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**D-transposition of the great arteries: post-operative evaluation by breath-by-breath analysis of ventilation and pulmonary gas exchange during exercise**

See page 1052 for the article to which this Editorial refers

Over the past decade, anatomical correction has been the treatment of choice for d-transposition of the great arteries. Mobilization and translocation of the coronary arteries is the most difficult aspect of the arterial switch operation and late mortality has been associated with coronary events such as acute myocardial infarction (0–2%). Although there are other forms of residual pathology (supravalvar pulmonary stenosis, bronchopulmonary collaterals and aortic valve insufficiency), post-operative follow-up has focused on the anatomy of the coronary arteries, myocardial perfusion and left ventricular function.

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Since the anatomical correction is performed during the neonatal period, exercise evaluation has not been an option until recently, when the first of these patients were old enough to participate in such studies. In one study of 23 children, aged 4·2–7·9 years, all had normal exercise tolerance (Bruce treadmill protocol) without symptoms or ECG changes. However, all but one showed some abnormality of myocardial perfusion by radionuclide study. In another study of 50 selected patients (asymptomatic, without medication) 47 had a normal exercise capacity (Bruce treadmill protocol) and normal exercise parameters (heart rate, systemic BP, and ECG). In these studies exercise was utilized primarily to determine exercise capacity, to facilitate radionuclide scans and to detect arrhythmias.

The study of Reybrouck and colleagues in the current issue[1] takes a different approach to exercise testing, by facilitating detection of residual pathology from an analysis of breath-by-breath ventilation and pulmonary gas exchange during submaximal treadmill exercise. The authors compared patients with d-transposition of the great arteries who had either undergone atrial repair (Senning operation) or anatomical correction (arterial switch operation) to normal children of similar age and body size. All exercised at a constant speed with stepwise increasing 2% grade changes at 1 min intervals. Exercise was terminated at a heart rate of 170 beats. min⁻¹. No attempt was made to obtain a maximal effort because the authors believe that such an end-point is too subjective and too dependent on motivation to be of value.

The data were evaluated with respect to four parameters: the anaerobic ventilatory threshold (VAT), the regression slope of oxygen uptake (VO₂) on work rate, the regression slope of ventilation (VE) on CO₂ production (VCO₂) and the heart rate response. The concept of the VAT was first described by Beaver and colleagues[3]. Its determination requires a protocol of small work rate increments of short duration, as was used in this study. The VAT has been widely accepted as a measure of aerobic fitness and defines the maximum VO₂ that can be maintained during sustained effort.

The slope of the VO₂ on work rate during exercise with small work rate increments of short duration is one of a number of ways to evaluate VO₂ kinetics in response to a step input of increased metabolic demand, which reflect the cardiac output response, since by the Fick principle \( \text{VO}_2 = \text{CO} \times (a - \tau) \text{O}_2 \). Sietsma and colleagues[3] examined the VO₂ kinetics in response to a sudden change from rest to a constant work rate exercise. They identified three distinct phases. Phase 1 represents the sudden increase in VO₂ at the onset of work, which is generally completed after approximately 20 s, i.e. before systemic recirculation changes \( C(a - \tau) \text{O}_2 \). It thus represents the change in cardiac output. In phase 2, VO₂ rises exponentially due to an increasing \( C(a - \tau) \text{O}_2 \) difference and cardiac output rises further, until the steady-state response is reached (phase 3). In adult patients with cyanotic congenital heart disease both the phase 1 and phase 2 response was significantly slowed as compared to normal subjects. Similarly, Gildein and colleagues[4] observed in children with d-transposition of the great arteries after atrial repair, a significant slowing of the exponential rate of rise of VO₂ in response to transition from rest to steady-state work, corresponding to 80% and 90% of maximal VO₂.

In normal subjects the breath-by-breath VO₂ in response to submaximal work can be approximated by a single exponential, which approaches a steady-state value asymptotically such that:

\[
\text{VO}_2(t) = \text{VO}_2(ss) \left[ 1 - e^{-\tau} \right]
\]

where \( \text{VO}_2(t) \) is the VO₂ increment at time \( t \) above the resting VO₂ and \( \text{VO}_2(ss) \) the steady-state increment. The exponential time constant \( \tau \) increases with increasing work rates and is shortened by cardiovascular fitness. The equation predicts that \( \text{VO}_2(ss) \) is largely independent of \( \tau \) and increases linearly with increasing work rate increments at a constant slope. The steady-state slope appears largely independent of age, gender, body size and cardiovascular fitness, and for cycle work has been found to be approximately slightly above 2 ml O₂/kg in many studies.

However, for small work rate increments of short duration, such as used in this study, the slope \( \text{VO}_2/\text{WR} \) is sensitive to changes in \( \tau \), decreasing as \( \tau \) increases. In accordance with previous studies[5] Reybrouck and colleagues[1] found a markedly decreased slope \( \text{VO}_2 \) on work rate in their patients after atrial repair of d-transposition of the great arteries. By contrast, in the patients with anatomical repair the slope was significantly greater but remained slightly reduced compared to the normal controls.

In the patients with atrial repair of d-transposition of the great arteries there was also a markedly increased ventilatory response to exercise, expressed as the regression slope of VE on VCO₂, which is inherently linear for submaximal work rates. The relationship of VE and alveolar ventilation (VA) to VCO₂ is given by: \( \text{VA}/\text{VCO}_2 = 1/[\text{FACO}_2 \times (1 - \text{VD}/\text{VT})] \). FACO₂ is the fractional alveolar CO₂ concentration which equals PACO₂ × 868 at body temperature. \text{VD}/\text{VT} is the ratio of dead-space to tidal volume. Thus, at a given

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rate of CO₂ elimination, VE must increase if arterial PCO₂ decreases (low PCO₂ set point), dead space ventilation increases or both.

Evaluation of previous cardiac catheterization data, simultaneous determination of breath-by-breath ventilation and pulmonary gas exchange and transcutaneous PCO₂ have implicated both mechanisms in patients with severe pulmonary vascular disease[5] and tricuspid atresia after Fontan correction[5], conditions also characterized by an inability to increase effective pulmonary blood flow appropriately in response to an increased metabolic demand. Thus in these patients an increased ventilatory response to exercise (VE/VCO₂ slope) is usually also associated with a reduced VO₂/WR slope. In d-transposition of the great arteries after atrial repair, an increased VE/VCO₂ slope has been attributed to ventilation/perfusion mismatch in the lungs, pulmonary vascular disease and broncho-pulmonary collaterals. In a study of 63 patients with d-transposition of the great arteries Muster and colleagues[7] demonstrated, in approximately half of the patients, development of progressive maldistribution of pulmonary blood flow with preferential perfusion of the right lung.

There was a high degree of correlation between preferential perfusion of the right lung and abnormal angulation between the main and right pulmonary arteries, a process which was more pronounced in the presence of pulmonary stenosis. In some cases, 90% of the blood flow was to the right. There was concomitant hypoplasia with relatively increased resistance and decreased compliance of the left lung pulmonary vascular bed. Since the disparity between the perfusion of the two lungs was not present in the newborn period, it was surprising to find, in the current study, an increased average ventilatory response to exercise in the patients with anatomical correction in early infancy. Review of Table 2 in this paper suggests that 5/15 of the patients in this group had an increased ventilatory response to exercise, assuming that a slope of 40 L VE/L VCO₂ is approximately the upper limit of normal in this age group. It is unclear from the data if these were also patients with decreased VO₂ kinetics, as measured by the VO₂/WR slope. While the average data provided in this study are revealing, there is clearly a need to correlate this information in the individual patient with pre- and post-operative anatomy and functional studies such as cardiac catheterization data, angiograms etc. These early long-term results after anatomical correction of d-transposition of the great arteries suggest an entirely normal exercise response in the majority of the patients. However, in about one third the data revealed evidence of an abnormal pulmonary vasculature and a reduced cardiac output response to exercise. Exercise evaluation of breath-by-breath ventilation and pulmonary gas exchange can be a valuable adjunct to other modes of post-operative evaluation of these patients. Since the studies are non-invasive they are eminently suitable for serial long-term follow-up, a sine qua non in this patient group.

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References