Pulmonary hemodynamic and tidal volume changes during exercise in heart failure

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Key words:
Exercise; Heart failure; Oxygen consumption; Ventilation.

Background. **Impairment of lung mechanics, increase of pulmonary artery pressure and limitation of exercise capacity are common findings in chronic heart failure. The objective of the present study was to evaluate whether pulmonary mechanics are correlated with pulmonary hemodynamics, whether both are correlated with the functional capacity and whether the time course of their changes during exercise correlates with the exercise capacity.**

Methods. **We performed a cardiopulmonary exercise test (breath by breath analysis of ventilation and gas exchange, cycloergometer, 25 W increments every 3 min) with pulmonary hemodynamic monitoring in 38 heart failure patients. The parameters were analyzed at rest, 1 min after the work rate increase and at peak exercise.**

Results. **A significant linear correlation with peak oxygen consumption was found at rest for: mean pulmonary artery pressure (mPAP, r = -0.56), right atrial pressure (RAP, r = -0.42), pulmonary wedge pressure (PWP, r = -0.53), and total pulmonary (TPR, r = -0.53) and pulmonary vascular resistances (PVR, r = -0.45); after 1 min of exercise for: cardiac index (CI, r = 0.49), mPAP (r = -0.57), RAP (r = -0.60), PWP (r = -0.45), and TPR (r = -0.67) and PVR (r = -0.38); at peak exercise for: tidal volume (r = 0.63), CI (r = 0.63), RAP (r = -0.43), TPR (r = -0.65) and PVR (r = -0.43). A significant linear correlation with peak oxygen consumption was found, for the increment between rest and 1 min of exercise, for RAP (r = -0.58) and CI (r = 0.42) and, for the increments between rest and peak exercise, for tidal volume (r = 0.79) and CI (r = 0.61) and, for the ratio between the increment between rest and 1 min of exercise/increment between rest and peak exercise, for mPAP (r = -0.42), RAP (r = 0.51) and CI (r = -0.54). The same ratio of increment of mPAP (r = 0.39) and CI (r = 0.36) correlated with that of tidal volume.**

Conclusions. **This study provides evidence of a strong correlation between the respiratory function and pulmonary vascular pressure changes during exercise in heart failure.**

(Ital Heart J 2002; 3 (2): 104-108)

Received November 12, 2001; revision received January 18, 2002; accepted January 30, 2002.

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Introduction

In chronic heart failure, the impairment of lung mechanics and pulmonary hemodynamics and the limitation of exercise capacity are common findings. Although it is widely acknowledged that pulmonary mechanics and vascular pressures are mutually related[1-3], little is known about their interdependence and whether their changes during exercise correlate with exercise capacity.

Methods

We analyzed 38 patients (30 males, 8 females, mean age 50 ± 9 years) with chronic heart failure due to ischemic (n = 23) or idiopathic (normal coronary angiography, n = 15) cardiomyopathy. Patients underwent a cardiopulmonary exercise test in a fully climatized laboratory with hemodynamic monitoring as part of the evaluation in view of possible cardiac transplant. The Institutional Ethics Committee approved the exercise protocol and the study. These 38 subjects are all the patients who fulfilled the study inclusion/exclusion criteria at our heart failure unit between August 1999 and August 2000. Treatment was optimized and clinical conditions were stable since at least 3 months. In particular, patients received ACE-inhibitors (n = 30), AT_1 blockers (n = 12), diuretics (n = 38), digitalis (n = 18), β-blockers (n = 20), and amiodarone (n = 25). In no case was therapy discontinued before the study. Patients who had angina pectoris, a recent myocardial infarction (< 1 year), primary valvular heart disease, pericardial effusion, peripheral vascular diseases, primary lung disease [including the clinical diagnosis of chronic bronchitis and laboratory measurements of a forced expiratory volume in 1 s (FEV_1) < 80% to that predicted and a lung diffusion capacity for car-

bon monoxide (DLCO) < 60% to that predicted], atrial fibrillation or flutter, severe ventricular arrhythmias, an artificial pacemaker, sinus or atrioventricular node dysfunction or who were unable to pedal for at least 6 min were not enrolled. The cardiopulmonary exercise test was performed in the sitting position using a cycloergometer (Sensor Medics Ergometrics 800 S, Anaheim, CA, USA) and with breath by breath monitoring of ventilation and gas exchange. Under local anesthesia, a 7F Swan-Ganz catheter was introduced into the internal jugular vein and advanced into the pulmonary artery. Pressures were recorded on an 8 channel recorder (Gould TA 5000, Valley View, OH, USA); the cardiac output was measured by thermodilution in triplicate (rapid injection of 10 ml of iced saline) and with pressure recording always preceding cardiac output measurements. The mean pulmonary artery pressure (mPAP) and the pulmonary vascular (PVR) and total pulmonary resistances (TPR) were calculated using standard formulae. The protocol was characterized by 25 W increments every 3 min until fatigue or limiting dyspnea. The data analyzed were those obtained at rest (on the cycloergometer), after the first minute of exercise and at peak exercise; the reported values are the means obtained over 30 s ± SD. Differences were evaluated using the paired Student's t-test and applying the Bonferroni correction for multiple comparisons; correlations were analyzed by linear regression analysis.

Results

Pulmonary function tests showed only a mild or no lung function impairment (FEV_1 94 ± 7% of that predicted, FEV_1/forced vital capacity 87 ± 10% of that predicted and DLCO 83 ± 9% of that predicted). Data from all subjects were considered for the analysis as they all performed maximal or near maximal exercise (respiratory equivalent > 1.05 in all subjects)[4] without untoward effects. The peak exercise oxygen consumption was 17.1 ± 4.7 ml/kg/min (range 8.8-27.4 ml/kg/min). The tidal volume was 0.54 ± 0.14 l at rest, 0.88 ± 0.20 l after 1 min of exercise and 1.50 ± 0.46 l at peak exercise ($p < 0.01$ vs rest, $p < 0.01$ vs 1 min of exercise). Hemodynamic data are reported in table I. The correlations of the peak oxygen consumption vs the tidal volume and the pulmonary hemodynamic measurements at the three exercise steps analyzed are reported in table II. At peak exercise, none of the evaluated hemodynamic parameters except for the cardiac index (CI) correlated with the tidal volume. The correlations of peak oxygen consumption vs the increment

Table II. Correlations of the peak oxygen consumption to the tidal volume, the mean pulmonary artery pressure, the right atrial pressure, the pulmonary wedge pressure, the cardiac index, the total pulmonary resistance and the pulmonary vascular resistance.

	r	p
Tidal volume		
At rest	0.10	0.6
After 1 min of exercise	0.22	0.25
At peak exercise	0.63	0.0001
mPAP		
At rest	-0.56	0.0001
After 1 min of exercise	-0.57	0.0001
At peak exercise	-0.30	0.06
RAP		
At rest	-0.42	0.01
After 1 min of exercise	-0.60	0.0001
At peak exercise	-0.43	0.008
PWP		
At rest	-0.53	0.001
After 1 min of exercise	-0.45	0.005
At peak exercise	-0.28	0.09
CI		
At rest	0.28	0.09
After 1 min of exercise	0.49	0.002
At peak exercise	0.63	0.0001
TPR		
At rest	-0.53	0.001
After 1 min of exercise	-0.67	0.0001
At peak exercise	-0.65	0.0001
PVR		
At rest	-0.45	0.005
After 1 min of exercise	-0.38	0.02
At peak exercise	-0.43	0.008

Abbreviations as in table I.

Table I. Hemodynamic variables at rest, after 1 min of exercise and at peak exercise.

	Rest	1 min of exercise	Peak exercise
HR (b/min)	83 ± 15	117 ± 21*	139 ± 25*§
CI (l/min/m^2)	2.3 ± 0.5	3.7 ± 1.1*	4.4 ± 1.7*§
PWP (mmHg)	20 ± 11	32 ± 12*	38 ± 13*§
RAP (mmHg)	3.5 ± 3.6	8.8 ± 6.1*	12 ± 6.3*§
mPAP (mmHg)	28.3 ± 13	37.7 ± 12*	48.8 ± 13*§
TPR (dynes·s·cm^{-5}·m^2)	1075 ± 667	912 ± 484	1008 ± 476
PVR (dynes·s·cm^{-5}·m^2)	330 ± 202	142 ± 208	222 ± 158

CI = cardiac index; HR = heart rate; mPAP = mean pulmonary artery pressure; PVR = pulmonary vascular resistance; PWP = pulmonary wedge pressure; RAP = right atrial pressure; TPR = total pulmonary resistance. * = $p < 0.01$ vs rest; § = $p < 0.01$ vs 1 min of exercise.

between rest and 1 min of exercise and throughout the entire exercise of tidal volume, mPAP, right atrial pressure (RAP), pulmonary wedge pressure (PWP), CI, PVR and TPR are reported in table III. Peak oxygen consumption was significantly related to the ratio of the tidal volume increment between rest and 1 min over the tidal volume increment between rest and peak exercise (r = -0.49, p = 0.008) and to the same ratio of increments for mPAP (r = -0.42, p = 0.009), RAP (r = -0.51, p = 0.001) and CI (r = -0.54, p = 0.001) (Fig. 1). The ratio of the tidal volume increment between rest and 1 min to the tidal volume increment between rest and peak exercise also correlated with the same ratio applied to mPAP (r = 0.39, p = 0.03) and CI (r = 0.36. p = 0.04; Fig. 2).

Table III. Correlations of the peak oxygen consumption to the tidal volume, the mean pulmonary artery pressure, the right atrial pressure, the pulmonary wedge pressure, the cardiac index, the total pulmonary resistance and the pulmonary vascular resistance changes during exercise.

	r	p
ΔTidal volume		
From rest to 1 min of exercise	0.15	0.42
From rest to peak exercise	0.79	0.0001
ΔmPAP		
From rest to 1 min of exercise	0.25	0.12
From rest to peak exercise	0.04	0.78
ΔRAP		
From rest to 1 min of exercise	-0.58	0.0001
From rest to peak exercise	-0.26	0.12
ΔPWP		
From rest to 1 min of exercise	0.04	0.79
From rest to peak exercise	0.17	0.32
ΔCI		
From rest to 1 min of exercise	0.42	0.008
From rest to peak exercise	0.61	0.0001
ΔTPR		
From rest to 1 min of exercise	0.07	0.64
From rest to peak exercise	0.10	0.56
ΔPVR		
From rest to 1 min of exercise	0.05	0.75
From rest to peak exercise	0.12	0.45

Abbreviations as in table I.

Discussion

The main goals of the present work were to evaluate whether changes in pulmonary hemodynamic and respiratory parameters are related to each other and to exercise capacity. It is known, in fact, that pulmonary vascular pressure at rest, but not at peak exercise, correlates with exercise capacity[5], that pulmonary vascular pressure and lung mechanics are mutually related[1], and that indexes of lung function obtained at rest and at peak exercise correlate with exercise capacity[6]. In particular, we evaluated the hypothesis that with respect to the exercise capacity and lung function/pulmonary hemodynamic relationship, what is important is not the absolute change of one parameter but rather the time course of this change. In other words, the faster the change the worse, as a "dip and plateau lung

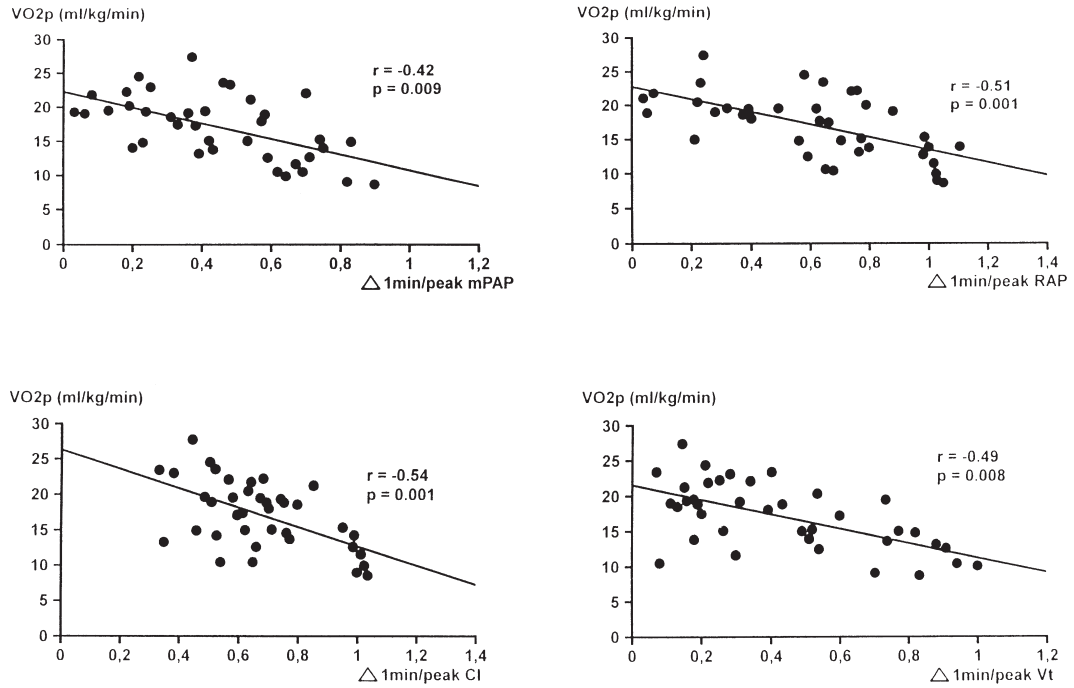

Figure 1. Left top panel: *correlation between the peak oxygen consumption (VO_2p) and the ratio of the mean pulmonary artery pressure (mPAP) increment between rest and 1 min over the mPAP increment between rest and peak exercise (Δ1 min/peak mPAP);* right top panel: *same correlation between the VO_2p and the right atrial pressure (RAP);* left lower panel: *same correlation between the VO_2p and the cardiac index (CI);* right lower panel: *same correlation between the VO_2p and the tidal volume (Vt).*

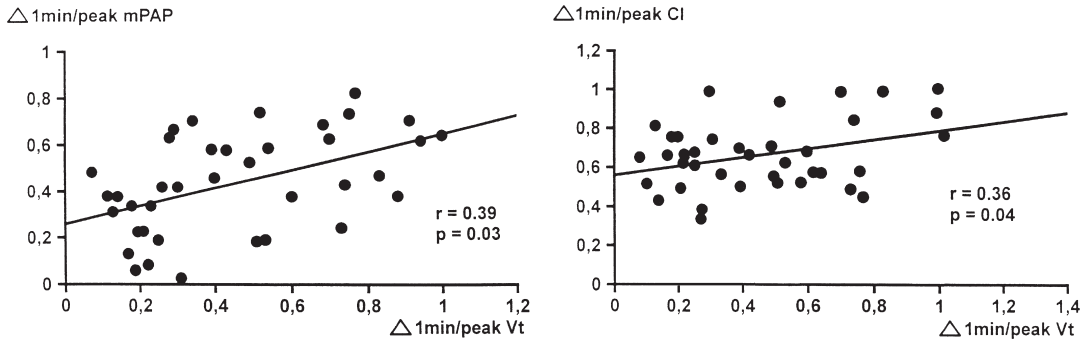

Figure 2. Left panel: *correlation between the ratio of the mean pulmonary artery pressure (mPAP) increment between rest and 1 min over the mPAP increment between rest and peak exercise (Δ1 min/peak mPAP) and the same ratio for the tidal volume (Vt).* Right panel: *correlation between the ratio of the cardiac index (CI) increment between rest and 1 min over the CI increment between rest and peak exercise (Δ1 min/peak CI) and the same ratio for the Vt.*

behavior". We chose an exercise protocol with moderate load increments in order to reach steady state conditions at submaximal exercise. Indeed, after 1 min of a 25 W load increment (i.e. data collection between 1 min and 1 min and 30 s), phase 3 (steady state) is usually reached. Furthermore, we analyzed data of patients who were able to pedal for at least 6 min, in other words 50 W. Thus, we have not included patients with extremely severe heart failure. We did this purposely so as to be sure that the first exercise measurement, which was performed after 1 min of exercise, was obtained in steady state conditions and that it was representative of an early phase of exercise. As an index of lung mechanics during exercise, we chose the tidal volume which is easy to obtain and which, at peak exercise, has been reported to be reduced in heart failure patients[7]. Our finding of a positive correlation between tidal volume and oxygen consumption at peak exercise and between the total tidal volume increment and peak oxygen consumption substantiates previous published data[7-9] and provides further evidence of a link between respiratory function and exercise capacity in heart failure.

The correlation between hemodynamic pulmonary parameters and exercise capacity has been extensively studied and the failure of PVR to fall during exercise has been considered as an important determinant of exercise limitation in heart failure patients[5,9]. In our population, peak oxygen consumption was correlated to mPAP, RAP and PWP at rest and after 1 min of exercise. Among these pressures, at peak exercise only RAP was related to peak oxygen consumption; this suggests that the value of mPAP at peak exercise is independent of the level of physical performance[5,9]. Vice versa, CI, PVR and TPR correlated with oxygen consumption at peak exercise, but not at rest while only CI correlated with tidal volume at peak exercise. We devoted our attention not only to the absolute value of the hemodynamic and respiratory parameters at rest and during exercise but also to their increment at the beginning (first minute) and throughout the entire exercise. Furthermore, we investigated the behavior of the changes in hemodynamic and respiratory measurements which occur during the first minute of exercise with respect to the entire changes throughout exercise. We did so in the belief that if the stiffness of the lung and pulmonary hemodynamics are both determinants of exercise capacity[1-3] and interrelated, the magnitude and the temporal behavior of their changes must be similar. Indeed, the ratio of the mPAP increment at the beginning of exercise versus the total exercise mPAP increase, as well as the same ratio of CI, RAP and tidal volume (Fig. 1) correlate with peak oxygen consumption; this implies that the behavior of mPAP, CI, RAP and tidal volume during exercise are relevant to exercise performance. However, at rest, during and at peak exercise, none of the evaluated hemodynamic parameters correlated with tidal volume. This, at a first glance, suggests that pulmonary hemodynamic and respiratory parameters, which both correlate with the peak oxygen consumption, are not interrelated. Nonetheless, during exercise, the patterns of changes of mPAP, CI and tidal volume were similar and were linearly related (Fig. 2). These findings, albeit a correlation does not imply causality, reinforce the concept that pulmonary hemodynamic changes[1-3] during exercise are related to the changes in lung mechanics and that the latter are a determinant of exercise capacity in heart failure patients.

Study limitations. This study has several limitations. First of all, the number of patients is relatively small; however, the complexity of the study measurements limits the number of subjects. Secondly, because of the need of a precise temporal correspondence when determining the pulmonary and hemodynamic parameters and because of the need of steady state conditions at each measurement, the exercise protocol used had discrete load increments. This is not the best exercise protocol to use for the determination of the peak oxygen consumption. Third, we did not perform a sophisticated pulmonary function evaluation because we wanted an easy-to-perform protocol with some clinical applicability. Finally, the pulmonary pressure was not re-

ferred to esophageal pressure, owing to the fact that ethical considerations do not permit the positioning of an esophageal balloon for routine hemodynamic evaluation.

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