217. Cardio-pulmonary interactions

1708
Late-breaking abstract: The diaphragm and abdominal muscles act on the abdomen to displace blood to the extremities during exercise

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We have recently demonstrated (Aliverti et al, J Appl Physiol, 2010) that during quiet breathing the diaphragm serves the double function to ventilate the lung and to shift blood from the splanchnic vascular bed to the extremities.
We hypothesized that with simultaneous contraction of abdominal muscles, such as occurs during exercise, the circulatory function of the diaphragm can be considerably enhanced.
Six healthy subject performed a submaximal constant exercise workload test (repeated foot flexion at ∼60% of max workload) within a whole body plethysmography (WBP) measuring changes in body volume (dVb). Simultaneously, changes in volume of the trunk (dVtr) were measured by optoelectronic plethysmography. Blood shifts between trunk and extremities (Vbs), were determined

as dVtr-dVb.In all subjects, intra-breath variations of Vbs were bimodal. Vbs initially decreased and then increased during inspiration; Vbs then decreased in the first part of expiration, and increased again in the second part. After 1 min of exercise, within-breath tidal Vbs increased by 175±122 ml ($p<0.018$) from rest, the blood accumulated into the extremities was 304±338 ml ($p<0.05$) and abdominal volume at end-expiration decreased by 0.50±0.32 L ($p<0.012$).
We conclude that a precise control mechanism of the diaphragm and abdominal muscles determines intra-breath variations of Vbs during exercise. Due to the high frequency of tidal Vbs there is not adequate time for a complete refilling of the splanchnic blood reservoir at each abdominal compression, and this results into a significant shift of blood from the trunk to the extremities during exercise. When needed, this should be clinically useful.

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Right ventricular contractility at rest and during exercise in COPD

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Rationale: COPD patients show a limited stroke volume response to exercise. This is thought to be due to an increased right ventricular (RV) afterload. Whether an impairment to increase RV contractility contributes to the impaired stroke volume response is unknown.
Therefore, the aim of this study is to determine whether RV contractility changes during exercise in COPD patients.
Methods: Nine patients with COPD (GOLD II-IV) underwent right heart catheterisation and subsequently cardiac MRI at rest and during submaximal exercise. With cardiac MRI RV volumes were measured. During right heart catheterisation RV pressure curves were continuously measured. As a measure of contractility, the maximum rate of rise of RV pressure (dP/dt_{max}) was obtained from an averaged RV pressure waveform over several respiratory cycles, see figure 1. Then, dP/dt_{max} was normalized for RV end-diastolic volume, i.e. dP/dt_{max}/EDV (1).
Results: In all patients dP/dt_{max}/EDV increased with exercise. At rest mean dP/dt_{max}/EDV was 3.6±1.3 mmHg/s/ml, while during exercise it was 6.9±3.7 mmHg/s/ml (p=0.001). RV end-systolic volume did not change with exercise.

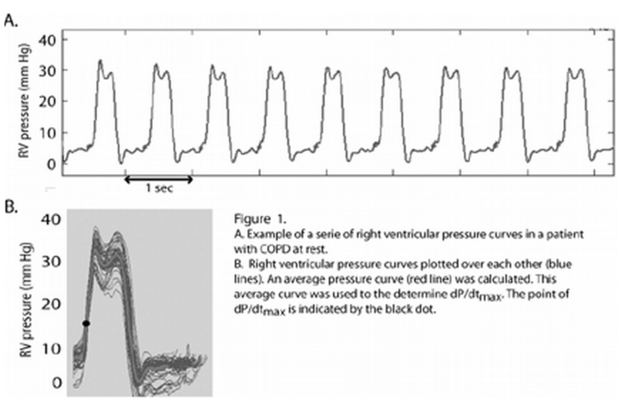

Figure 1.
A. Example of a serie of right ventricular pressure curves in a patient with COPD at rest.
B. Right ventricular pressure curves plotted over each other (blue lines). An average pressure curve (red line) was calculated. This average curve was used to the determine dP/dt_{max}. The point of dP/dt_{max} is indicated by the black dot.

Conclusions: COPD patients show an increase in RV contractility. The increase in contractility does not result in a decrease in RV end-systolic volume.

Reference:

[1] Kass DA, Maughan WL, Guo ZM, et al. *Circulation* 1987 Dec; 76(6):1422-36.

1710

Right ventricular output in chronic obstructive pulmonary disease during expiration is impaired by reduced venous return

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Background: High positive airway pressure impedes venous return and right ventricular (RV) output in mechanically ventilated patients. Whether this is also the case in normally breathing COPD-patients, where the expiratory intrathoracic pressure is increased due to airway obstruction, is unknown. We investigated the effects of intrathoracic pressure on venous return and how this perturbs RV output during expiration at rest and during exercise.
Methods: Fourteen COPD-patients (GOLD II-IV) underwent simultaneous measurements of intrathoracic, right atrial (RA) and pulmonary artery pressures at rest and during exercise. Intrathoracic and RA pressure were used to calculate RA filling pressure. Dynamic changes in pulmonary artery pulse pressure during expiration were examined to evaluate changes in RV output.
Results: Pulmonary artery pulse pressure decreased up to 40% during expiration (figure 1). This decline was associated with a low RA filling pressure (r^2= 0.64). During exercise, a similar decline in pulmonary artery pressure was observed. Intrathoracic pressure and RA pressure increased similar, resulting in an unchanged RA filling pressure.

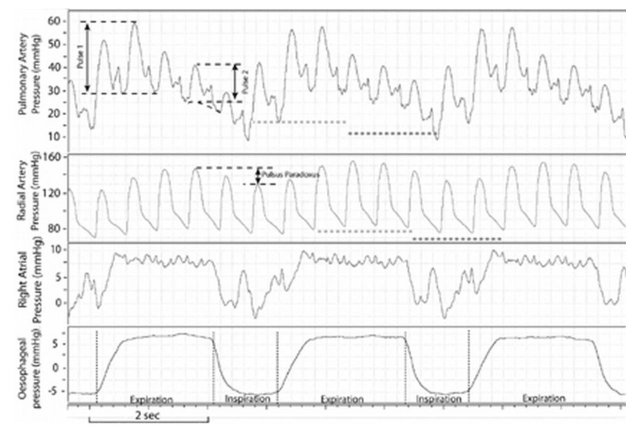

Figure 1. Example of the behavior of the pulmonary artery pressure over the respiratory cycle in a COPD patient. In the upper channel we show the decline in pulse pressure (pulse 1 - pulse 2) in the pulmonary artery during expiration, which is a consistent phenomenon over all respiratory cycles. The second channel shows the pressure in the radial artery. The decline in pulse pressure in the radial artery seems to follow the decline in the pulmonary artery pressure. (red dotted lines). During expiration, the intrathoracic pressure (channel 4) probably exceeds the central venous pressure, which would explain the flatline of the right atrial pressure (channel 3).

Conclusions: We show that in COPD, pulmonary artery pulse pressure declines during expiration; most prominent in patients with a low RA filling pressure. This implies that, spontaneous breathing already impairs venous return and by that RV output in COPD.

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Effects of hyperoxia and helium-hyperoxia on the cardiocirculatory responses to incremental exercise in hypoxaemic patients with advanced COPD

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Heliox breathing might positively impact upon the haemodynamic responses to exercise in non-hypoxaemic patients with moderate-to-severe chronic obstructive pulmonary disease (COPD) (Chiappa, GR *et al. Am J Respir Crit Care Med, 179:1004, 2009*). There is, however, a lack of evidence of whether these beneficial effects would also be found in patients with more advanced cardiovascular impairment, *i.e.*, hipoxaemic, GOLD stage IV patients. On a double-blind study, 13 patients (FEV_1= 35.4±9.1% pred; PaO_2= 57.7±7.0 mmHg) were submitted to maximum incremental cardiopulmonary exercise tests while breathing hyperoxia (HiOX= 40% O_2) or helium-hyperoxia (He-HiOX= 60% He/40% O_2). Stroke volume (SV, mL) and cardiac output (CO, L/min) were non-invasively monitored by impedance cardiography (*PhysioFlow*®, Manatec Inc, France). Peak work rate (WR) was improved with He-HiOX compared to HiOX (52±21 W vs. 46±18 W); in addition, end-expiratory lung volume (EELV) was slightly, albeit significantly, reduced (5.50±1.25 vs 5.61±1.30 L; $p<0.05$). At iso-WR, He-HiOX was associated with higher SV and CO than HiOX (92±8 mL vs. 84±2 mL and 9.6±1.3 L/min vs. 8.7±1.9 L/min, $p<0.05$). Improvement in CO with He-HiOX was negatively related to resting EELV (r= - 0.72, p= 0.01) but not with baseline CO and PaO_2 ($p>0.05$). In conclusion, hyperoxic heliox enhances the cardiocirculatory responses to exercise compared to hyperoxia alone in less hyperinflated patients with advanced, hypoxaemic COPD. These data indicate that increased operational lung volumes are related to deleterious haemodynamic effects in this patient sub-population.

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Predictors of improvement in peak exercise capacity with helium-hyperoxia in severely-impaired COPD patients under long-term oxygen therapy

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Heliox can improve exercise tolerance in ventilatory-limited patients with chronic obstructive pulmonary disease (COPD). Unfortunately, however, these benefits are quite heterogeneous in patients with similar levels of resting airflow obstruction. In order to gain further insight into the determinants of such variability in hypoxaemic patients with advanced COPD, we evaluated 24 males (GOLD stage IV) who were under long-term O_2 therapy. Patients underwent maximum incremental cardiopulmonary exercise tests while breathing hyperoxia (HiOX= 40% O_2) or helium-hyperoxia (He-HiOX= 60% He/40%O_2). Peak work rate (WR) was significantly improved with He-HiOX compared to HiOX (54±26 W vs. 48±23 W). This was associated with increased mean ins and expiratory flows and larger tidal volumes; in addition, end-expiratory lung volume was lower at peak exercise (5.57±1.12 L vs 5.65±1.13 L; $p<0.05$). Δ(He-HiOX – HiOX) WR was positively related to markers of lung hyperinflation including total lung capacity and residual volume (r= 0.52 and r= 0.40; $p<0.05$). Interestingly, however, fat-free mass (FFM) also showed to be strongly related to ΔWR; in fact, FFM was the only independent predictor of ΔWR on a multiple regression analysis (r^2= 0.66; $p<0.001$). We conclude that once patients with advanced COPD are relieved from the "central" ventilatory constraints by breathing hyperoxic heliox, appendicular muscle mass becomes an important determinant of maxinal exercise capacity. These data lend support to the notion that preserved muscle mass is important for improved respiratory mechanics be translated into enhamced peak exercise capacity in these patients.

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Tissue deoxygenation kinetics induced by acute hypoxic exposure at rest in humans

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The impact of hypoxemia on tissue oxygenation per se involves complex mechanisms. How muscle and brain face the hypoxemic stress over several hours of hypoxic exposure (HE) remain unknown. Therefore, this study aimed to investigate the effects of 4-hours HE at rest on muscle and cerebral (de)oxygenation kinetics. Twelve healthy males seated quietly while breathing the appropriate gas mixtures. After 10-min of normoxia (FiO_2=0.21), subjects were exposed for 4 h to hypoxia (HE, FiO_2=0.12) or normoxia (control condition), and then again to normoxia for 15 min. Muscle and cerebral oxygenation (NIRS), pulse oxygen saturation (SpO_2) and heart rate variability were measured continuously. Relative concentration changes of oxy-(Δ[HbO_2]), deoxy-(Δ[HHb]) and total-hemoglobin (Δ[HbTot]) were measured from baseline level.

SpO_2 fell from 96±1% to 83±3% during the first 20 min of HE and then remained stable. In the same time, HE resulted in general sympathoexcitation. After a transient rise at 20 min of HE, muscle Δ[HHb] restored to baseline values whereas Δ[HbO_2] and Δ[HbTot] were reduced from 120 to 240 min of HE only. Cerebral Δ[HHb] rose markedly at 20 min of HE and remained constant until the end of HE. Cerebral Δ[HbO_2] was reduced over the first 120 min of HE but re-increased afterwards towards baseline values together with an increase in Δ[HbTot]. Muscle and brain both showed hyper-oxygenation status post HE.

This study provided new insights on *i)* differential (de)oxygenation kinetics in brain and muscle in response to sustained HE, *ii)* a biphasic cerebral tissue adaptation in the first hours probably to counter balance initial impairments and *iii)* a tissue hyper-oxygenation after return to normoxia.

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Blood shift during cough in healthy subjects

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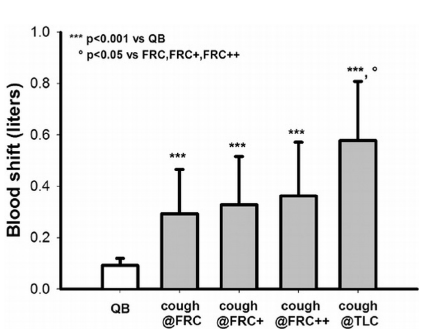
Double Body Plethysmography (DBP), which combines total body plethysmography and opto-electronic Plethysmography, has been recently developed to measure the amount of blood displaced from the thorax to the extremities (Aliverti et al, PLoS One. 2009). By using DBP, we have recently shown that significant blood shifts (BS) occur during expulsive maneuvers and that abdominal pressure controls the outflow of blood from the splanchnic vasculature (Aliverti et al, J Appl Physiol, 2010).

We hypothesized that also during cough a significant amount of blood can be displaced from the trunk to the extremities. We studied 7 healthy subjects (age: 28.6±2.5 yrs) during series of voluntary coughs at four different operating volumes: functional residual capacity (FRC), total lung capacity (TLC) and two intermediate volumes between FRC and TLC (namely, FRC+ and FRC++). BS from the thorax to the extremities were measured by DBP during quiet breathing and during cough at each operating lung volume. The results are shown in figure. BS during cough resulted significantly higher than during QB ($p<0.001$). BS increase with increasing operating volume, being maximal at total lung capacity (figure).

These findings might help to better understand the cardiopulmonary interactions during cough and the mechanism by which coughing during asystolic cardiac arrest can maintain consciousness in human subjects.



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Regional chest wall volume variations in heart failure patients during inspiratory muscle training

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It is unknown how heart failure (HF) and cardiomegaly associated with diaphragmatic weakness affects chest wall function. Therefore, we evaluated in these patients the distribution of volume variations into the different thoracoabdominal compartments during quiet breathing and during inspiratory muscle training. Thirty-one individuals were evaluated and divided into two groups: HF (17 patients with functional class II and III chronic heart failure associated with cardiomegaly) and control (12 healthy volunteers). All subjects were evaluated by spirometry, six-minute walking test (6MWT), and optoelectronic plethysmography (OEP) during threshold inspiratory muscle training (IMT). OEP allowed to assess right-left asymmetries in the volume changes of upper thoracic (Vrcp), lower thoracic (Vrca), and abdominal (Vab) compartments. While no significant differences were present between right and left sides in the control group during IMT, in HF patients volume variations of Vrca were 45.30%±9.10 and 54.33%±12.9, respectively in the left and right sides (p=0,03). This was associated to a significant decrease, compared to normals, of Vrca variations; in addition, a positive correlation between the%Vra,left and ejection fraction of left ventricle (r=0.468 and p=0.049), and a negative correlation between the Borg scale after the 6MWT and the%Vra, left side (r=-0.878 and $p<0.01$) were found. In conclusion, HF patients have a reduced displacement of the lower rib cage of the left compared to right side, suggesting the influence of cardiomegaly on diaphragmatic weakness and increased perception of dyspnea during submaximal exercise.