CARDOVASCULAR MEDICINE

Does lung diffusion impairment affect exercise capacity in patients with heart failure?

P G Agostoni, M Bussotti, P Palermo, M Guazzi

Objective: To determine whether there is a relation between impairment of lung diffusion and reduced exercise capacity in chronic heart failure.

Design: 40 patients with heart failure in stable clinical condition and 40 controls participated in the study. All subjects underwent standard pulmonary function tests plus measurements of resting lung diffusion (carbon monoxide transfer, Tlco), pulmonary capillary volume (Vc), and membrane resistance (Dm), and maximal cardiopulmonary exercise testing. In 20 patients and controls, the following investigations were also done: (1) resting and constant work rate Tlco; (2) maximal cardiopulmonary exercise testing with inspiratory O2 fractions of 0.21 and 0.16; and (3) rest and peak exercise blood gases. The other subjects underwent Tlco, Dm, and Vc measurements during constant work rate exercise.

Results: In normoxia, exercise induced reductions of haemoglobin O2 saturation never occurred. With hypoxia, peak exercise uptake (peak VO2) decreased from (mean (SD)) 1285 (395) to 1081 (396) ml/min (p < 0.01) in patients, and from 1861 (563) to 1771 (457) ml/min (p < 0.05) in controls. Resting Tlco correlated with peak VO2 in heart failure (normoxia < hypoxia). In heart failure patients and normal subjects, Tlco and peak VO2 correlated with O2 arterial content at rest and during peak exercise in both normoxia and hypoxia. Tlco, Vc, and Dm increased during exercise. The increase in Tlco was greater in patients who had a smaller reduction of exercise capacity with hypoxia. Alveolar–arterial O2 gradient at peak correlated with exercise capacity in heart failure during normoxia and, to a greater extent, during hypoxia.

Conclusions: Lung diffusion impairment is related to exercise capacity in heart failure.

METHODS

Patient population

Forty patients with stable heart failure (mean (SD) age 61.9 (6.4) years; 30 male, 10 female) and 40 healthy controls (57.6 (9.6) years; 28 male, 12 female) participated in the study.

All the heart failure patients were in New York Heart Association (NYHA) functional class II or III and belonged to a cohort of heart failure patients regularly followed in our heart failure clinic. Heart failure aetiology was: ischaemic cardiomyopathy (15), idiopathic (11), alcoholic (7), HIV related (4), and related to antitumour drugs (3). Exclusion criteria included: a left ventricular ejection fraction > 35% by echocardiography, the presence of periodic breathing during exercise, primary pulmonary disease, unstable angina, recent myocardial infarction, and artificial pacemakers. Ten patients were active smokers, 20 were previous smokers (defined as patients who quit smoking more than five years ago), and 10

Abbreviations: Cao2, arterial oxygen content; DM, membrane resistance; △P[A–aO2], alveolar–arterial oxygen pressure gradient; FEV1, forced expiratory volume in one second; Finh, inspired oxygen fraction; FVC, forced vital capacity; MVV, maximum voluntary ventilation; PaO2, systemic arterial oxygen tension; Sao2, haemoglobin saturation with oxygen; Tlco, carbon monoxide transfer; Vc, pulmonary capillary blood volume; VO2, oxygen uptake

S

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regulate

CaO2, including the following: the systemic arterial Po2 (Pao2), which depends on alveolar Po2, the gas exchange surface area, and the alveolar–arterial oxygen pressure gradient (AP[A–aO2]); the haemoglobin concentration; and the shape of the haemoglobin dissociation curve for oxygen. All these factors undergo exercise induced changes. Further exchange surface and AP[A–aO2] are reflected by Tlco. To evaluate the relation between lung diffusion impairment and exercise intolerance in chronic heart failure we studied in the correlations between Tlco, Cao2, and exercise capacity during normoxic and hypoxic conditions both at rest and during exercise. Different levels of inspired oxygen fraction (FiO2) were chosen because during hypoxia, both PaO2 and haemoglobin saturation with oxygen (Sao2) are in the linear portion of the S shaped haemoglobin dissociation curve for oxygen, making it easier to study and understand the role of Tlco in regulating CaO2 and exercise capacity.
had never smoked. Treatment was stable and included: digitalis (13), diuretics (34), ACE inhibitors (29), angiotensin 1 blockers (8), β blockers (18), and amiodarone (18).

Healthy controls were chosen from patients’ relatives and hospital employees or their friends. Eighteen were smokers, eight were previous smokers, and 14 never smoked. None was involved in regular exercise programmes.

The study was approved by the local ethics committee and all subjects provided their written informed consent.

Pulmonary function evaluation
Forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) were measured in triplicate and calculated according to the American Thoracic Society criteria, using a mass flow sensor (2200 Sensor Medicis, Yorba Linda, California, USA). Maximum voluntary ventilation (MVV) was assumed to be either MVV measured in 12 seconds or FEV1 × 40, whichever was highest. Predicted values are from Quanjer and colleagues, and Jones. Molecular diffusion of carbon monoxide across the alveolar-capillary membrane (Dm) and pulmonary capillary blood volume (VC) were measured according to the method of Roughton and Forster. TLCO, Dm, and VC are linked by the following equation:

\[ \frac{1}{\text{TLCO}} = \frac{1}{\text{Dm}} + \frac{1}{\theta \text{VC}} \]

where \( \theta \) is the rate of reaction of carbon monoxide with haemoglobin and is inversely proportional to \( P_{O2} \) in the alveolar air (\( P_{A02} \)). Therefore subjects inspired a gas mixture with 0.3% \( CH_4 \), 0.3% CO, and 0.3% \( C_2H_2 \) balanced with nitrogen with an FiO2 of 21% or 16% (equivalent to the oxygen tension \( \theta \text{PaO2} \) at different \( P_{A02} \) values, thereby causing \( \theta \) to vary and enabling calculation of Dm and VC graphically.

Cardiopulmonary exercise testing
Maximal cardiopulmonary exercise tests (VMAX 29C, Sensor Medicis) were done on a cycle ergometer (Ergometrics-800, Sensor Medicis), using a personalised ramp protocol aimed at achieving peak exercise in around 10 minutes.

Data are reported as absolute values or as a percentage of predicted. Molecular diffusion of carbon monoxide across the alveolar-capillary membrane (Dm) and pulmonary capillary blood volume (VC) were measured according to the method of Roughton and Forster. TLCO, Dm, and VC are linked by the following equation:

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Study design
The first part of the protocol was the same for all subjects. Both patients and control subjects underwent standard pulmonary function tests, resting TLCO, Dm, and VC measurements (in the sitting position) and an incremental cardiopulmonary exercise test. At least one cardiopulmonary exercise test was performed before the formal study to familiarise the subjects with the techniques and procedures. Subjects were then randomly allocated into two groups, A and B, each comprising 20 heart failure patients and 20 normal controls.

Investigations in group A
In group A, TLCO was also measured with the subjects sitting on the ergometer and after three and five minutes of light exercise (20% of the maximum workload achieved). The cardiopulmonary exercise tests, with an FiO2 of 21% and 16%, were done on the following days. The order of the two tests was randomised and a resting interval of more than six hours was allowed between each test.

Investigations in group B
In group B, only one cardiopulmonary exercise test was performed to assess exercise capacity while the subjects were breathing room air. TLCO, Dm, and VC were measured with the subjects sitting on the cycle ergometer and during light exercise (20% of maximum workload achieved) which lasted around five minutes.

Statistical analysis
Data are presented as mean (SD). Correlations were obtained by linear regression analysis and the best fit method. Differences were evaluated by analysis of variance (ANOVA) and the unpaired t test, applying the Bonferroni correction for multiple comparisons as appropriate. Multivariate stepwise regression model (SPSS 9.0) was used to identify independent predictors of TLCO and peak exercise oxygen consumption (peak \( VO_2 \)). All variables with a univariate probability value of \( p < 0.05 \) were included.

RESULTS
Pulmonary function and exercise capacity (all subjects)
Results of the pulmonary function tests were consistent with a mild restrictive defect in the heart failure patients (table 1). Compared with the normal controls, resting TLCO was reduced in the heart failure group owing to a reduction in Dm with a normal VC (table 1). \( VO_2 \) at peak exercise and at anaerobic threshold was 1285 (376)/800 (140) and 1866 (540)/1010 (290) ml/min in patients and controls, respectively (\( p < 0.01 \) for both conditions). Oxygen pulse at peak exercise was 10.0 (2.7) and 12.5 (3.5) ml/beat in patients and normal subjects, respectively (\( p < 0.05 \)). In heart failure patients (fig 1, upper panel) but not in normal subjects (lower panel) resting TLCO was significantly correlated with normoxic peak \( VO_2 \). To avoid

| Table 1 Standard pulmonary function and lung diffusion tests in the whole study population |
|-----------------|-----------------|-----------------|
|                  | Heart failure patients (n=40) | Normal controls (n=40) |
| FEV1 (% pred)    | 86 (20)          | 114 (21)        |
| FVC (% pred)     | 74 (12)*         | 106 (12)        |
| FEV1 / FVC       | 115 (15)         | 108 (10)        |
| MVV (% pred)     | 85 (20)          | 118 (17)        |
| TlCO (ml/min/mm Hg) | 19.9 (5.5)*   | 28.0 (6.1)      |
| TlCO (% pred)    | 77 (19)*         | 108 (17)        |
| Dm (ml/min/mm Hg) | 29.0 (10.6)*   | 45.4 (12.8)     |
| VC (ml)          | 103.8 (40.8)     | 103.3 (38.2)    |

Data are presented as mean (SD).

\* p < 0.05 vs normal controls.

Dm, molecular diffusion for carbon monoxide across the alveolar-capillary membrane; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; MVV, maximum voluntary ventilation; pred, TLCO, lung transfer capacity for carbon monoxide; VC, capillary blood volume.
confounding by variables such as age, sex, or anthropometric measurements, both resting TLCO and peak $\dot{V}O_2$ are reported as per cent of predicted normal values.

Exercise capacity in hypoxic condition (group A)

With normoxia, peak exercise $\dot{V}O_2$ was 1285 (395) and 1861 (563) ml/min in patients and controls, respectively. The maximum work rate achieved was 101 (36) W in the patients and 163 (54) W in the controls. With hypoxia (FiO$_2$ = 16%), peak $\dot{V}O_2$ reduced to 1081 (396) in patients and to 1771 (457) in normal subjects, respectively ($p < 0.01$ and $p < 0.05$ v normoxic condition); the maximum work rate was reduced to 87 (34) W in patients and to 157 (52) W in normal subjects ($p < 0.01$ and $p < 0.05$ v normoxic condition). With hypoxia, in both patients and normal subjects ventilation was increased at rest and throughout the test compared with normoxic levels, but not at peak exercise (table 2). Resting TLCO was correlated with peak $\dot{V}O_2$ obtained under hypoxic conditions (fig 2), with an R value greater than in normoxic conditions (0.725 and 0.619, respectively). Resting TLCO, DM, and Vc did not predict the reduction in exercise capacity with hypoxia, either in patients or in controls.

Blood gas values and exercise capacity in normoxic and hypoxic conditions

Haemoglobin concentration, Po$_2$, SaO$_2$, CaO$_2$, alveolar po$_2$, and ΔP[A–ao$_2$] at rest and peak exercise in normoxic and hypoxic conditions are reported in table 4; each datum is the mean of three measurements. In the normoxic condition Po$_2$, CaO$_2$, alveolar po$_2$, and ΔP[A–ao$_2$] increased during exercise in both patients and normal controls. With hypoxia the resting data were comparable between the normal subjects and the patients. At peak exercise, Po$_2$ and SaO$_2$ decreased compared with resting values in both patients and normal controls.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Ventilation, tidal volume, and respiratory rate at rest and on peak exercise under normoxic and hypoxic conditions in patients with heart failure (n = 20) and normal controls (n = 20) (group A)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normoxia</td>
</tr>
<tr>
<td></td>
<td>Rest</td>
</tr>
<tr>
<td>Heart failure patients</td>
<td></td>
</tr>
<tr>
<td>Ventilation (/min)</td>
<td>11 (2)</td>
</tr>
<tr>
<td>Tidal volume (l)</td>
<td>0.6 (0.1)</td>
</tr>
<tr>
<td>Respiratory rate (beats/min)</td>
<td>19 (4)*</td>
</tr>
<tr>
<td>Normal controls</td>
<td></td>
</tr>
<tr>
<td>Ventilation (/min)</td>
<td>10 (2)</td>
</tr>
<tr>
<td>Tidal volume (l)</td>
<td>0.6 (0.1)</td>
</tr>
<tr>
<td>Respiratory rate (beats/min)</td>
<td>15 (4)</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD).

* $p < 0.01$ v normal controls; †p < 0.01 v normoxia.

Figure 1  Peak $\dot{V}O_2$ during normoxia v resting lung transfer capacity for carbon monoxide (TLCO) (reported as per cent of predicted) in heart failure patients (upper panel, n = 40) and healthy controls (lower panel, n = 40).

Figure 2  Peak $\dot{V}O_2$ during hypoxia v resting lung transfer capacity for carbon monoxide (TLCO) (both reported as per cent of predicted) in heart failure patients (upper panel, n = 20) and healthy subjects (lower panel, n = 20) (group A). In chronic heart failure, the correlation between TLCO and peak $\dot{V}O_2$ increased further during hypoxia.
In group A patients there was a weak but significant correlation between resting TLCO and (1) SaO₂, (2) CaO₂, and (3) arterial P0₂ at rest and at peak exercise, in both normoxic and hypoxic conditions; resting TLCO was also weakly correlated with haemoglobin at peak exercise in the patients, in normal subjects, respectively (NS). There was a significant correlation between resting TLCO and ΔP[A–aO₂] at peak exercise in normoxia and at rest and peak exercise in hypoxia in patients but not in normal subjects (table 7). Adjusting ΔP[A–aO₂] for peak VO₂ strengthened this correlation at peak exercise in the patients, and made it evident in the normal subjects (table 7). Best fit analysis showed that a curvilinear relation significantly improved the correlation of ΔP[A–aO₂], adjusted for peak VO₂, with TLCO in both normoxic (fig 5, upper panel) and hypoxic conditions (fig 5, lower panel).

**DISCUSSION**

This study contains several observations aimed at elucidating the complex interplay between lung diffusion abnormalities and impairment of exercise capacity in patients with heart failure. In the first place, our study confirms that in patients with heart failure, resting TLCO correlates with peak VO₂. Although we were only able to show a correlation and not a cause–effect link, we believe that a causal relation between impaired TLCO and reduced exercise capacity exists; indeed when the physiological impact of TLCO reduction is increased, as with hypoxia, the correlation between TLCO and peak VO₂ is high. Second, our study provides evidence that in heart failure patients, even though resting and peak exercise SaO₂, P0₂, and CaO₂ are in the normal range, their values correlate with TLCO, that TLCO increases during exercise as a result of increases in both VC and DM, and that patients who have the greatest capability to increase their TLCO during exercise are those who have the smallest reduction in exercise capacity with hypoxia. Finally, in both normoxic and hypoxic conditions, the value of the ΔP[A–aO₂] differences is related to TLCO, so when oxygen flow across the alveolar capillary membrane has to increase, as with exercise, or is impaired, as in hypoxia, the ΔP[A–aO₂] difference increases more the lower the resting TLCO value.

The patients we studied belong to a cohort of subjects regularly followed in our heart failure clinic. They were in stable clinical condition and, as in several previous reports, results of standard pulmonary function tests and TLCO showed mild restrictive lung disease and impairment of diffusion. As previously reported, TLCO impairment at rest correlates with exercise capacity. However, even if several pieces of evidence suggest a link between TLCO and exercise capacity, the physiological meaning of this correlation remains controversial because, in contrast with patients with pulmonary disease,

![Figure 3: Lung transfer capacity for carbon monoxide (TLCO) at rest (on the bicycle ergometer) and at the third and fifth minute of constant workload exercise (20% of peak workload exercise). Circles, normal subjects; diamonds, chronic heart failure patients. *p < 0.01 v; †p < 0.01 v 3rd minute value; ‡p < 0.01 v normal subjects; †p < 0.01 v normal controls; †p < 0.01 v 3rd minute value.](image)

![Figure 4: Reduction of exercise capacity with hypoxia. ΔW/W = [maximum workload achieved in normoxia – maximum workload achieved in hypoxia]/maximum workload achieved in normoxia. ΔTLCO = differences in lung diffusing capacity for carbon monoxide between the fifth minute of exercise and rest in heart failure patients. Patients with the greatest capability to increase TLCO during exercise are those who show the smallest reduction in exercise capacity in hypoxia.](image)

**Table 3**

<table>
<thead>
<tr>
<th>CO transfer (TLCO) subcomponents during submaximal exercise (group A, 20 heart failure patients and 20 normal controls)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure subjects</td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>DM (ml/min/mm Hg)</td>
</tr>
<tr>
<td>DM/VO₂</td>
</tr>
<tr>
<td>VC (ml)</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD).

* p < 0.01 v normal controls; †p < 0.01 v values at rest.

Lung diffusion and exercise capacity in heart failure

Table 4  Haemoglobin concentration, PO2, SaO2, CaO2, and PaCO2 at rest and during peak exercise under normoxic and hypoxic conditions (group A, 20 heart failure patients and 20 normal controls)

<table>
<thead>
<tr>
<th></th>
<th>Normoxia Rest</th>
<th>Normoxia Peak exercise</th>
<th>Hypoxia Rest</th>
<th>Hypoxia Peak exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>14.1 (1.4)</td>
<td>14.5 (1.7)*</td>
<td>14.1 (1.3)</td>
<td>14.7 (2.0)*</td>
</tr>
<tr>
<td>PO2 (mm Hg)</td>
<td>86 (6)</td>
<td>99 (11)*</td>
<td>68 (9)*</td>
<td>61 (8)*</td>
</tr>
<tr>
<td>SaO2 (%)</td>
<td>97.2 (0.8)</td>
<td>97.7 (1.2)</td>
<td>94.9 (2.0)</td>
<td>92.1 (3.1)*</td>
</tr>
<tr>
<td>CaO2 (ml/100 ml)</td>
<td>183 (2.0)</td>
<td>185 (2.2)*</td>
<td>181 (1.9)</td>
<td>185 (2.3)*</td>
</tr>
<tr>
<td>pH</td>
<td>7.42 (0.03)</td>
<td>7.40 (0.40)*</td>
<td>7.46 (0.03)</td>
<td>7.44 (0.04)*</td>
</tr>
<tr>
<td>PaCO2 (mm Hg)</td>
<td>100 (8)</td>
<td>110 (7)*</td>
<td>79 (5)*</td>
<td>84 (4)*</td>
</tr>
</tbody>
</table>
| Hb, arterial oxygen content; PaCO2, arterial oxygen pressure; PO2, arterial oxygen tension; SaO2, haemoglobin saturation with oxygen.

Table 5  Correlations between resting carbon monoxide transfer (TLCO) and haemoglobin saturation, arterial oxygen content, haemoglobin, and arterial oxygen tension (group A, 20 heart failure patients and 20 normal controls)

<table>
<thead>
<tr>
<th></th>
<th>SaO2</th>
<th>CaO2</th>
<th>Hb</th>
<th>PO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normoxia, rest</td>
<td>R=0.633, p&lt;0.01</td>
<td>R=0.438, p=0.06</td>
<td>R=0.394, NS</td>
<td>R=0.674, p&lt;0.01</td>
</tr>
<tr>
<td>Normoxia, peak exercise</td>
<td>R=0.503, p&lt;0.02</td>
<td>R=0.499, p=0.03</td>
<td>R=0.483, p&lt;0.03</td>
<td>R=0.488, p&lt;0.02</td>
</tr>
<tr>
<td>Hypoxia, rest</td>
<td>R=0.479, p&lt;0.03</td>
<td>R=0.503, p&lt;0.03</td>
<td>R=0.425, NS</td>
<td>R=0.417, p=0.06</td>
</tr>
<tr>
<td>Hypoxia, peak exercise</td>
<td>R=0.541, p&lt;0.01</td>
<td>R=0.300, p&lt;0.03</td>
<td>R=0.476, p&lt;0.03</td>
<td>R=0.541, p&lt;0.01</td>
</tr>
<tr>
<td>Normal controls</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normoxia, rest</td>
<td>R=0.140, NS</td>
<td>R=0.645, p&lt;0.01</td>
<td>R=0.655, p&lt;0.01</td>
<td>R=0.148, NS</td>
</tr>
<tr>
<td>Normoxia, peak exercise</td>
<td>R=0.216, NS</td>
<td>R=0.688, p&lt;0.01</td>
<td>R=0.690, p&lt;0.01</td>
<td>R=0.164, NS</td>
</tr>
<tr>
<td>Hypoxia, rest</td>
<td>R=0.210, NS</td>
<td>R=0.678, p&lt;0.01</td>
<td>R=0.684, p&lt;0.01</td>
<td>R=0.192, NS</td>
</tr>
<tr>
<td>Hypoxia, peak exercise</td>
<td>R=0.087, NS</td>
<td>R=0.563, p&lt;0.01</td>
<td>R=0.603, p&lt;0.01</td>
<td>R=0.148, NS</td>
</tr>
</tbody>
</table>

Data were obtained from means of three samples.

exercise induced haemoglobin desaturation is rare in patients with heart failure. A cardiopulmonary exercise test with a reduced O2 fraction is a safe test used to assess exercise capacity at moderate altitude. With hypoxia, peak VO2 and maximum work rate were reduced in both heart failure patients and normal controls. It is noteworthy that the correlation between TLCO and exercise capacity was high in the hypoxic tests (fig 2), a condition where TLCO impairment is likely to become more important.

In normal subjects we found a correlation between TLCO and CaO2, arterial oxygen content, haemoglobin, and arterial oxygen tension (table 4). Values at the lower end of this range are functionally relevant. In other words, it makes a difference for a heart failure patient whether they have a haemoglobin of 12 mg/dl or 15 mg/dl, or an SaO2 of 94% or 98%. Furthermore, our data confirm the role of an increase in haemoglobin as a determinant of exercise capacity. To our knowledge, blood gas analyses during exercise in hypoxia have not previously been reported in patients with heart failure. In normal subjects as well as in heart failure patients, resting TLCO was significantly correlated with haemoglobin and CaO2 measured at peak exercise, suggesting that in hypoxia CaO2 becomes a relevant determinant of exercise capacity. The observed reduction of PO2 and SaO2 is counterbalanced by an increase in haemoglobin concentration, which serves to obviate an undesirable reduction of CaO2 during exercise. Two explanations for the decrease in arterial PO2 at peak exercise with hypoxia are likely. In the first place, there could be a hypoxia induced increase in pulmonary shunting because of hypoxic pulmonary vasoconstriction enhancing the ventilation–perfusion mismatch; secondly, the pulmonary

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capillary transit time could be too short for a reduced alveolar PO₂ to achieve an equilibrium between alveolar and capillary transit time, so that alveolar–arterial O₂ differences at a reduced alveolar PO₂ pressures. Indeed with hypoxia the A–a O₂ gradient increased compared with normoxia, both at rest and during peak exercise (table 6). An inadequate exercise induced increase in ventilation during hypoxia is unlikely because Paco₂ levels did not increase.

Smith and colleagues recently showed that TLCO increases during light exercise in heart failure patients. Our findings are consistent with that report and provide new information about the cause of the exercise induced increase in TLCO. TLCO depends on membrane diffusion capacity and capillary volume, and both were increased during exercise in our heart failure patients and normal controls. The increase in VC is likely to be caused by pulmonary vessel recruitment. The exercise induced increase in Dm is more difficult to understand. The increase in Dm during exercise confirms that Dm is not a fixed value but can increase. This observation is in line with the suggestion that TLCO should be used as an antifailure treatment target. It is not possible to measure TLCO or its components reliably at peak exercise when haemoconcentration can further increase TLCO by increasing the surface of the alveoli in contact with the red blood cells. We measured TLCO during light exercise (around 20% of the maximum workload achieved) and therefore we cannot say whether this value represents the maximum possible increase in TLCO or not. We used a light workload to show that TLCO can be increased and that at the same increment of work rate the increase in TLCO correlates with the capacity of the subjects to adjust to exercise under hypoxic conditions. Indeed we showed that patients who increase TLCO most during exercise are those with the least reduction in hypoxia induced exercise capacity—meaning that the increase in TLCO during exercise can be viewed as a compensatory mechanism.

Conclusions

While none of the present evidence, when considered in isolation, proves a causal role of TLCO impairment in the reduced...
exercise capacity of patients with heart failure, collectively the following findings strongly suggest that its role is indeed causal:

- the resting $T\text{LCO}$ correlates with exercise capacity and that this correlation is increased with hypoxia
- a low but “normal” arterial haemoglobin content, $S\text{ao}_2$, and $C\text{ao}$, are associated with reduced exercise performance in heart failure patients
- a reduced capacity to increase $T\text{LCO}$ during submaximal effort correlates with the reduction of exercise capacity with hypoxia
- if resting $T\text{LCO}$ is low at peak exercise with hypoxia, then the $\Delta [A-\text{ao}_1]$ difference shows the greatest oxygen gradient.

References


Images in Cardiology

Subaortic stenosis caused by two discrete membranes

A 15 year old girl presented with fatigue and dyspnoea on exertion. She had an ejection murmur at the left sternal border. A chest radiograph showed cardiomegaly and the ECG showed left ventricular hypertrophy with a strain pattern. The echocardiogram confirmed left ventricular hypertrophy, with outflow obstruction caused by subaortic stenosis at two separate levels, one immediately proximal to the aortic valve appearing as a fibrous ridge (upward arrow) and the other as a discrete membrane. Cardiac catheterisation confirmed two discrete intracavitary pressure gradients. Subaortic stenosis is usually caused by a discrete membrane or fibromuscular ridge and may very rarely be due to a fibrous tunnel involving the whole left ventricular outflow tract. Obstruction caused by two separate but very discrete membranes as occurred in our patient also appears to be very rare. At operation both obstructions were resected and the patient made a good recovery. She will, however, require long term follow up as recurrence of subaortic stenosis after surgical treatment is known to occur in a proportion of cases.

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Subaortic stenosis caused by two discrete membranes

M B Yilmaz, E Akarca and Ü Güray

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