Comparing four non-invasive methods to determine the ventilatory anaerobic threshold during cardiopulmonary exercise testing in children with congenital heart or lung disease

Naomi. C. A. Visschers¹, Erik. H. Hulzebos³, Marco. van Brussel¹ and Tim. Takken¹,²

¹Child Development & Exercise Centre, Wilhelmina Children's Hospital, University Medical Center Utrecht, and ²Partner of Shared Utrecht Pediatric Exercise Research (SUPER) Lab, Utrecht, The Netherlands

Summary

Background The ventilatory anaerobic threshold (VAT) is an important method to assess the aerobic fitness in patients with cardiopulmonary disease. Several methods exist to determine the VAT; however, there is no consensus which of these methods is the most accurate.

Objective To compare four different non-invasive methods for the determination of the VAT via respiratory gas exchange analysis during a cardiopulmonary exercise test (CPET). A secondary objective is to determine the interobserver reliability of the VAT.

Methods CPET data of 30 children diagnosed with either cystic fibrosis (CF; N = 15) or with a surgically corrected dextro-transposition of the great arteries (asoTGA; N = 15) were included.

Results No significant differences were found between conditions or among testers. The RER = 1 method differed the most compared to the other methods, showing significant higher results in all six variables. The PET-O₂ method differed significantly on five of six and four of six exercise variables with the V-slope method and the VentEq method, respectively. The V-slope and the VentEq method differed significantly on one of six exercise variables. Ten of thirteen ICCs that were >0.80 had a 95% CI > 0.70. The RER = 1 method and the V-slope method had the highest number of significant ICCs and 95% CIs.

Conclusion The V-slope method, the ventilatory equivalent method and the PET-O₂ method are comparable and reliable methods to determine the VAT during CPET in children with CF or asoTGA.

Introduction

Aerobic fitness is one of the most relevant prognostic factors for morbidity and mortality in patients with pulmonary or cardiac diseases, such as cystic fibrosis or congenital heart diseases (Nixon et al., 1992; Giardini et al., 2007, 2009; Inuzuka et al., 2012; Perez et al., 2013; Hulzebos et al., 2014). The maximal oxygen uptake (VO₂peak), the highest rate at which an individual can consume oxygen during exercise, is widely recognized as the golden standard to assess an individual’s level of aerobic fitness (Shephard et al., 1968). Maximal oxygen uptake conventionally implies the existence of a VO₂ plateau. However, this response is not typical of children and adolescents (Rowland, 1993; Armstrong et al., 1996), and so it has gradually become more common to determine the VO₂peak, being the highest VO₂ elicited during a cardiopulmonary exercise test (CPET), to describe the aerobic fitness of children (Fawkner & Armstrong, 2007). Achieving this VO₂peak, however, requires maximal effort, which might not be attainable for every paediatric patient with a cardiac or pulmonary impairment. Therefore, in these patients, supplementary approaches to determine the level of physical fitness, such as quantifying the ventilatory anaerobic threshold (VAT), are being implemented (Hebestreit et al., 2000).

Maintaining and improving a certain level of aerobic fitness (within a frame of reference suitable for cardiopulmonary impaired patients) is a fundamental pillar in the multidisciplinary treatment of the above mentioned diseases. Therefore,
these patients are recommended to perform a CPET on a regular basis (Binder et al., 2008; Baumgartner et al., 2010). Next to the assessment of aerobic fitness, the VAT is frequently used to determine a patient’s exercise intensity level in order to develop and prescribe an individually tailored exercise training programme, thereby making it a multi-purpose tool (Gaskill et al., 2001; Binder et al., 2008; Baumgartner et al., 2010).

In general, the anaerobic threshold (AT) is defined as a time point, which emerges during incremental exercise, that indicates a shift in the type of metabolism in muscle cells (Wasserman et al., 2005). From this point on, a solely aerobic metabolism will not be sufficient to deliver enough energy, thereby generating additional energy from anaerobic glycolysis (Wasserman et al., 2005). During anaerobic glycolysis, lactic acid is formed, which, in aqueous solutions, will almost completely dissociate into lactate and H+ ions. In anaerobic circumstances, levels of lactate and H+ will rapidly augment. The production of lactic acid is most prominent in type 2 ‘fast-twitch’ muscle fibres, which are mainly recruited during high-intensity exercise (Philp et al., 2005). At first, the accumulation of lactate and H+ is compensated by binding to NaHCO3 in the cytoplasm of myocytes and in blood plasma. This prevents drastic alterations in the blood lactate concentrations. However, once the buffering capacity of NaHCO3 has reached its maximum, and the H+ concentration in the blood will rise. This latter rise causes the pH to drop, and metabolic acidosis threatens to occur. Automatically, ventilation will increase and deepen to make sure more carbon dioxide is exhaled, so that the pH-decline will be compensated (Gaskill et al., 2001; Binder et al., 2008).

When determining the AT, it is important to take two points into consideration. Firstly, there is a large diversity in terminology to address the concept of the anaerobic threshold, which can cause misapprehension. For example, terms such as the ventilatory threshold, the lactate threshold or the point of optimal ventilatory efficiency are all applied to point out the anaerobic threshold. Moreover, there is no clear-cut definition on what the so-called first and second anaerobic thresholds behold. Thus, to avoid confusion, in this study the first and second anaerobic thresholds will be defined as following:

First anaerobic threshold or VAT: that point in time, which indicates an augmentation in ventilation to eliminate more carbon dioxide to compensate for the rising blood lactate concentration. After this point, for a certain period, the carbon dioxide exchange is equal to the production of lactate, which results in a near constant blood lactate concentration (Wasserman et al., 2005; Binder et al., 2008). Second anaerobic threshold or respiratory compensation point (RCP): once the lactate accumulation starts to exceed the carbon dioxide elimination, lactate levels in the blood will excessively augment. Relative hyperventilating will no longer be sufficient to maintain a constant pH level in the blood (Wasserman et al., 2005; Binder et al., 2008). Secondly, there are several techniques to determine the VAT during CPET. Wassermann and McIlroy were in 1964 the first ones to describe the anaerobic threshold (Wasserman & McIlroy, 1964). Since then, different techniques have been suggested as a tool to determine the VAT. Quantifying blood lactate levels is considered to be the golden standard for determining the VAT. As this method is invasive, time-consuming and not patient-friendly, non-invasive methods are preferred, especially in children. Previous research postulates that assessing the VAT via respiratory gas exchange parameters are as accurate as measuring blood lactate levels (Nikolaizik et al., 1998; Santos & Giannella-Neto, 2004; Plato et al., 2008; Nikoosie et al., 2009; Gravier et al., 2014).

Various non-invasive methods using respiratory gas exchange variables are available; however, the most frequently utilized methods are the ventilatory equivalent method (Vent-Eq) and the V-slope method (Wasserman et al., 2005). The PET-O2 method and the respiratory exchange ratio = 1 method (RER = 1) are regularly applied as well. Clinical exercise physiologists indicate that the combination of different methods seems to increase the reliability of the determination of the VAT (Hebestreit et al., 2000; Gaskill et al., 2001). However, little literature is available on comparing the results of the different methods to determine the VAT in children with pulmonary or cardiac conditions.

Therefore, the aim of this study is to compare the four most clinically applied non-invasive methods for determining the VAT via respiratory gas exchange analysis during a CPET in children with impaired cardiopulmonary function. A secondary objective is to determine the interobserver reliability of experienced clinical exercise physiologists for assessing these four non-invasive methods for determining the VAT.

Methods

Study sample

The CPET data of a convenience sample of 30 children, either diagnosed with cystic fibrosis (CF; N = 15) or with a dextrotransposition of the great arteries for which they received arterial switch surgery shortly after birth (asoTGA; N = 15), were selected for this study. Patients were aged between 5-0 and 18-4 years at the time of performing the CPET. Patients >18 years or who had other comorbidities were excluded. Clinical characteristics of the patients are depicted in Table 1a, b. All procedures were approved by the Medical Ethics Board of our institution.

Cardiopulmonary exercise testing

Participants performed a CPET by bicycle ergometry according to a ramped Godfrey protocol, with possible intensities of 10, 15, 20 or 25 Watt min⁻¹ (based on the height and estimated fitness of the patient) (Godfrey, 1974). All CPETs were performed on the Lode Corival cycle ergometer (Lode BV, Groningen, the Netherlands) and gas exchange was measured using the ZAN 600 metabolic cart (Accuramed BVBA, Lummen, 2008; Baumgartner et al., 2008; Santos & Giannella-Neto, 2004).
### Table 1
(a) Clinical characteristics of the patients with CF. (b) Characteristics of the patients with asoTGA.

| Patient | Age on test date | Height (cm) | Weight (kg) | Sex | Proscntol | Peak Watt | Peak Watt % | Peak Watt/kg | VO<sub>2</sub> peak | VO<sub>2</sub> peak % | VO<sub>2</sub> peak/kg | VO<sub>2</sub> peak/kg % | HF peak | RER peak |
|---------|------------------|-------------|-------------|-----|-----------|-----------|------------|-------------|----------------|-----------------|----------------|-------------------|------------------|---------|---------|
| 1       | 15-6             | 172         | 58          | F   | 20        | 180       | 87         | 3-1         | 87             | 2.41            | 98             | 41.6              | 99                | 184     | 1-04    |
| 2       | 15-0             | 178         | 59          | M   | 25        | 230       | 101        | 3-9         | 97             | 2.86            | 108            | 48.2              | 98                | 182     | 1-16    |
| 3       | 13-8             | 172         | 58          | F   | 15        | 180       | 115        | 3-1         | 99             | 2.34            | 117            | 40.3              | 102               | 202     | 1-16    |
| 4       | 14-2             | 166         | 46          | F   | 15        | 137       | 74         | 3           | 85             | 1.41            | 63             | 30.7              | 74                | 192     | 1-03    |
| 5       | 13-2             | 173         | 53          | M   | 15        | 210       | 117        | 4           | 112            | 2.44            | 102            | 46                | 97                | 205     | 1-27    |
| 6       | 12-1             | 138         | 31          | F   | 15        | 81        | 60         | 2-6         | 87             | 1.12            | 70             | 36.2              | 95                | 184     | 1-12    |
| 7       | 13-2             | 160         | 48          | M   | 15        | 139       | 73         | 3-9         | 71             | 1.76            | 71             | 36.7              | 74                | 173     | 1-1     |
| 8       | 11-5             | 154         | 47          | F   | 15        | 150       | 118        | 3-2         | 108            | 1.88            | 112            | 40.1              | 98                | 183     | 1-06    |
| 9       | 11-1             | 143         | 33          | M   | 10        | 99        | 67         | 3           | 80             | 1.34            | 75             | 40.7              | 85                | 187     | 1-13    |
| 10      | 10-0             | 142         | 35          | F   | 15        | 111       | 104        | 3-2         | 111            | 1.27            | 88             | 36.2              | 88                | 179     | 1-18    |
| 11      | 9-4              | 135         | 30          | F   | 10        | 96        | 88         | 3-2         | 102            | 1.22            | 90             | 40.7              | 102               | 176     | 1-05    |
| 12      | 8-9              | 143         | 39          | M   | 15        | 105       | 100        | 2-7         | 79             | 1.27            | 101            | 32.5              | 72                | 177     | 1-09    |
| 13      | 7-8              | 126         | 25          | F   | 10        | 88        | 106        | 3-5         | 116            | 0.92            | 76             | 36.7              | 82                | 198     | 1-26    |
| 14      | 6-1              | 118         | 23          | F   | 10        | 54        | 96         | 2-3         | 81             | 0.76            | 84             | 32.9              | 76                | 170     | 0-99    |
| 15      | 5                | 111         | 18          | M   | 10        | 49        | 99         | 3-2         | 97             | 0.74            | 82             | 2.7                | 97                | 184     | 0-91    |
| Mean    | 9-59             | 147         | 38-9        |     |           | 13-9      | 123-5      | 94-1         | 13-13          | 94-6            | 15-2           | 88-5              | 35-8             | 88-6    | 185-1   |
| SD      | 3-33             | 20-9        | 13-1        |     |           | 4-0       | 54-4       | 18-9         | 0-46           | 14-3            | 0-65           | 17-1              | 10-7             | 11-2    | 10-65   |

(b) Comparing four VAT methods, N. C. A. Visschers et al.
Comparing four VAT methods, N. C. A. Visschers et al.

Belgium) and analysed using the ZAN® GPI 3-00 Cardiopulmonary Exercise software (Accuramed BVBA, Lummen, Belgium). Preceding and during the CPET, arterial oxygen saturation (SpO2; Masimo Rad 8; Masimo BV, Tilburg, the Netherlands), cardiac rhythm via a 12-lead ECG (CardioPerfect; IT-Medical, Veenendaal, the Netherlands) and blood pressure (Suntech Tango; Suntech Medical Inc, Morrisville, NC, USA) were continuously measured and prior to the CPET, all parameters were measured in a resting state. Each test included a three-minute warming up consisting of unloaded cycling. The workload increased according to the ramped Godfrey protocol (Godfrey, 1974). Every patient continued until (leg) fatigue or dyspnea appeared, as long as they did not experience any chest pain, vertigo, near-fainting or nausea. All participants were verbally encouraged to exercise until volitional exhaustion. The recovery phase included 3 min of unloaded cycling and a 1–2 min cooling down.

For this study, the following variables were relevant for determining the different VATs: the workload (Watt), the heart frequency (HF), the oxygen uptake in litres per minute (VO2), the ratio between ventilation and oxygen uptake (VE/VO2), the ratio between ventilation and CO2 exhalation (VE/VCO2) and the ventilation in litres per minute (VE). Data were averaged using 10 s averages. All exercise tests were standardized and supervised by an experienced paediatric exercise physiologist.

Procedure

Three paediatric exercise physiologists, from here on designated as testers, with, respectively, 9, 9 and 15 years of experience in performing paediatric CPETs, assessed the results of the CPETs independently from one another. Two of them specialized in exercise physiology in patients with cardiac and/or pulmonary diseases, one of them in musculoskeletal disease. All testers analysed the same CPET from each patient. For every CPET, they determined the time point at which the VAT occurred in four different ways (via the V-slope method, the VentEq method, the PET-O2 method and the RER = 1 method, respectively). Data were displayed and analysed using a nine panel plot (Wasserman et al., 2005). In the V-slope method, the VO2 was plotted against VCO2 (plot 5). The VAT is where the slope of the relationship between VO2 and VCO2 is steeper than 1-0 (Wasserman et al., 2005). The VentEq method is determined using the VE/VO2 and the VE/VCO2 (plot 6). When VE/VCO2 is observed to increase without a simultaneous increase in VE/VCO2, this was the point where the VAT occurred according to the VentEq method (Wasserman et al., 2005). Using the PET-O2 method (plot 9), the VAT was determined at the point where PET-O2 increased without concomitant increase in PET-CO2 (Wasserman et al., 2005).

The variables corresponding with the time point of the four determined VATs (Watt, HF, VO2, VE/VO2, VE/VCO2 and VE) were determined and used for statistical analysis.

Data analysis

Statistical analysis was performed using SPSS 20.0 for Windows (SPSS, Chicago, IL, USA). Standard statistical methods were used to calculate means and standard deviations. Two-way repeated measures ANOVA were performed to compare key variables obtained during CPET. Two different conditions (CF and asoTGA) were compared by the three independent testers. Assumptions for the repeated measures ANOVA were checked using Mauchly’s test of sphericity.

Interobserver variability

The means and standard deviations for all three testers are depicted in Table 3. No significant differences were found among the testers. Table 4 shows the level of agreement.
Lactate concentrations were not assessed during exercise for the VAT determination in children. However, blood other three methods and resulted in significantly higher val-
trast, the RER and the PET-O2 method. All results were statistically significant

### Table 2: Mean and SD values for all variables using the four VAT methods.

<table>
<thead>
<tr>
<th>Method</th>
<th>V-slope</th>
<th>VentEq</th>
<th>PET-O2</th>
<th>RER = 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watt</td>
<td>82&lt;sup&gt;CD&lt;/sup&gt;</td>
<td>79&lt;sup&gt;CD&lt;/sup&gt;</td>
<td>74&lt;sup&gt;ABD&lt;/sup&gt;</td>
<td>108&lt;sup&gt;ABC&lt;/sup&gt;</td>
</tr>
<tr>
<td>SD</td>
<td>4.4</td>
<td>3.8</td>
<td>3.5</td>
<td>4.4</td>
</tr>
<tr>
<td>HF</td>
<td>130&lt;sup&gt;CD&lt;/sup&gt;</td>
<td>134&lt;sup&gt;CD&lt;/sup&gt;</td>
<td>130&lt;sup&gt;ABD&lt;/sup&gt;</td>
<td>153&lt;sup&gt;ABC&lt;/sup&gt;</td>
</tr>
<tr>
<td>SD</td>
<td>1.9</td>
<td>2.0</td>
<td>2.2</td>
<td>1.7</td>
</tr>
<tr>
<td>VO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>1.15&lt;sup&gt;CD&lt;/sup&gt;</td>
<td>1.13&lt;sup&gt;CD&lt;/sup&gt;</td>
<td>1.06&lt;sup&gt;ABD&lt;/sup&gt;</td>
<td>1.40&lt;sup&gt;ABC&lt;/sup&gt;</td>
</tr>
<tr>
<td>SD</td>
<td>0.05</td>
<td>0.05</td>
<td>0.04</td>
<td>0.06</td>
</tr>
<tr>
<td>VE/V&lt;sub&gt;O&lt;/sub&gt;2</td>
<td>23.3&lt;sup&gt;B&lt;/sup&gt;</td>
<td>22.7&lt;sup&gt;A&lt;/sup&gt;</td>
<td>22.7&lt;sup&gt;AD&lt;/sup&gt;</td>
<td>26.0&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>SD</td>
<td>0.28</td>
<td>0.30</td>
<td>0.29</td>
<td>0.26</td>
</tr>
<tr>
<td>VE/V&lt;sub&gt;CO&lt;/sub&gt;2</td>
<td>25.27&lt;sup&gt;D&lt;/sup&gt;</td>
<td>24.94&lt;sup&gt;D&lt;/sup&gt;</td>
<td>25.08&lt;sup&gt;B&lt;/sup&gt;</td>
<td>25.69&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>SD</td>
<td>0.22</td>
<td>0.27</td>
<td>0.27</td>
<td>0.24</td>
</tr>
<tr>
<td>VE</td>
<td>27.89&lt;sup&gt;CD&lt;/sup&gt;</td>
<td>26.48&lt;sup&gt;CD&lt;/sup&gt;</td>
<td>25.40&lt;sup&gt;ABD&lt;/sup&gt;</td>
<td>38.50&lt;sup&gt;ABC&lt;/sup&gt;</td>
</tr>
<tr>
<td>SD</td>
<td>1.24</td>
<td>0.92</td>
<td>0.83</td>
<td>1.31</td>
</tr>
</tbody>
</table>

A: significantly different from the V-slope method (P<0.05); B: significantly different from the ventilatory equivalent method (P<0.05); C: significantly different from the PET-<sub>O2</sub> method (P<0.05); D: significantly different from the RER = 1 method (P<0.05). HF, heart rate; VO<sub>2</sub>, oxygen uptake; VE/V<sub>O</sub>2, ventilatory equivalent for oxygen uptake; VE/V<sub>CO</sub>2, ventilator equivalent for carbon dioxide exhalation; VE, minute ventilation.

among testers through the intraclass correlation coefficient test (ICC). Besides one, all ICCs were >0.60, and 13 of 24 ICCs were >0.80. Therefore, nearly all ICCs showed a good or excellent degree of similarity among testers. Ten of 13 ICCs that were >0.80 had a 95% CI > 0.70, which supports the previous findings of a notable high degree of similarity among testers. The RER = 1 method and the V-slope method had the highest incidence of significant ICCs and 95% CIs. In addition, the variable Watt showed significant results for the ICCs for all the four methods. The VO<sub>2</sub> showed statistically significant ICCs and 95% CIs for the V-slope method, the VentEq method and the PET-<sub>O2</sub> method. All results were statistically significant at the P<0.05 level.

### Discussion

When comparing most clinically applied non-invasive methods for determining the VAT, the V-slope method and the VentEq method showed the greatest similarities with regard to the results of the gas exchange variables in children with impaired cardiopulmonary function. The PET-<sub>O2</sub> method gave slightly lower values compared to these two methods. In contrast, the RER = 1 method differed significantly from the other three methods and resulted in significantly higher values. This questions, whether the RER = 1 method is appropriate for the VAT determination in children. However, blood lactate concentrations were not assessed during exercise because of the burden or repeated blood sampling. Therefore, it is not possible to draw definite conclusions regarding the validity of the RER = 1 method in children.

The results of the ICC indicate a remarkable degree of similarity among the testers. The RER = 1 method showed the best results for the ICCs and 95% CIs. Considering the other three methods, the VO<sub>2</sub> at the VAT using the V-slope method, showed the best agreement. According to Wasserman et al. (2005) the VO<sub>2</sub> is the most physiologically meaningful parameter to report on the VAT.

These findings implicate that the V-slope method, the VentEq method and the PET-<sub>O2</sub> method are remarkably comparable for determining the VAT during CPET. When further specified, the V-slope and the VentEq methods are the most alike, although the differences among these two methods and the PET-<sub>O2</sub> methods are very small. The V-slope method has shown to be the method with the least interobserver variability. In addition, the VO<sub>2</sub> is the most reliable variable to report the VAT, as it shows the lowest variability among assessors. This implies that the V-slope method is the method least prone to differences in results due to interobserver differences.

Previously, Yeh et al. (1983) concluded that, due to the large range of interobserver variability, determining the VAT via gas exchange variables might not be an appropriate method (Yeh et al., 1983). In contrast, we found an excellent level of agreement among testers.

Several studies are available regarding exercise testing in patients with cystic fibrosis or a surgically corrected transposition of the great arteries; however, these studies report predominantly from a prognostic perspective (Nikolaizik et al., 1998; Shah et al., 1998; Reybrouck et al., 2001; Thin et al., 2002; Sexauer et al., 2003; Buys et al., 2012; Muller et al., 2013; Gruber et al., 2014). Furthermore, most studies on patients with CF included adult patients instead of paediatric patients (Shah et al., 1998; Sexauer et al., 2003; Gruber et al., 2014). Recently, Saynor et al. (2013) reported a good test–retest reliability for assessing the VAT in children with CF (Saynor et al., 2013) and strengthen our current findings.

Furthermore, most studies on patients with CF included adult patients instead of paediatric patients (Shah et al., 1998; Sexauer et al., 2003; Gruber et al., 2014). These studies emphasize that VAT is an appropriate method to estimate a person’s physical fitness in multiple populations.

Merely a few studies are known that compare different methods to determine the VAT (Plato et al., 2008; Nikooie et al., 2009; Gravier et al., 2014); however, these studies predominantly compare two or three methods, or methods that are not included in the current study (i.e. the Conconi test method) (Nikolaizik et al., 1998). Moreover, these method comparing studies often included healthy individuals instead of patients with impaired cardiopulmonary function. Nonetheless, a few studies made comparisons with blood lactate levels, in these studies referred to as the golden standard for determining the anaerobic threshold (Caiozzo et al., 1982; Beaver et al., 1986). For example, Ohuchi et al. (1996) found
a significant correlation for the V-slope method and the VentEq method compared to blood lactate concentrations in patients with congenital heart disease (Ohuchi et al., 1996). The correlation coefficients for these comparisons were 0.80 and 0.91 for the V-slope and the VentEq method, respectively. The authors also found a correlation coefficient of 0.93 when comparing the V-slope method and the VentEq method (Ohuchi et al., 1996). This study depicts that non-invasive ways to determine the VAT are an excellent option to predict the lactate threshold, which has been confirmed by several other studies (Nikolaizik et al., 1998; Santos & Giannella-Neto, 2004; Plato et al., 2008; Nikooie et al., 2009; Gravier et al., 2014). Nonetheless, studies differ on which method seems to be the most suitable for clinical application.
Future research

Future research should also include children with other (cardiac or pulmonary) diseases, and/or compare different methods to a golden (invasive) standard, although the invasive methods are not preferred in children. Furthermore, also less
experience that physiologists should be included in the interobserver reliability study.

**Strengths and limitations**

The current study compared methods that are frequently applied in the clinical setting to determine the VAT during CPET, to an extent that has not been performed before in pediatric patients with cardiopulmonary disease. Whereas other studies compare two or three methods, our study provides the most extensive and complete comparison of VAT-determining methods, thereby answering an actual and clinically relevant question. Secondly, we included a study sample that represents a wide range of patient characteristics: for example, age differed between 5 and 18 years old, the level of fitness reached from 61 to 116% of predicted VO2 peak kg⁻¹, and both boys and girls were included.

Furthermore, we used the standard analysing software that came with our metabolic cart to analyse the VATs. This latter mimics daily clinical practice and enhances generalization to other systems because many of the software functionalities are comparable between manufacturers of metabolic carts.

There are a few limitations to this study. We did not compare the different methods to determine the VAT to a golden standard method, such as measuring the blood lactate concentration. Finally, our results are applicable on patients with cystic fibrosis or a transposition of the great arteries and might not be for other cardiac or pulmonary diseases.

**Conclusion**

The V-slope method, the ventilatory equivalent method and the PET-O2 method are comparable methods to determine the VAT non-invasively during cardiopulmonary exercise testing in children with cystic fibrosis or a surgically corrected transposition of the great arteries. In contrast, the RER = 1 method differed significantly from the other three methods and questions whether the RER = 1 method is appropriate for the VAT determination in children. The RER = 1 method gave significantly higher values compared to the other three methods. In addition, the four employed non-invasive methods for the determination of the VAT showed high inter-rater reliability.

The current study provides additional evidence to use the V-slope method, the ventilatory equivalent method and the PET-O2 method to determine the VAT non-invasively in children with congenital heart or lung disease.

**Conflict of interest**

The authors have no conflict of interest.

**References**


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Giraudouz B, Mary JY. Planning a reproducibility study: how many subjects and how many replicates per subject for an expected width of the 95% confidence interval of the intraclass correlation coefficient. Stat Med (2001); 20: 3205–3214.


Giraudouz B, Mary JY. Planning a reproducibility study: how many subjects and how many replicates per subject for an expected width of the 95% confidence interval of the intraclass correlation coefficient. Stat Med (2001); 20: 3205–3214.


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