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Prolonged exhaustive exercise induces diastolic dysfunction with preserved systolic function mediated by oxidative stress

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Intense physical practices like marathon or triathlon result in transient left ventricular (LV) dysfunction, characterized by transient reduction of LV diastolic relaxation without changes in systolic function by unknown mechanisms. Our study aimed to investigate in vivo and in vitro the involvement of known regulators of diastolic function such as eNOS and oxidative stress signalling pathways in a rat model. Wistar rats experienced prolonged exhaustive exercise (PEE) (3 hours; 65% of maximal aerobic velocity), in association or not with an antioxidant treatment (N-acetylcysteine, 50 mg.kg⁻¹, i.p.). Systolic cardiac function evaluated in vivo by echocardiography and ex vivo in Langendorff isolated heart was unchanged by PEE, while parameters of diastolic function were severely altered. At the cellular level, PEE had no effect on myofilament calcium sensitivity, TnI expression and phosphorylation. However, PEE was associated with marked alteration of calcium handling during contraction. The amplitude of calcium transient was reduced in PEE hearts when compared to Ctrl ones and both Tau and time to baseline50 (TTBI50), two indexes reflecting the kinetic of Ca²⁺ reuptake by the SR were increased by PEE. Finally, an interesting point is that antioxidant treatment with NAC during PEE totally prevents the alteration of the diastolic function. To conclude, the present results show that PEE induced oxidative stress that targeted preferentially calcium handling rather than myofilaments, and may be responsible for transient diastolic dysfunction.

0401

Which parameters can predict the response to exercise training in cardiac patients?

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Aims: Benefit effects of exercise training are well known and validated after a cardiac event, but some patients fail to ameliorate their functional capacity. This retrospective study determined which parameters in the initial cardio pulmonary exercise test could predict an improvement of functional capacity after training in cardiac patients.

Methods and results: 292 cardiac patients with a complete training intervention were divided in two groups at the end of their rehabilitation : one group with a gain equal or more than 1 MET (148 patients) and one group with a gain less than 1 MET (144 patients) when the initial and final cardio pulmonary exercise tests were compared. The cardiac event (coronary revascularization 38 %, aortic valvular surgery 23%, coronary stenting 18%) was similar in both group. The initial peak VO₂ was not different (100 watts vs 110 watts, 15.6ml/kg/min vs 16.1ml/kg/min) neither the ventilator threshold nor the training intervention (19.3 sessions vs 17.9). At the end of the exercise training intervention, the gain of peak VO₂ was 4.1ml/kg/min (+28%) in the global population and 6.8 ml/kg/min (+46%) in the group ≥1 METS vs 1.29ml/kg/min (9.3%) in the group < 1 MET. Clinical predictor factors for a gain ≥1 MET were: age (58.3 years vs 62*), sex male (92 % vs 83 %*), ejection fraction (LVEF 52,5 % vs 49,9 %**). The initial discriminated exercise parameters were the energetic cost per watt (VO₂/watt) 11,4 vs 12,2**, the ventilatory cost (VE/watt) 0.62 vs 0.67*, the intensity per body kilogram (watts/kg) 1.43 vs 1.31* and the cardiac frequency per 1 liter of VO₂ was lower 102 vs 110*.

Conclusion: The benefit on functional capacity after exercise training intervention depended more of the initial physical condition than of the cardiac pathology in patients discharged in our cardiac rehabilitation centers. The exercise training should be more directed by the initial exercise test.

*: p < 0,05, **: p < 0,001

0032

Exercise failed to improve NO pathway in SHR rats and markedly increases eNOS dependent ROS production

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Aim: The spontaneously hypertensive rat (SHR) is widely described as an animal model which shares with human essential hypertension several similarities and notably endothelial dysfunction. This study investigated whether exercise, a recognized strategy to prevent endothelial dysfunction, could have beneficial effects on arterial vasomotricity and blood pressure in SHR rats. A specific attention was paid to endothelium-dependent relaxing factors.

Method: Arterial blood pressure was assessed by tail-cuff method in WKY, SHR and SHR exercised (1 hour 70% of VO₂max; 5 days/week for 6 weeks) rats. Arterial function was evaluated on isolated aortic rings in response to ACh or SNP in presence or not of different inhibitors (L-NAME, indomethacin, TRAM34 and Apamine) to discriminate the role of different vasodilator triggers (NO, PGI₂, EDHF). Finally, aortic total and NOS-dependent ROS production were measured using Electron paramagnetic resonance.

Results: An unexpected result was that exercise training did not moderate hypertension in SHR rats. Although, endothelium-dependent vasorelaxation was altered in SHR, no beneficial effect of exercise was observed. This altered response to ACh in SHR rats was mainly explained by COX, since inhibition of this enzyme markedly correct endothelium dysfunction. However, COX pathways were not impacted by exercise. Although exercise is largely recognized as increasing eNOS activity, we reported that exercise has no effect on eNOS-dependent vasorelaxation. Especially, exercise in SHR rats resulted in increased NOS-dependent ROS production suggesting increased eNOS uncoupling and resulting then in increased total ROS production in arterial tissue.

In conclusion, we can postulate that, the lack of positive effect of exercise training on essential hypertension could be explained by unexpected eNOS uncoupling with exercise. This hypothesis has to be confirmed by the use of a recoupling agent and by biochemical assays of eNOS dimerized state.

0115

Correlation between right ventricular function and exercise capacity in patients with chronic heart failure

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Aim of this study: to define a correlation between echocardiographic parameters of right ventricular (RV) function and exercise capacity in a group of patients with stable chronic heart failure (CHF).

Methods: 30 patients with CHF (age=58.3±13 years, 29 men), defined as a left ventricular ejection fraction (LVEF) ≤0.45, had an echocardiographic examination followed by a 6-min walk test. RV function was evaluated by two parameters: Tricuspid annular plane systolic excursion (TAPSE) and tricuspid lateral annular systolic velocity derived by tissue Doppler (S').

Results: Sixteen patients (53%) had ischemic CHF. 22 patients (73%) were in NYHA class II and 7 in class III. Average distance traveled in walk test was 393±135 m. Mean LVEF was 43±11%. 20 patients had an S'≤10cm/s and 9 had a TAPSE≤16mm. There was a significant positive correlation between TAPSE and the distance traveled during the walk test (r=0.43; p=0.02). There was no correlation between S' and exercise capacity (p=0.20).

Conclusion: TAPSE is a significant determinant of physical performance in CHF patients.