Exercise hyperpnea in chronic heart failure: relationships to lung stiffness and expiratory flow limitation

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PATIENTS AFFECTED BY chronic heart failure (CHF) often exhibit excessive ventilation for a given workload during exercise (4, 8, 11, 14, 21, 33, 34), mostly sustained by an increase in breathing frequency rather than in tidal volume (VT) (4, 8, 14, 33). Several mechanisms have been proposed to explain the increased ventilatory response to exercise in CHF, including ventilation-perfusion abnormalities, altered control of breathing, impaired central and peripheral hemodynamics, early onset of anaerobic metabolism, and respiratory and skeletal muscle fatigue (6). The reasons and the mechanisms causing exercise hyperpnea to be achieved by increasing breathing frequency more than VT in CHF are unknown and represent the object of this study.

The most prominent pulmonary abnormality in CHF is an increased lung stiffness (9, 14, 21, 24, 26, 34, 35). This may result from a number of mechanisms, including vascular congestion, interstitial edema and fibrosis, increased alveolar surface tension, ventilation inhomogeneities, and activation of contractile elements. An increased lung stiffness may contribute to alter the pattern of breathing during exercise by different mechanisms. First, vascular congestion and interstitial edema, either preexisting or developing during exercise, may trigger rapid and shallow breathing by direct stimulation of irritant or J receptors (8, 25). Second, an increase in breathing frequency may be necessary from the beginning of exercise because the increase in VT is limited by mechanical constraints. These are represented by 1) an excessive elastic work of breathing, which limits the increase of end-inspiratory lung volume, and 2) premature occurrence of expiratory flow limitation (EFL) (15), which prevents the physiological decrease of functional residual capacity (FRC) during exercise.

This study was undertaken to investigate whether differences in ventilation during an incremental exercise test between CHF and normal subjects are related to differences in lung stiffness, EFL, or both. Both static and dynamic lung compliance were measured at rest and during exercise in an attempt to separate the effects of various determinants of increased lung stiffness. The occurrence of EFL was inferred from the reduction of the expiratory flow reserve (EFR), i.e., the difference between tidal and forced expiratory flows in the range of tidal breathing.
Table 1. Main anthropometric data

<table>
<thead>
<tr>
<th>CHF Subjects</th>
<th>Normal Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>14</td>
</tr>
<tr>
<td>Male/female</td>
<td>12/2</td>
</tr>
<tr>
<td>Age, yr</td>
<td>60 – 9</td>
</tr>
<tr>
<td>Height, cm</td>
<td>171 – 8</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>76 ± 13</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.3 ± 4.0</td>
</tr>
<tr>
<td>Smoking habit</td>
<td>Yes/No/Former</td>
</tr>
<tr>
<td>pack-yr</td>
<td>9 ± 12</td>
</tr>
</tbody>
</table>

Values are means ± SD. CHF, chronic heart failure; BMI, body mass index; NS, not significant.

METHODS

Subjects

The study included 14 CHF and 15 normal subjects (Table 1). Inclusion criteria for CHF subjects were to have a history of congestive heart failure and to have been in stable clinical conditions in the 2 mo preceding the study. Exclusion criteria were primary pulmonary disease, peripheral vascular disease, primary pulmonary hypertension, primary valvular disease, artificial pacemaker, exercise-induced arrhythmias, chronic obstructive pulmonary disease, and bronchial asthma. The cause of CHF was ischemic dilated cardiomyopathy in 3 cases and primary dilated cardiomyopathy in 11 cases. All CHF subjects were under pharmacological treatment: 6 with digitalis, 13 with diuretics, 14 with angiotensin-converting enzyme inhibitors, and 4 with β-blockers. All normal subjects were physically active in recreational activities. The protocol was approved by the local Ethics Committee, and written consent was obtained from each participant before the study.

Lung Function Measurements

Forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC) were measured in triplicate by a mass flow sensor (Vmax, SensorMedics, Yorba Linda, CA) following the American Thoracic Society recommendation (3). Maximum forced expiratory flows at 50% and 25% of FVC from a full flow-volume curve were calculated after volume had been corrected for the difference between predicted and measured total lung capacity (TLC). TLC, residual volume (RV), and FRC were measured by multibreath nitrogen washout (2200 Pulmonary Function Laboratory, SensorMedics). Diffusion capacity for carbon monoxide was measured by single-breath constant-expiratory flow technique (SensorMedics 2200) (13). Arterial oxygen and carbon dioxide tensions and pH were measured by a gas analyzer (ABL 520, Radiometer, Copenhagen, Denmark).

Lung mechanics before and during exercise were measured by using a Direc/NEP 200A recording system (Raytech, Vancouver, BC). Flow was measured by a screen-type pneumotachograph placed between mouthpiece and mass flow sensor and connected to a differential pressure transducer (±5 cmH₂O). Transpulmonary pressure (Ptp) was estimated from the difference between esophageal and mouth pressures. Esophageal pressure was measured by positioning a 10-cm-long thin latex balloon in the esophagus, 38–42 cm from the nostrils. Volume and pressure channels were calibrated before each study according to the recommendations of the manufacturer by using a 3-liter syringe and a water-filled manometer, respectively. The balloon was connected to a pressure transducer (±100 cmH₂O) and filled with 0.8 ml of air. Its positioning was considered correct if Ptp remained constant while mouth pressure increased during a gentle effort against a small orifice (20). Mouth pressure was measured by a pressure transducer (±100 cmH₂O). Care was taken to avoid thermal drift by zeroing the flow and volume signals immediately before recording tidal breathing necessary to compute dynamic compliance (CLdyn) and before recording quasi-static pressure-volume (PV) curves. The latter were measured by intermittent manual occlusion of the expiratory port of the pneumotachograph with the patient slowly expiring from TLC. Quasi-static lung compliance (CLst) was measured only at rest and within 2 min from the end of maximum exercise, whereas CLdyn was measured at rest and at each step of the incremental exercise test. The frequency responses of flow- and Ptp-measuring systems had been determined to be flat up to 10 Hz. All signals were recorded at a frequency of 100 Hz and digitized by a computer for subsequent analysis.

During exercise, minute ventilation (Ve), oxygen consumption (VO₂), and carbon dioxide output (VCO₂) were measured by breath by breath (Vmax, SensorMedics). Sets of simple and very reproducible maneuvers consisting of four to six regular tidal breaths immediately followed by a forced expiration from end-tidal inspiration to near RV (partial forced expiration) and a forced inspiration to TLC were performed in triplicate at rest and once over the last 20 s at the end of each step to estimate the changes in FRC, end-inspiratory lung volume (EILV), EFR, partial forced expiratory flow at 50% of FVC (V₂ fifty), and maximal inspiratory flow at 50% of FVC. Specifically, changes in FRC and EILV during exercise were defined as the changes in dynamically determined lung volumes at end-tidal expiration and inspiration, respectively. Both FRC and EILV were related to TLC, which was assumed to remain constant during exercise. This assumption was verified by measuring Ptp at TLC. EFR was determined at each step of the test from the difference between partial and tidal expiratory flows near FRC (27). In the case that FRC tended to increase when tidal expiratory flow near FRC impinged on partial flow at some level of ventilation, EFR was computed as the difference between the tidal expiratory flow near the increased lung volume and the partial flow measured at the level of the lowest FRC attained during the test. Thus EFR becomes negative if FRC increases.

Predicted values are from Quanjer et al. (29) for lung function tests and from Jones (16) for the exercise test.

Study Protocol

Screening day. All subjects attended the laboratory for clinical history and physical examination, electrocardiogram, and lung function measurements. CHF subjects also underwent an echocardiography. All subjects were taught how to perform reproducibly the partial forced expiratory maneuvers required for the study and underwent an incremental cardiopulmonary exercise test to have their maximum exercise capacity determined.

Study day. The subjects attended the laboratory in the midafternoon after a light meal. Partial and full forced expiratory flow-volume curves were recorded in triplicate through the mass flow sensor. Blood pressure and heart rate were measured. All CHF and six normal subjects accepted to have an esophageal balloon positioned after topical anesthesia of the nose and throat. Before starting the exercise test, at least three quasi-static PV curves, two sets of CLdyn, and several regular breaths followed by three sets of reproducible

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tidal, partial, and maximal flow-volume curves were obtained.

A symptom-limited exercise test was performed on an electronically braked cycle ergometer (Ergometrics 800S, SensorMedics), with the subject wearing a nose clip and breathing through a mass flow sensor (dead space 75 ml) connected to a saliva trap. A 12-lead electrocardiogram was continuously recorded (MAX1, SensorMedics). After 3 min of resting and 2 min of warm-up, the exercise load was increased every 2 min by 10 or 15 W for the CHF patients, depending on the previous exercise test, and by 25 W for the normal subjects until exhaustion. The subjects pedaled at ~50–60 revolutions/min. Ptp, flow, and volume were recorded during tidal breathing to compute CLdyn, at least twice at rest for ~2 min and once during the first 40 s of the second minute at each step. Tidal and partial flow-volume loops were measured at rest and during the last 20 s of each work level. Special care was taken to maintain the position of the trunk fairly constant during the test. A second set of three quasi-static PV curves was recorded within 2 min from the end of exercise.

Data Analysis

Quasi-static PV curves were constructed by taking the relevant signals at zero flow. Clat was the slope of the best fit of the curves between FRC and 0.5 liters above it. CLdyn was estimated on at least six tidal breaths by playing back the files recorded at each step. Irregular breaths, sighs, swallows, and portions of the files with volume drift were discarded before analysis. With the aid of a cursor, Vr and Ptp were measured at end-inspiratory lung volume (PtpEILV) and at FRC (PtpFRC) for each breath. CLdyn was computed by dividing Vr by the difference between PtpEILV and PtpFRC (31).

Only representative breaths recorded during the exercise test before the partial forced expiratory maneuver were used for analysis of breathing pattern. Vr and inspiratory and expiratory times (Ti and Te, respectively) were calculated breath by breath and averaged over several breaths, thus allowing minute ventilation (VE), breathing frequency, and ratio of inspiratory time to total respiratory cycle duration (TV/Ttot) to be computed.

To allow comparison between subjects with different respiratory volumes, Vr and VE were normalized to TLC, which is the most representative index of lung volumes in CHF, and were referred to as adjusted Vr (Vraadj) and adjusted VE (VEaadj), respectively. Differences in breathing pattern during exercise between groups were assessed by regressing breathing frequency, Ti, Te, TV/Ttot, Vraadj, CLadj, Vpar50, Vco2, and EFR against Vco2, rather than considering their single values at maximum exercise as conventionally done. Such an analysis is expected to give an accurate estimate of the changes in breathing pattern during exercise, because it takes into account all the values recorded during the test and minimizes the high variability of a single value. The reason for regressing the variables against Vco2 rather than the more conventional VE or VEaadj relies on the fact that, for a given Vco2, VE is much higher in CHF than in normal subjects. Thus using VE instead of Vco2 would have led to a systematic overestimation of the relationship of the relevant variables with the respiratory stimulus in the normal subjects and possibly blurred the mechanisms causing tachypnea in the CHF.

The regression of EFR against Vco2 was taken as an index of EFL during exercise on the basis of the following reasoning. When ventilation increases, EFR tends to decrease because tidal expiratory flow increases and FRC decreases. When EFR is reduced to zero, flow is limited and greater ventilation can be achieved only by increasing FRC. Thus a lower intercept and/or a greater slope of the regression of EFR vs. Vco2 in CHF compared with normal individuals would suggest occurrence of premature EFL and/or worsening of it with the increase in ventilatory stimulus, or both.

Statistics

Student’s paired and unpaired t-tests and χ2 test with Yates correction were used to analyze resting differences between groups. Correlations were assessed by Pearson’s test. P < 0.05 was considered statistically significant. All values are expressed as means ± SD.

RESULTS

Pulmonary Function Tests at Rest

Although within predicted normal limits, lung volumes tended to be slightly less in CHF than in normal subjects (Table 2). The EFR of CHF subjects was on average less than half of that of normal subjects (P < 0.05), but this difference was apparently not due to a decrease in maximal expiratory flows (similar maximum forced expiratory flows at 50% and 25%). Breathing pattern, PtpFRC, Clat, and CLdyn were similar in CHF and normal subjects, although CLdyn tended to be less in the former (P < 0.06). Diffusion capacity for carbon monoxide was slightly but significantly reduced in CHF patients (P < 0.02). FRC as percent of predicted was significantly correlated with CLdyn (r = 0.48, P < 0.05). Arterial PO2, arterial PCO2, and pH were similar in the two groups. According to maximum exercise tests

Table 2. Pulmonary and cardiovascular function data at rest

<table>
<thead>
<tr>
<th>CHF</th>
<th>Subjects</th>
<th>P Value</th>
<th>Normal Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1, %predicted</td>
<td>95 ± 17</td>
<td>NS</td>
<td>105 ± 16</td>
</tr>
<tr>
<td>FVC, %predicted</td>
<td>101 ± 16</td>
<td>NS</td>
<td>107 ± 17</td>
</tr>
<tr>
<td>FRC, %predicted</td>
<td>94 ± 17</td>
<td>NS</td>
<td>106 ± 20</td>
</tr>
<tr>
<td>RV, %predicted</td>
<td>78 ± 19</td>
<td>NS</td>
<td>87 ± 22</td>
</tr>
<tr>
<td>TLC, %predicted</td>
<td>93 ± 15</td>
<td>NS</td>
<td>102 ± 13</td>
</tr>
<tr>
<td>DLco, %predicted</td>
<td>81 ± 24</td>
<td>&lt;0.02</td>
<td>100 ± 10</td>
</tr>
<tr>
<td>Vmax50, l/s</td>
<td>4.13 ± 2.03</td>
<td>NS</td>
<td>4.41 ± 1.96</td>
</tr>
<tr>
<td>Vmax25, l/s</td>
<td>1.84 ± 1.10</td>
<td>NS</td>
<td>1.60 ± 1.03</td>
</tr>
<tr>
<td>MIF50, l/s</td>
<td>4.63 ± 1.44</td>
<td>&lt;0.01</td>
<td>6.66 ± 2.22</td>
</tr>
<tr>
<td>EFR, l/s</td>
<td>0.72 ± 1.13</td>
<td>&lt;0.05</td>
<td>1.77 ± 1.08</td>
</tr>
<tr>
<td>Ccl, l/cmH2O</td>
<td>0.34 ± 0.16</td>
<td>NS</td>
<td>0.25 ± 0.08</td>
</tr>
<tr>
<td>Ptplecl, cmH2O</td>
<td>22.4 ± 7.1</td>
<td>NS</td>
<td>28.7 ± 7.9</td>
</tr>
<tr>
<td>Cldyn, l/cmH2O</td>
<td>0.16 ± 0.06</td>
<td>&lt;0.06</td>
<td>0.22 ± 0.06</td>
</tr>
<tr>
<td>Pao2, Torr</td>
<td>85 ± 16</td>
<td>NS</td>
<td>85 ± 13</td>
</tr>
<tr>
<td>Paco2, Torr</td>
<td>34 ± 4</td>
<td>NS</td>
<td>37 ± 1</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>32.5 ± 7.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD. FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; FRC, functional residual capacity; RV, residual volume; TLC, total lung capacity; DLco, single-breath carbon monoxide diffusion capacity; Vmax50 and Vmax25, forced expiratory flows at 50% and 25% of FVC, respectively; MIF50, maximal inspiratory flow at 50% of FVC; EFR, expiratory flow reserve; Ccl, static lung compliance; Ptplecl, transpulmonary pressure at TLC; Cldyn, dynamic lung compliance; Pao2, arterial PO2; Paco2, arterial PCO2; LVEF, left ventricle ejection fraction.
performed before the study, seven patients were in class A of the New York Heart Association (NYHA) classification (peak $\dot{V}_{O_2} > 20$ ml·min$^{-1}$·kg$^{-1}$), five in NYHA class B (peak $\dot{V}_{O_2} = 15$–20 ml·min$^{-1}$·kg$^{-1}$), and two in NYHA class C (peak $\dot{V}_{O_2} < 10$ ml·min$^{-1}$·kg$^{-1}$).

Table 3. Main respiratory and cardiovascular variables at maximum exercise

<table>
<thead>
<tr>
<th>Variable</th>
<th>CHF Subjects</th>
<th>P Value</th>
<th>Normal Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Workload</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$W$</td>
<td>$73 \pm 21$</td>
<td>$&lt;0.001$</td>
<td>$174 \pm 42$</td>
</tr>
<tr>
<td>% predicted</td>
<td>$50 \pm 19$</td>
<td>$&lt;0.001$</td>
<td>$98 \pm 24$</td>
</tr>
<tr>
<td>$\dot{V}_{O_2}$</td>
<td>$1.35 \pm 0.31$</td>
<td>$&lt;0.001$</td>
<td>$2.39 \pm 0.62$</td>
</tr>
<tr>
<td>% predicted</td>
<td>$62 \pm 13$</td>
<td>$&lt;0.001$</td>
<td>$100 \pm 20$</td>
</tr>
<tr>
<td>$\dot{V}_{E}$</td>
<td>$42.2 \pm 10.8$</td>
<td>$&lt;0.001$</td>
<td>$76.4 \pm 25.4$</td>
</tr>
<tr>
<td>% predicted</td>
<td>$44 \pm 13$</td>
<td>$&lt;0.001$</td>
<td>$62 \pm 17$</td>
</tr>
<tr>
<td>$FRC$, % TLC</td>
<td>$11.4 \pm 2.9$</td>
<td>$&lt;0.001$</td>
<td>$16.7 \pm 3.8$</td>
</tr>
</tbody>
</table>

Maximum Exercise Test

In the CHF group there was a mild to moderate degree of exercise impairment, as evidenced by reduced power output and lower $\dot{V}_{O_2}$ peak (Table 3). At end exercise, $\dot{V}_E$ was $<50$% of MVV, estimated as FEV$1 \cdot 35$, and HR and $O_2$ pulse were also low. $C_{L_{st}}$ decreased significantly from rest to end exercise in CHF but not in normal subjects, although this difference was not significant between groups, likely because of the small number of normal subjects ($n = 4$) who made reproducible PV curves both at rest and at maximum exercise. In neither group was $P_{tp_{TLC}}$ modified by exercise. No intergroup differences in the slope of the relationships between $C_{L_{dy}}$ or $P_{tp_{EILV}}$ vs. $V_{CO_2}$ were observed.

Analysis of the most important variables of breathing pattern during exercise (Fig. 1) revealed that exertional hyperpnea was achieved by proportionally more rapid breathing in CHF than in normal subjects, as documented by a significantly greater slope of breathing frequency vs. $V_{CO_2}$ (10.9 ± 5.5 in CHF and 5.7 ± 2.6 in normal subjects, $P < 0.01$) and a similar slope of $\dot{V}_{T_{adj}}$ vs. $V_{CO_2}$. In the CHF group, the slope of breathing frequency vs. $V_{CO_2}$ was inversely correlated with resting $C_{L_{dy}}$ ($r = -0.61, P < 0.05$) (Fig. 2). FEV$1$ %predicted ($r = -0.58, P < 0.05$), FVC %predicted ($r = -0.67, P < 0.01$), TLC %predicted ($r = -0.74, P < 0.01$), and FRC %predicted ($r = -0.56, P < 0.05$).

Inset, the slope of breathing frequency vs. $V_{CO_2}$ did not correlate with baseline $C_{L_{st}}$, change in $C_{L_{st}}$ at end exercise, slope of $C_{L_{dy}}$ vs. $V_{CO_2}$, and regression param-

Fig. 1. Mean regression lines of some of the respiratory variables plotted against $CO_2$ production ($\dot{V}_{CO_2}$) during exercise in chronic heart failure patients (CHF; solid lines) and in the control group (dashed lines). A: tidal volume ($\dot{V}_{T_{adj}}$). B: breathing frequency ($f$). C and D: inspiratory and expiratory times (Ti and Te, respectively). E: respiratory duty cycle (Ti/Ttot). F: partial forced expiratory flow at 50% of control forced vital capacity ($V_{part_{50}}$). G: expiratory flow reserve (EFR). H: lung dynamic compliance ($C_{L_{dy}}$). Significant differences of intercept (Int) and slopes (Sl) are reported.
Fig. 2. Slope of the linear regression of \( f \) vs. \( \dot{V}CO_2 \) during exercise plotted against \( CL_{dy} \) at control in the CHF group \((r = -0.61, P < 0.05)\).

The major findings of this study are that exercise tachypnea in CHF was 1) inversely correlated with resting dynamic compliance but not with quasi-static compliance, either at rest or at maximum exercise, 2) not correlated with the occurrence of EFL, and 3) characterized by a greater rate of decrease in expiratory time than in the normal subjects.

It is well accepted that lung parenchyma is commonly involved in CHF for a series of reasons. Pulmonary congestion and hypertension, edema, increased perivascular pressure, vascular thrombosis, increased heart size, and neurohumoral mechanisms may increase lung stiffness both at rest and during exercise (9, 14, 21, 24, 26, 34, 35). In addition, regional hypoperfusion may result in pneumatic constriction with local decrease in lung compliance (22). Altogether these mechanisms are deemed to decrease lung compliance, thus causing a restrictive lung abnormality (34). In the present study, lung restriction was present only in two patients, as documented by a TLC <80% of predicted, whereas the average lung function of the other subjects...
was unexpectedly maintained within the normal range. This finding may be explained by the fact that average $C_{\text{dyn}}$ in CHF was similar to that of normal subjects and is in line with similar values reported by others for CHF patients with similar NYHA class (2, 8, 34).

If the range of operational lung volume is restricted, $V_T$ may not be able to increase sufficiently to meet the ventilatory demands during exercise and the required $V_E$ may be achieved mostly by increasing breathing frequency. A given increase in $V_E$ attained with increase in frequency rather than in $V_T$ would result in an increase in dead space, thus requiring a greater $V_E$ for a given power output. Moreover, if we accept that breathing pattern is regulated in a way to minimize the work of breathing (19), then we could speculate that the increase in frequency for a given $V_E$ is more advantageous in CHF than an increase in $V_T$.

In the present study, the rate of increase of breathing frequency with $VCO_2$ was inversely correlated with resting $C_{\text{dyn}}$, but not with $C_{\text{lat}}$. Although these findings seem to be discrepant at a first sight, it may be speculated that exercise tachypnea is related to an increase in lung parenchyma hysteresis rather than to lung stiffness itself. A decrease in $C_{\text{dyn}}$ is known to reflect an involvement of lung parenchyma as a result of exaggerated growth of inextensible fibrotic tissue, vascular congestion and edema, altered alveolar surface tension, activation of contractile elements, recruitment/derecruitment of alveolar units, and ventilation inhomogeneities (12). Whether tachypnea was predominantly triggered by one or more of the above factors cannot be inferred from the present data, although vascular congestion, alteration in surface tension together with large differences between opening and closing pressures, and parenchymal and airways contractile elements appear to be the most plausible ones. Indeed, exaggerated growth of fibrotic tissue, which is known to cause decrease in $C_{\text{lat}}$ in addition to $C_{\text{dyn}}$, is unlikely to have occurred in the subjects of the present study given that baseline $C_{\text{lat}}$ was similar between groups and did not correlate with the increase in breathing frequency vs. $VCO_2$. Also ventilation inhomogeneities, which are known to cause decrease in $C_{\text{lat}}$ with increase in frequency, were likely of little importance in the present study, because $C_{\text{lat}}$ increased with $VCO_2$ similarly in CHF and normal subjects. Therefore, these data would substantiate at least in part the accepted notion that exercise tachypnea in CHF may be either the most economic breathing adaptation to the high elastic load due to the primary cardiovascular disease (14) or the consequence of neural reflexes evoked by stimulation of the irritant and/or J receptors because of chronic excess of extravascular fluid in the lungs (25).

That perturbed breathing frequency during exercise is linked to involvement of the lungs in CHF is also supported by two additional observations. First, the rate of increase of breathing frequency with $VCO_2$ correlated with most of the lung function parameters measured at rest. Second, the relationship between the rate of increase in breathing frequency and resting $C_{\text{dyn}}$ remained significant when the former was expressed as a function of $V_E$ ($r = -0.53, P < 0.05$).

At variance with a previous study (8), the significant decrease in $C_{\text{lat}}$ recorded in CHF at maximum exercise did not correlate with an increase of ventilation and especially of breathing frequency. Presumably, such a decrease was due to pulmonary congestion, likely because of high intravascular hydrostatic pressures developed at high ventilation (30). If this is the case, then one would wonder why exercise-induced increase in lung stiffness did not evoke tachypnea as much as preexisting involvement of lung parenchyma. One possible reason is that the tachypnoic response to exercise occurs with a certain time delay and becomes more visible in the recovery phase (8).

Although EFL occurred fairly soon with exercise in CHF, as suggested by a significantly lower intercept of EFR vs. $VCO_2$ than in the control group, there was no relationship between this and exercise tachypnea. Studies in chronic obstructive pulmonary disease during exercise demonstrate that, when EFR occurs, FRC is accommodated to higher lung volume to allow greater ventilation (18, 23, 27). This adaptation entails a mechanical constraint of $V_T$ with exercise, so that for a given ventilation breathing frequency has to increase. The fact that in our CHF patients none of the indexes of EFL were associated with rapid shallow breathing does not rule out that EFL may contribute to tachypnea. Other triggers, such as lung stiffness, could have been more predominant in this respect. Alternatively, comparison of tidal and maximal flow measured at the mouth is not sensitive enough to detect the occurrence of regional EFLs, as suggested by a recent study (28).

We observed that the rate of increase of TI/T_tot with $VCO_2$ in the CHF was abnormally higher than in the normal subjects. TI decreased with $VCO_2$ similarly in CHF and normal group, but $T_E$ decreased as twice as fast in the former. Thus the increase in TI/T_tot was mostly due to excessive shortening of $T_E$ with constant decrease in TI. Although we do not have a clear explanation for this finding, we speculate that the greater decrease in $T_E$ with exercise may reflect a complex respiratory adaptation tending to limit or contrast functional events specifically arising late on expiration, such as dynamic compression of the airways, which occurred in most of the CHF patients. Under these conditions, increased TI/T_tot could have limited the dangerous effects on the cardiovascular system (10), even though such a strategy may burden the inspiratory muscles. Certainly, any decrease in $T_E$ should increase breathing frequency, unless compensated by a change in TI. Thus it is not unreasonable to suspect that what caused the rate of TI/T_tot with $VCO_2$ to increase more in CHF than in the control group also contributed to tachypnea, had TI not blurred the effect.

Dynamic lung hyperinflation is almost mandatory when EFL occurs but has several side effects. Increasing FRC would necessarily decrease $V_T$, unless EILV mutually increased by the same magnitude. In the present study, EILV at maximum load was signifi-
cantly less in CHF than in normal subjects, thus preventing VTadj from further increase. One reason for this could be that the decrement in C\textsubscript{Lst} recorded at end exercise in CHF, possibly due to regional hyperperfusion and consequent pneumoconstriction (22, 35) or engorged pulmonary vascular bed (1), was such as to impose an extra end-inspiratory load intolerable to the inspiratory muscles, thus prematurely terminating inspiration. Dynamic lung hyperinflation could put the inspiratory muscles in an unfavorable condition to generate force (32); edema formation as a result of increased pulmonary vascular pressure could stimulate lung parenchyma receptors, thus prematurely interrupting ventilation; and, finally, respiratory muscle deoxygenation (17) could lead to inability to sustain lung expansion over an adequate period of time. Alternatively, external factors such as leg fatigue could have contributed to interrupt exercise prematurely and prevented EILV in CHF from increasing as much as in normal subjects.

Although most of the differences in lung function at rest between CHF and normal subjects were quantitatively trivial, EFR was <50% compared with the control group. Its decrement was not likely due to airway narrowing, because forced expiratory flows were similar between groups. More likely, it was the small increase in lung stiffness that caused FRC to accommodate at a lower lung volume at which EFR is necessarily low, as suggested by a significant relationship between FRC as percent of predicted and C\textsubscript{Ldyn}. A still-positive EFR at rest in the CHF patients would explain why VT increased similarly to that of the normal subjects at the beginning of exercise, because it was not such to prevent EILV and FRC from expanding adequately. However, with EFR becoming zero at lower V\textsubscript{O2} than in the normal subjects, breathing pattern had to adapt with a gradual increase in FRC to achieve greater expiratory flow and with a decrease in VT and increase in breathing frequency.

Normal individuals tend to increase maximal flows during exercise (15, 27), likely because of an increase in airway caliber. Catecholamines, decreased vagal tone with exercise, and tidal stretching of airway smooth muscle could be responsible for the phenomenon. If catecholamines in exercising CHF subjects are assumed to increase at least as much as in healthy subjects (1, 7), a lack of increment in forced expiratory flow in CHF would suggest that vagal tone persists in CHF (5) and/or that tidal stretching is ineffective to distend the airways, or that airway walls are inextensible with lung expansion. Whatever the underlying mechanisms, the inability to increase flow during exercise heavily weighted on the choice of breathing adaptation.

In conclusion, the present data are consistent with the notion that lung stiffness may lead to a mainly tachypnoic response to exercise in CHF. This pattern of response seems to be attributable to longstanding decrease in C\textsubscript{Ldyn}, reflecting chronic perivascular and alveolar edema, surface phenomena, and recruitment/derecruitment. According to the present data, dynamic compression of the airways during expiration is not directly involved in tachypnea, although it may contribute to alter breathing pattern.

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