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 V˙O₂) 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 V˙O₂ in heart failure (normoxia < hypoxia). In heart failure patients and normal subjects, TLCO and peak V˙O₂ 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; ΔP[A–Ao], alveolar–arterial oxygen pressure gradient; FEV₁, forced expiratory volume in one second; FICO₂, inspired oxygen fraction; FVC, forced vital capacity; MVV, maximum voluntary ventilation; PAO₂, systemic arterial oxygen tension; SaO₂, haemoglobin saturation with oxygen; TICO, carbon monoxide transfer; VC, pulmonary capillary blood volume; VO₂, oxygen uptake.
had never smoked. Treatment was stable and included:
digoxin (13), diuretics (34), ACE inhibitors (29), angiotensin
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 (FEV.) and forced
dilution capacity (FVC) were measured in triplicate and
calculated according to the American Thoracic Society
criteria, using a mass flow sensor (2200 Sensor Medics, Yorba
Linda, California, USA). Maximum voluntary ventilation
(MVV) was assumed to be either MVV measured in 12 seconds
or FEV. x 40, whichever was higher. Predicted values are
from Quanjer and colleagues, and Jones. Molecular diffusion
across the alveolar-capillary membrane (DM) and
pulmonary-capillary blood volume (VC) were measured
according to the method of Roughton and Forster. TLCO, DMO,
and VC are linked by the following equation:

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

where θ is the rate of reaction of carbon monoxide with
haemoglobin and is inversely proportional to PaO2 in the alveolar
air (PAO2). Therefore subjects inspired a gas mixture with
0.3% CH4, 0.3% CO, and 0.3% C2H2 balanced with nitrogen with
three different O2 fractions equal to 20%, 40%, and 60%,
respectively. This procedure allows measurement of TLCO at
different PaO2 values, thereby causing θ to vary and enabling
calculation of DMO and VC graphically.

**Cardiopulmonary exercise testing**

Maximal cardiopulmonary exercise tests (VMAX 29C, Sensor
Medics) were done on a cycle ergometer (Ergometrics-800,
Sensor Medics) were done on a cycle ergometer (Ergometrics-800,
Maximal cardiopulmonary exercise tests were performed while they breathed a gas mixture
with an FiO2 of 21% or 16% (equivalent to the oxygen tension
around five minutes. 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.

**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 VO2). 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 DMO with a normal VC (table 1). VO2 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 VO2. To avoid

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Standard pulmonary function and lung diffusion tests in the whole study population</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV ( % pred)</td>
<td>86 (20)</td>
</tr>
<tr>
<td>FVC ( % pred)</td>
<td>74 (12)</td>
</tr>
<tr>
<td>FEV / FVC</td>
<td>115 (15)</td>
</tr>
<tr>
<td>MVV ( % pred)</td>
<td>85 (20)</td>
</tr>
<tr>
<td>TLCO (ml/min/mm Hg)</td>
<td>19.9 (5.5)</td>
</tr>
<tr>
<td>DMO (ml/min/mm Hg)</td>
<td>29.0 (10.6)</td>
</tr>
<tr>
<td>VC (ml)</td>
<td>103.8 (40.8)</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD). *p < 0.01 v normal controls. **D MO, molecular diffusion for carbon monoxide across the alveolar capillary membrane; FEV, 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 VO\(_2\) are reported as per cent of predicted normal values.

**Exercise capacity in hypoxic condition (group A)**

With normoxia, peak exercise VO\(_2\) 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 VO\(_2\) 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 VO\(_2\) 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\(_2\), Sa\(_O_2\), Ca\(_O_2\), alveolar PO\(_2\), and ΔP[A–a\(_O_2\)] 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\(_2\), Sa\(_O_2\), Ca\(_O_2\), alveolar PO\(_2\), and ΔP[A–a\(_O_2\)] 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 Sa\(_O_2\) decreased compared with resting values in both patients and normal controls.

**Table 2** 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)

<table>
<thead>
<tr>
<th></th>
<th>Normoxia</th>
<th>Hypoxia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rest</td>
<td>Peak exercise</td>
</tr>
<tr>
<td>Heart failure patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilation (l/min)</td>
<td>11 (2)</td>
<td>58 (18)*</td>
</tr>
<tr>
<td>Tidal volume (l)</td>
<td>0.6 (0.1)</td>
<td>1.6 (0.4)*</td>
</tr>
<tr>
<td>Respiratory rate (beats/min)</td>
<td>19 (4)*</td>
<td>37 (7)</td>
</tr>
<tr>
<td>Normal controls</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilation (l/min)</td>
<td>10 (2)</td>
<td>69 (19)</td>
</tr>
<tr>
<td>Tidal volume (l)</td>
<td>0.6 (0.1)</td>
<td>2.1 (0.6)</td>
</tr>
<tr>
<td>Respiratory rate (beats/min)</td>
<td>15 (4)</td>
<td>34 (5)</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD).

* p < 0.01 v normal controls; † p < 0.01 v normoxia.
hypoxic conditions; resting TLCO was also weakly correlated

tion between resting TLCO and (1) SaO2, (2) CaO2, and (3) arterial PO2 at rest and at peak exercise, in both normoxic and

tions (mean SaO2 at rest 97.2 (0.8)%, range 94.7–98.4%; mean

desaturation either at rest or peak exercise in normoxic condi-
tions 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

In group A patients there was a weak but significant corre-
laration between resting TLCO and (1) SaO2, (2) CaO2, and (3) arterial PO2 at rest and at peak exercise, in both normoxic and

hypoxic conditions; resting TLCO was also weakly correlated with haemoglobin at peak exercise during both normoxia and

hypoxia (table 5). In contrast to the patients, in normal

subjects resting TLCO was significantly correlated only with haemoglobin and CaO2, measured during normoxia and

hypoxia both at rest and at peak exercise. None of the heart

failure patients showed significant (> 3%) haemoglobin

desaturation either at rest or peak exercise in normoxic condi-
tions (mean SaO2, at rest 97.2 (0.8)%, range 94.7–98.4%; mean

SaO2, at peak exercise 97.5 (1.4)%, range 93.2–99.0%). Correla-
tions between peak VO2 and SaO2, haemoglobin, CaO2, and PO2

in both patients and normal controls are reported in table 6.
The correlations between peak VO2 and CaO2, and haemoglobin

were significant in patients and controls in all the conditions

studied.

The ΔP[A–aO2] value in the patients was greater at rest with

normoxia than in the normal controls (table 4). However, the

increase at peak exercise was greater in the controls than in

the patients (14.4 (6.4) v 5.8 (10.0) mm Hg, p < 0.01). With

hypoxia the increase in the ΔP[A–aO2] value from rest to peak

was 11.9 (5.9) mm Hg and 15.9 (9.1) mm Hg in patients and

in normal subjects, respectively (NS). There was a significant

correlation between resting TLCO and ΔP[A–aO2] at peak exer-
cise 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 physio-

logical 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, PO2, 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] dif-

ference increases more the lower the resting TLCO value.

The patients we studied belong to a cohort of subjects regu-

larly followed in our heart failure clinic. They were in stable

clinical condition and, as in several previous reports,21–23

results of standard pulmonary function tests and TLCO showed

mild restrictive lung disease and impairment of diffusion. As

previously reported,21 TLCO impairment at rest correlates with

exercise capacity. However, even if several pieces of evidence

suggest a link between TLCO and exercise capacity, the physiolog-

ical meaning of this correlation remains controversial because,
in contrast with patients with pulmonary disease,

Table 3 CO transfer (TLCO) subcomponents during submaximal exercise (group A, 20 heart failure patients and 20 normal controls)

<table>
<thead>
<tr>
<th></th>
<th>Heart failure subjects</th>
<th>Normal controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rest</td>
<td>5th minute</td>
</tr>
<tr>
<td>DM (ml/min/mm Hg)</td>
<td>29.1 (8.4)*</td>
<td>36.4 (12.8)†</td>
</tr>
<tr>
<td>DM/VA</td>
<td>5.4 (1.3)*</td>
<td>6.6 (2.5)†</td>
</tr>
<tr>
<td>VC (ml)</td>
<td>109 (42)</td>
<td>145 (65)†</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD).

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


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 exercise workload). Circles, normal subjects; diamonds, chronic heart failure patients. * p < 0.01 v rest; † p < 0.01 v 3rd minute value; ‡ p < 0.01 v chronic heart failure patients.

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.
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 patients and normal controls. It is noteworthy that the correlation between TLCO and exercise capacity was high in the patients and normal controls.

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 ventilation–perfusion mismatch; secondly, the pulmonary arteriovenous shunting.

### 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>Hb (g/dl)</td>
<td>14.0 (1.5)</td>
<td>14.9 (1.6)*</td>
<td>14.3 (1.4)</td>
<td>15.0 (1.4)*</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>18.3 (2.0)</td>
<td>19.5 (2.2)*</td>
<td>18.1 (1.9)</td>
<td>18.5 (2.3)*</td>
</tr>
<tr>
<td>pH</td>
<td>7.42 (0.03)</td>
<td>7.40 (0.04)*</td>
<td>7.46 (0.05)</td>
<td>7.44 (0.04)*</td>
</tr>
<tr>
<td>PaCO2 (mm Hg)</td>
<td>100 (8)</td>
<td>119 (5)*</td>
<td>79 (4)*</td>
<td>84 (4)*</td>
</tr>
<tr>
<td>P[A-a O2] (mm Hg)</td>
<td>14.7 (7.6)</td>
<td>20.5 (10.0)*</td>
<td>11.1 (8.8)</td>
<td>23.0 (7.8)*</td>
</tr>
<tr>
<td>PaCO2 (mm Hg)</td>
<td>36.8 (4.5)</td>
<td>33.3 (5.5)*</td>
<td>31.2 (4.1)</td>
<td>32.1 (4.4)</td>
</tr>
</tbody>
</table>

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>Hb (g/dl)</td>
<td>14.1 (1.4)</td>
<td>15.1 (1.4)*</td>
<td>14.2 (1.5)</td>
<td>15.2 (1.3)*</td>
</tr>
<tr>
<td>PO2 (mm Hg)</td>
<td>92.9 (6.0)</td>
<td>98.5 (7.0)*</td>
<td>74.6 (9.5)*</td>
<td>67.6 (7.2)*</td>
</tr>
<tr>
<td>SaO2 (%)</td>
<td>97.8 (0.6)</td>
<td>97.8 (0.5)</td>
<td>96.2 (1.6)</td>
<td>93.8 (2.2)*</td>
</tr>
<tr>
<td>CaO2 (ml/100 ml)</td>
<td>18.5 (1.9)</td>
<td>19.8 (1.8)*</td>
<td>18.3 (1.8)</td>
<td>19.1 (1.7)*</td>
</tr>
<tr>
<td>pH</td>
<td>7.42 (0.02)</td>
<td>7.37 (0.04)*</td>
<td>7.46 (0.04)</td>
<td>7.39 (0.04)*</td>
</tr>
<tr>
<td>PaCO2 (mm Hg)</td>
<td>97.0 (4.8)</td>
<td>117.2 (4.5)*</td>
<td>77.4 (6.8)</td>
<td>88.1 (5.4)*</td>
</tr>
<tr>
<td>P[A-a O2] (mm Hg)</td>
<td>4.2 (6.5)</td>
<td>16.8 (5.6)*</td>
<td>3.0 (5.3)</td>
<td>20.4 (9)*</td>
</tr>
<tr>
<td>PaCO2 (mm Hg)</td>
<td>36.9 (3.3)</td>
<td>33.9 (3.8)*</td>
<td>30.6 (4.2)</td>
<td>30.5 (4.0)</td>
</tr>
</tbody>
</table>

Values are presented as mean (SD).

* p < 0.05 v rest; † p < 0.05 v normoxia.

CaO2, arterial oxygen content; P[A-a O2], alveolar–arterial pressure difference for oxygen; Hb, haemoglobin; PaCO2, arterial oxygen pressure; PO2, arterial oxygen tension; SaO2, haemoglobin saturation with oxygen.
capillary transit time could be too short for a reduced alveolar
Po2 to achieve an equilibrium between alveolar and capillary
Po2 pressures. Indeed with hypoxia the A–aO2 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 under-
stand. 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 haemoconcentra-
tion 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

| Table 6: Correlations of peak oxygen consumption with haemoglobin saturation with oxygen, arterial oxygen content, haemoglobin, and arterial oxygen tension (group A, 20 heart failure patients and 20 normal controls) |
|----------------|----------------|----------------|----------------|
|                | Sao2            | CaO2            | Hb             | Po2            |
| Heart failure patients |                |                |                |                |
| Normoxia, rest   | R=0.515, p<0.02 | R=0.509, p<0.02 | R=0.474, p<0.05 | R=0.549, p<0.01 |
| Normoxia, peak exercise | R=0.333, NS   | R=0.557, p<0.01 | R=0.561, p<0.01 | R=0.340, NS    |
| Hypoxia, rest    | R=0.243, NS    | R=0.478, p<0.04 | R=0.462, p<0.05 | R=0.187, NS    |
| Hypoxia, peak exercise | R=0.462, p<0.04 | R=0.542, p<0.01 | R=0.538, p<0.02 | R=0.525, p<0.02 |
| Normal controls  |                |                |                |                |
| Normoxia, rest   | R=0.315, NS    | R=0.597, p<0.01 | R=0.615, p<0.01 | R=0.003, NS    |
| Normoxia, peak exercise | R=0.143, NS   | R=0.674, p<0.01 | R=0.696, p<0.01 | R=0.434, NS    |
| Hypoxia, rest    | R=0.306, NS    | R=0.539, p<0.02 | R=0.662, p<0.02 | R=0.315, NS    |
| Hypoxia, peak exercise | R=0.291, NS   | R=0.532, p<0.02 | R=0.677, p<0.01 | R=0.231, NS    |

Data were obtained from means of three samples.
CaO2, arterial oxygen content; Hb, haemoglobin; Po2, arterial oxygen tension; Sao2, haemoglobin saturation with oxygen.

| Table 7: Correlation between resting carbon monoxide transfer (TLCO) and alveolar–arterial pressure difference for oxygen (group A, 20 heart failure patients and 20 normal controls) |
|----------------|----------------|----------------|
|                | Heart failure patients | Normal controls |
| ΔP[A–aO2]/V02 | R=0.439, p<0.06 | R=0.06, NS     |
| ΔP[A–aO2]/V02, normoxia, rest | R=0.516, p<0.02 | R=0.211, NS    |
| ΔP[A–aO2]/V02, hypoxia, rest    | R=0.502, p<0.02 | R=0.106, NS    |
| ΔP[A–aO2]/V02, hypoxia, peak exercise | R=0.625, p<0.01 | R=0.207, NS    |
| ΔP[A–aO2]/V02, normoxia, peak exercise | R=0.384, NS | R=0.022, NS    |
| ΔP[A–aO2]/V02, hypoxia, peak exercise | R=0.720, p<0.01 | R=0.488, NS    |
| ΔP[A–aO2]/V02, hypoxia, rest    | R=0.431, p=0.06 | R=0.049, NS    |
| ΔP[A–aO2]/V02, hypoxia, peak exercise | R=0.794, p<0.01 | R=0.791, p<0.01 |

ΔP[A–aO2], alveolar–arterial pressure difference for oxygen; V02, oxygen uptake.

Figure 5: Correlation between alveolar–arterial O2 differences at peak exercise divided by peak V02 (ΔP[A–aO2]/peak V02) v resting diffusing capacity for carbon monoxide (TLCO) in normoxia (upper panel) and hypoxia (lower panel).
exercise capacity of patients with heart failure, collectively the following findings strongly suggest that its role is indeed causal:

- the resting $T_{LCO}$ correlates with exercise capacity and that this correlation is increased with hypoxia
- a low but “normal” arterial haemoglobin content, $SaO_2$, and $CaO_2$ are associated with reduced exercise performance in heart failure patients
- a reduced capacity to increase $T_{LCO}$ during submaximal effort correlates with the reduction of exercise capacity with hypoxia
- if resting $T_{LCO}$ is low at peak exercise with hypoxia, then the $\Delta[P_{A-o_2}]$ 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.