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Letters

Exercise Cardiac Output Limitation in Pectus Excavatum

Indication of pectus excavatum (PE) surgical treatment is a much-debated subject, especially regarding functional impact of the deformation. The pulmonary consequences of PE have been found not to be the limiting factor in exercise for these patients. On the other hand, the hemodynamic consequences of PE have been sparingly studied, because of the difficulty to secure reliable exercise cardiac output (CO). Opinions, therefore, differ greatly as to the scope and the reversibility of hemodynamic exercise limitations for these patients (1,2).

Recently, transthoracic impedance has been extensively used to determine CO and provides a novel way to study pectus physiology. It is a noninvasive, easy-to-perform technique validated against the direct Fick method in exercise, which provides continuous measures from rest-to-peak exercise (3).

We designed a study in which patients seeking treatment for PE underwent exercise evaluation. Our aim was to compare exercise CO components to that of healthy sedentary control subjects (Ctrl), using the bioimpedance technique.

Two thoracic surgery centers promoted this prospective study, which was performed in accordance with the amended Helsinki declaration and local human ethics committee. Seventeen consecutive PE (mean Haller index 5.8 ± 3.9) were included from April 2013 to July 2014 and matched to 17 Ctrl of similar age, weight, and height.

Patients cycled to exhaustion in the upright position. We combined an incremental cycle ergometer test (Medgraphics Ultima Cardio$_2$C, Saint Paul, Minnesota) with gas-exchange measurements to a continuous, noninvasive, determination of the CO (PhysioFlow, Manatec Biomedical, Paris, France).

Data were analyzed using Statistics for Epidemiology and Medicine software (4). Data are presented as mean ± SD. PE and Ctrl values were compared using Student *t* test. Linear regression was used to test the relationship among oxygen consumption ($\dot{V}O_2$), stroke volume (SV), and arteriovenous oxygen difference ($a\bar{v}DO_2$). A difference was considered significant if $p < 0.05$.

There was no significant difference in age, weight, and height between PE (22 ± 7 years of age, 60 ± 9 kg, 175 ± 8 cm) and Ctrl. Both groups performed maximal exercise tests, with PE reaching 74 ± 14% and Ctrl reaching 101 ± 26% of their maximal theoretical $\dot{V}O_2$ ($p < 0.001$) as well as their maximal theoretical heart rates.

At peak exercise, CO was lower in PE (14.0 ± 3.9 l/min) compared with the Ctrl (19.5 ± 4.9 l/min), caused by a lower SV for PE (81 ± 19 ml) versus Ctrl (112 ± 22 ml). This SV reduction is persistent throughout exercise (**Figure 1**). PE is therefore unable to reach the SV values of Ctrl, whatever the exercise intensity.

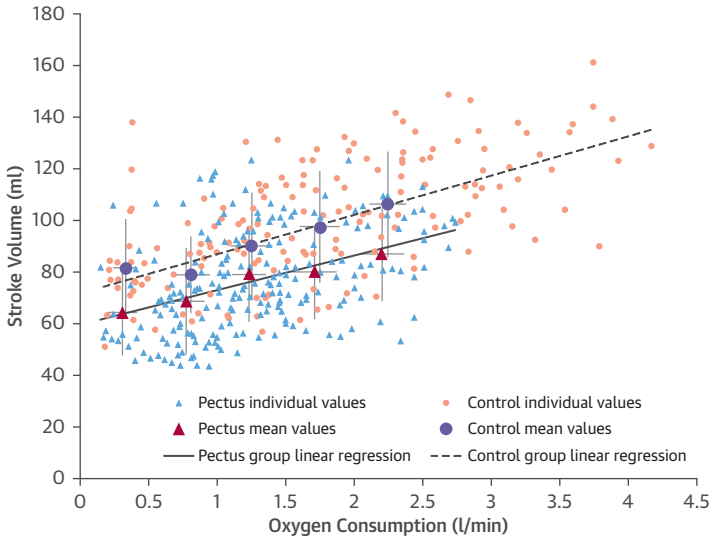
We describe a partial peripheral compensation mechanism in the guise of an increased $a\bar{v}DO_2$. Independent measures of CO and $\dot{V}O_2$ enabled us to calculate continuous $a\bar{v}DO_2$. Linear regression of $a\bar{v}DO_2$ plotted against $\dot{V}O_2$ for each group found significantly different slopes, the PEs being steeper ($\beta = 38.9$; $r = 0.625$) than the Ctrls ($\beta = 31.2$; $r = 0.778$; $p < 0.05$); intercepts were not significantly different. Rest $a\bar{v}DO_2$ are comparable, but PE increase sooner their $a\bar{v}DO_2$ than do Ctrl.

Our main result was the confirmation of PE exercise hemodynamic repercussions, rooted in the patients' lower SV: compression of the right ventricle by the caved-in chest wall restricts the available supplemental volume (5).

There is a clear limitation of peak exercise capacities; because all the subjects' exercise tests were maximal, it can be attributed to the CO restriction. At submaximal exercise, while CO is still decreased in PE, there is partial compensation by an increased $a\bar{v}DO_2$.

The natural heart rate limitation prevents a central compensation of SV restriction. Better $a\bar{v}DO_2$ is another compensation mechanism, but it is limited. All in all, central and peripheral adaptations are unable to overcome the bounds laid by a restricted SV and a set—albeit normal, maximal heart rate. The next step would be to study whether this CO limitation is reversible after remodeling treatments.

FIGURE 1 Stroke Volume Plotted Against $\dot{V}O_2$



For each 500 ml $\dot{V}O_2$ bracket, mean and SD were calculated. The values of the slope and intercept for pectus excavatum and the controls were respectively 13.4 versus 15.2 (p = NS) and 59.8 versus 71.8 ($p < 0.01$), with good correlation coefficients (0.413 and 0.618). NS = not significant; VO_2 = oxygen consumption.

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Vagal Modulation of Atrial Fibrillation

The study by Stavrakis et al. (1) is an interesting contribution to the emerging area of human neuromodulation. The complexity of interaction between the parasympathetic nervous system and the immune system (2), as well as the heart (3), is increasingly well recognized. As the authors highlight, atrial fibrillation is frequently associated with a chronic proinflammatory state. Concordant systematic reviews highlight that higher plasma C-reactive protein (CRP) levels are predictive of greater risk of failure to successfully cardiovert acutely and/or maintain sinus rhythm in the longer term (4). In the Stavrakis et al. trial, patients in the arm randomized to low-level transcutaneous electrical vagus nerve stimulation had an abnormal distribution of plasma CRP, as evident from the standard deviation being higher than mean CRP. In addition to presenting these data with regard to skewness, it may also be instructive for readers to be able to reassess the impact of these data by controlling for each individual patient's baseline