonstrated that patients with chronic heart failure tend to breathe at low lung volumes at rest and during activity.\textsuperscript{44} The reduced expiratory flow, particularly at these low lung volumes, reduces the breathing reserve and appears to contribute to expiratory flow limitation. We also found that it was difficult to increase end-expiratory lung volume during exercise, despite apparent room to do so, suggesting that the reduced lung and possibly chest wall compliance may reduce the ability to avoid expiratory flow limitation (by increasing end-expiratory lung volume), and this may contribute to an increased work of breathing and to an enhanced sensation of dyspnea.

\textbf{ACKNOWLEDGMENT:} The authors thank Becky Hughes-Borst and Sue Nelson, LPN, for help in data collection, and Audrey Schroeder for help with manuscript preparation.

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