CHD

Assumed oxygen consumption frequently results in large errors in the determination of cardiac output

Ullrich Fakler, MD,[a] Christian Pauli, MD,[a] Michael Hennig, PhD,[b] Walter Sebening, MD,[a] and John Hess, MD, PhD[a]

Objective: We sought to investigate the differences in assumed and measured oxygen consumption values for the determination of cardiac output by using the Fick principle in a pediatric population with congenital heart disease.

Methods: The patient population consisted of 143 patients with a mean age of 11.3 years (age range, 2 days to 23.8 years) undergoing cardiac catheterization during general anesthesia and with mechanical ventilation. Oxygen consumption was measured with a standard commercial analyzing system (Deltatrac II; Datex, Engström, Helsinki, Finland). Assumed oxygen consumption values were calculated according to the formulas of Krovetz and Goldbloom and LaFarge and Miettinen. Comparisons between measurements and assumptions were performed by Bland-Altman plots. Two-sided paired *t* tests were used to assess a difference of the assumed and measured values.

Results: The range of measured oxygen consumption values was between 55.2 and 249 $mL \cdot min^{-1} \cdot m^{-2}$. The Krovetz-Goldbloom formula led to systematically larger values compared with the measured values ($P = .0001$; mean difference of −53.3 $mL \cdot min^{-1} \cdot m^{-2}$; 95% confidence interval, −56.7 to −49.8 $mL \cdot min^{-1} \cdot m^{-2}$). The use of the LaFarge-Miettinen formula tends to overestimate oxygen consumption ($P = .0037$; mean difference of −15.9 $mL \cdot min^{-1} \cdot m^{-2}$; 95% confidence interval, −26.5 to −5.4 $mL \cdot min^{-1} \cdot m^{-2}$). A similarly poor agreement was found when analyzing a subgroup of 25 patients with Fontan-type circulation.

Conclusion: The use of assumed instead of measured oxygen consumption values introduces large errors in the determination of cardiac output.

The determination of hemodynamic parameters requires an exact measurement of cardiac output. The Fick method[1] is established as the clinical gold standard for measuring cardiac output and is most commonly used. It requires the determination of the difference of arterial–mixed venous oxygen content and the oxygen consumption (VO_2).

The Fick equation is as follows: $CO = VO_2/(CaO_2 - CvO_2)$, where CO is defined as cardiac output in liters per minute, VO_2 is defined as oxygen consumption in liters per minute, CaO_2 is defined as arterial oxygen content in milliliters per liter ($1.36 \times Hbg\ [g/L] \times SaO_2) + (PaO_2[mmHg] \times 0.003)$, CvO_2 is defined as mixed venous oxygen content in milliliters per liter ($1.36 \times Hbg\ [g/L] \times SvO_2) + (PvO_2[mmHg] \times 0.003)$.

It is common practice to use an estimate of VO_2 instead of measurements. Both Krovetz and Goldbloom,[2] carrying out multiple regression analysis, and LaFarge and Miettinen,[3] using multivariate analysis of covariance, derived empiric formulas to estimate VO_2, which remain the most commonly used equations for calculating assumed VO_2. Considerable errors introduced by using assumed VO_2 have been reported and discussed previously.[4-7] General anesthesia is sometimes necessary to perform cardiac catheterization in pediatric patients under stable conditions, thus affecting oxygen consumption and other parameters substantially.

Therefore, the aim of this study was to assess the quantity of error that might be introduced by using assumed VO_2 compared with measured VO_2 in a pediatric population with congenital heart disease undergoing cardiac catheterization.

From the Department of Pediatric Cardiology and Congenital Heart Disease,[a] German Heart Center, Technische Universität München, Munich, Germany, and the Institute of Medical Statistics and Epidemiology,[b] Technische Universität München, Klinikum r.d. Isar, Munich, Germany.

Received for publication Nov 20, 2004; revisions received Jan 15, 2005; accepted for publication Feb 8, 2005.

Address for reprints: Ullrich Fakler, MD, German Heart Center, Department of Pediatric Cardiology and Congenital Heart Disease, Technische Universität München, Lazarettstraβe 36, D-80636 Munich, Germany (E-mail: fakler@dhm.mhn.de).

J Thorac Cardiovasc Surg 2005;130:272-6

0022-5223/$30.00

doi:10.1016/j.jtcvs.2005.02.048

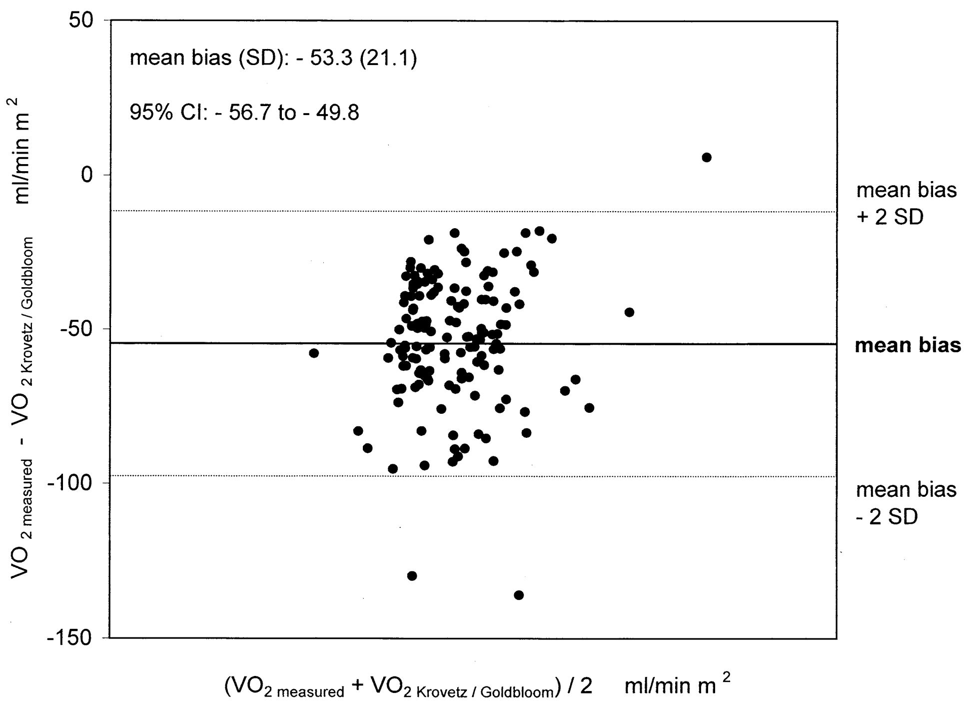

Figure 1. Bland-Altman plot showing the difference between VO_2 measured minus VO_2 Krovetz-Goldbloom and the mean of VO_2 measured plus VO_2 Krovetz-Goldbloom from 143 patients.

Subgroup analysis in patients with completed Fontan circulation was performed.

Methods

The study was performed in 143 patients (67 female and 76 male patient; mean [standard deviation [SD] age, 11.3 [8.1] years; age range, 2 days to 23.8 years; mean [SD] weight, 34.6 [23.1] kg; weight range, 2.9-96 kg). These patients were undergoing cardiac catheterization because of congenital heart disease. The study was approved from the institutional review board, and informed consent was obtained from patients or their guardians.

All patients received anesthesia, avoiding inhalant narcotics. Their lungs were mechanically ventilated in volume-controlled mode (IPPV ventilator, Siemens Servo Ventilator 900 D; Siemens, Erlangen, Germany), receiving an inhaled fraction of inspired oxygen of between 0.21 and 0.48. Twelve patients had to be excluded because of air leaks of the tube of more than 5% during the measurements. The LaFarge-Miettinen formula was derived in patients between 3 and 40 years of age. One hundred fifteen patients were of this age and were available for the comparison. A subset of 25 patients had a Fontan-type circulation.

Age, sex, height, weight, and heart rate (electrocardiography) were recorded, and body surface area was calculated according to the method of Dubois and Dubois.[8]

VO_2 was measured with the standard commercial analyzing system Deltatrac II (Datex-Engström, Helsinki, Finland). The Deltatrac Metabolic Monitor is an open-system, indirect calorimetry device equipped with a fast differential paramagnetic oxygen sensor to measure a differential signal between inspired and expired gases and a gas dilution system to measure flow.[9,10] The measurements were taken when the patient was in a stable state shortly after intubation over a period of 10 minutes, obtaining one measurement every minute. All sets of 10 single measurements showed an SD of less than 10%, so effects of a fluctuating FIO_2 on metabolic measurements could be excluded.[11] The mean of these single measurements was calculated and compared with the assumed VO_2 values.

Assumed VO_2 values were calculated according to the Krovetz-Goldbloom formula as follows: $VO_2/BSA = (1.39\times height[cm] + 0.84\times weight[kg] - 35.6)/BSA(mL/\text{min})/m^2$. The formula of LaFarge-Miettinen was used as follows: $VO_2/BSA = (138.1-17.04\times \ln(age) + 0.378\times HR)/BSA(mL/\text{min})/m^2$ for female subjects and $VO_2/BSA = (138.1 - 11.49\times \ln(age) + 0.378\times HR\_/BSA(mL/\text{min})/m^2$ for male subjects, where age is presented in years and HR is defined as heart rate (in minutes).

Comparisons between measurements and assumptions were performed by means of Bland-Altman plots[12] and comparative correlation plots. Two-sided paired *t* tests were used to assess a difference of the assumed and measured values. Because there were 2 such tests, the significance level was split to 2.5% for each test, according to the method of Bonferroni. Pearson correlation coefficients were calculated to assess the correlation of assumed and measured VO_2. The percent error introduced by using assumed VO_2 was calculated by dividing the difference of measured minus assumed VO_2 by the corresponding measured VO_2. Data are represented as means (SDs).

The subgroup of 25 patients with completed Fontan-type circulation was compared with the 118 patients without Fontan-type circulation by an unpaired *t* test.

Calculations were computed with SAS 6.12 software (Cary, NC).

CHD

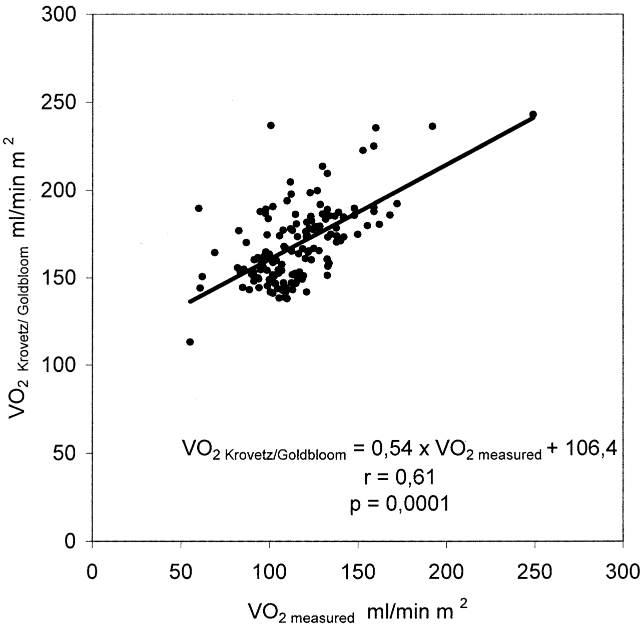

Figure 2. Comparative plot of VO_2 measured versus VO_2 Krovetz-Goldbloom and the corresponding correlation coefficient.

Results

The mean measured VO_2 was 115.7 mL · min^{-1} · m^{-2} (SD, 25.2 mL · min^{-1} · m^{-2}), with a range of 55.2 to 249 mL · min^{-1} · m^{-2} (n = 143). According to the Krovetz-Goldbloom formula, the mean assumed VO_2 was 169.0 mL · min^{-1} · m^{-2} (SD, 22.3 mL · min^{-1} · m^{-2}). Calculating with the Krovetz-Goldbloom formula led to a systematic and significant (P = .0001) overestimation of VO_2 values. The mean difference (bias) was −53.3 mL · min^{-1} · m^{-2} (SD, 21.1 mL · min^{-1} · m^{-2}; 95% confidence interval, −56.7 to −49.8 mL · min^{-1} · m^{-2}). The Pearson correlation coefficient of assumed VO_2 Krovetz-Goldbloom and measured VO_2 was an r value of 0.61 (P = .0001; VO_2 Krovetz-Goldbloom = 0.54 × VO_2 measured + 106.4).

A Bland-Altman plot of the difference between VO_2 measured minus VO_2 Krovetz-Goldbloom and the mean of VO_2 measured plus VO_2 Krovetz-Goldbloom is shown in Figure 1. Figure 2 presents a comparative plot of VO_2 measured versus VO_2 Krovetz-Goldbloom and the corresponding correlation coefficient.

With the LaFarge-Miettienen formula, a systematic and significant (P = .0037) overestimation of VO_2 values was observed. The mean difference was −15.6 mL · min^{-1} · m^{-2} (SD, 57.2 mL · min^{-1} · m^{-2}; 95% confidence interval, −26.3 to −5.4 mL · min^{-1} · m^{-2}). A correlation (r value) of 0.38 between VO_2 measured and VO_2 LaFarge-Miettinen was found with the following regression equation: *VO_2 LaFarge-Mietten = 1.28 × VO_2 LaFarge-Miettinen = 1.28 × VO_2 measured − 14.9.* A Bland-Altman plot of the difference between VO_2 measured minus VO_2 LaFarge-Miettinen and the mean of VO_2 measured plus VO_2 LaFarge-Miettinen and a comparative plot are shown in Figure 3. Figure 4 presents a

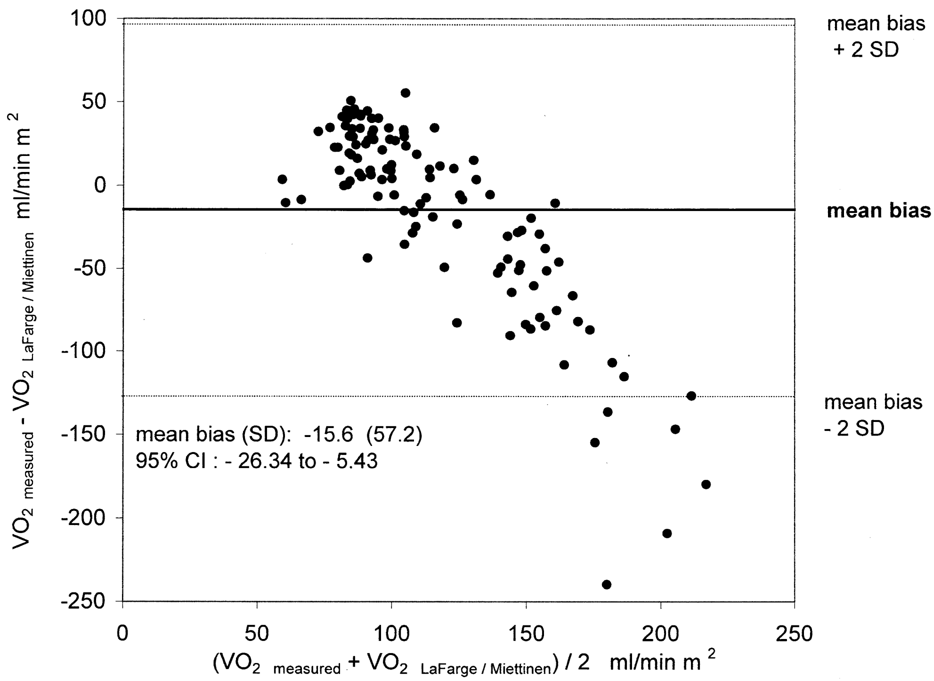

Figure 3. Bland-Altman plot showing the difference between VO_2 measured minus VO_2 LaFarge-Miettinen and the mean of VO_2 measured plus VO_2 LaFarge-Miettinen from 115 patients.

comparative plot of VO_2 measured versus VO_2 LaFarge-Miettinen and the correlation coefficient.

The distribution of the quantity of error related to the use of assumed VO_2 instead of measured VO_2 is shown in Figure 5. Absolute errors of more than 50% occurred in 38.5% (Krovetz-Goldbloom) or 19.1% (LaFarge-Miettinen) of the compared assumed and measured values.

Twenty-five patients with completed Fontan circulation had a significantly lower (mean, 101.27 $mL \cdot min^{-1} \cdot m^{-2}$ [SD, 17.68 $mL \cdot min^{-1} \cdot m^{-2}$]) VO_2 than patients without a Fontan circulation (n = 118; mean, 118.42 $mL \cdot min^{-1} \cdot m^{-2}$ [SD, 25.7 $mL \cdot min^{-1} \cdot m^{-2}$]; P = .0002). The mean difference found with the Krovetz-Goldbloom formula was −55.7 $mL \cdot min^{-1} \cdot m^{-2}$ (SD, 29.9 $mL \cdot min^{-1} \cdot m^{-2}$; P = .0001), leading to a mean relative error in the determination of VO_2 of 59% (range, 14%-136.5%). If the LaFarge-Miettinen formula was used, a nonsignificant difference (mean, 4.59 $mL \cdot min^{-1} \cdot m^{-2}$ [SD, 30.14 $mL \cdot min^{-1} \cdot m^{-2}$]; P = .453) was found. The limits of agreement were −55.69 to 64.87 $mL \cdot min^{-1} \cdot m^{-2}$, and the corresponding mean relative error was 22% (range, −57.3% to +41.7%), expressing a strong scattering of the assumed VO_2 values.

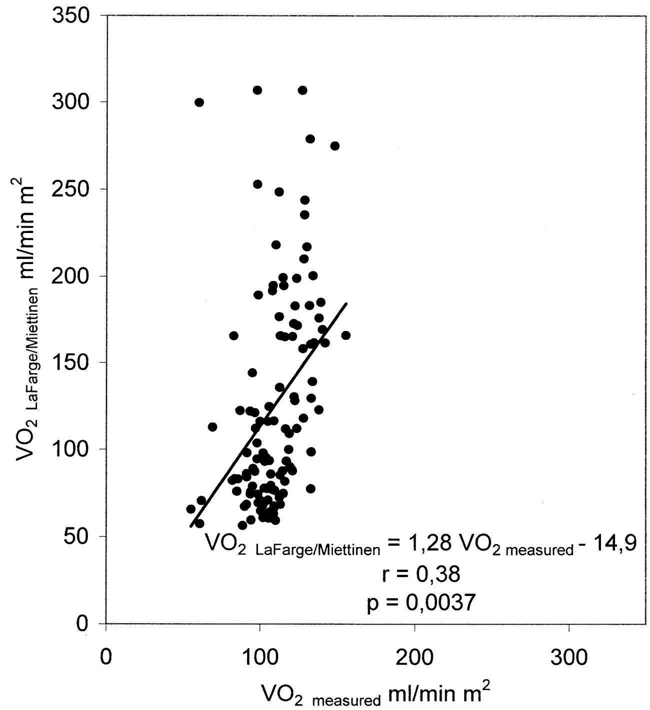

Figure 4. Comparative plot of VO_2 measured versus VO_2 LaFarge-Miettinen and the corresponding correlation coefficient.

Discussion

The results of this study emphasize a poor agreement of measured and assumed VO_2 values. This was already known in adult populations[13] and can now be demonstrated in a pediatric population. The use of standard empiric formulas for the calculation of assumed VO_2 resulted in a systematic error of overestimating VO_2 values. We found a wide spread of the limits of agreement. This indicates an unacceptable difference of the compared methods to determine VO_2. The magnitude of variability and the large errors of greater than 50% that occur in 19.1% (LaFarge-Miettinen) and 38.5% (Krovetz-Goldbloom) are clearly not acceptable for clinical purposes. With the Fick equation, this error in the VO_2 determination will subsequently lead to an error of the same order of magnitude in the calculation of cardiac output. In addition, these wrong values will influence the calculation of systemic or pulmonary vascular resistance, of valve area with the Gorlin formula,[14] and of shunt ratio, as well as the determination of the regurgitant fraction.[15]

In the patient in whom a Fontan-type repair is planned, the accurate determination of vascular resistance values is of even more substantial clinical importance. Looking at the results of the subgroup of patients with Fontan circulation, it can be demonstrated that the errors found in the determination of cardiac output will lead to wrong values of vascular resistance, especially pulmonary vascular resistance.

Calculations of vascular resistance are obtained by relating the mean pressure change across a circuit to the flow across the circuit. An error in the determination of VO_2 as demonstrated (eg, in the Fontan subgroup; mean error, 59% with the Krovetz-Goldbloom formula and 22% with the LaFarge-Miettinen formula) affects the calculation of cardiac output (flow) and pulmonary vascular resistance. In patients with Fontan circulation, it might lead to an overestimation of cardiac output and an underestimation of vascular resistance. This quantity of error obviously cannot be accepted, considering the narrow limits of pulmonary vascular resistance values, planning a further management of a completed Fontan-type circulation.[16,17] A former study showed that in patients with bidirectional Glenn anastomoses, assumed VO_2 led to underestimation of pulmonary vascular resistance to an extent that could significantly influence clinical decision making.[18]

The poor agreement of measured and assumed VO_2 from the formulas might be due to a difference of population and the fact that the patients in this study were undergoing general anesthesia and were mechanically ventilated. However, these formulas were used thus far in sedated patients, as well as in patients under the effects of anesthesia. LaFarge and Miettinen determined their formula in patients between 3 and 40 years of age. Therefore, the formula cannot be applied in younger children. If the Krovetz-Goldbloom formula is used in children less than 3 years of age (n = 28), we found a mean error of 42%. The use of this formula can be questioned, especially in neonates and infants.

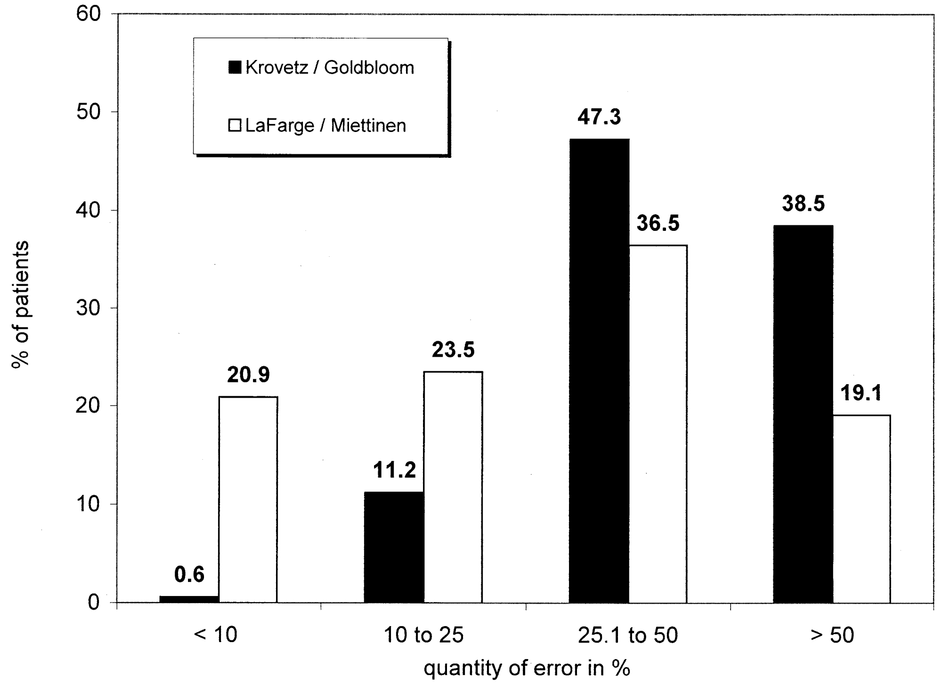

Figure 5. The distribution of the quantity of error related to the use of assumed VO_2 instead of measured VO_2 calculated by dividing measured-assumed VO_2 by the corresponding measured VO_2.

Looking at recently published regression-based estimates, both bias and precision showed similar results.[19]

A comparison of assumed VO_2 with the Krovetz-Goldbloom or the LaFarge-Miettinen formula demonstrates poor agreement with measured VO_2 in a pediatric population undergoing cardiac catheterization under general anesthesia and with mechanical ventilation. Routine use of assumed VO_2 when calculating cardiac output with the Fick equation might frequently result in large errors in the determination of cardiac output and dependent parameters. Therefore, VO_2 should be measured.

References

1. Fick A. Über die Messungen des Blutquantums in den Herzventrikeln. *Sitzungsberichte der Phys–Med. Gesellschaft.* Würzburg: 1870. XVI-XVII.
2. Krovetz LJ, Goldbloom S. Normal standards for cardiovascular data. I. Examination of the validity of cardiac index. *Johns Hopkins Med J.* 1972;130:174-86.
3. LaFarge CG, Miettinen OS. The estimation of oxygen consumption. *Cardiovasc Res.* 1970;4:23-30.
4. Kendrick AH, West J, Papouchado M, et al. Direct Fick cardiac output: are assumed values of oxygen consumption acceptable? *Eur Heart J.* 1988;9:337-42.
5. Berger RMF, van Popellen R, Kruit M, van Vliet A, Witzenburg M, Hess J. Impact of discrepancy between assumed and measured oxygen consumption for the calculation of cardiac output in children during cardiac catheterization. *Neth J Cardiol.* 1992;4:156-60.
6. Mocellin R, Mühlstein V, Bühlmeyer K. Der Sauerstoffverbrauch von herzkranken Säuglingen und Kindern. *Herz.* 1980;5:385-92.
7. Dehmer GJ, Firth BG, Hillis LD. Oxygen consumption in adult patients during cardiac catheterization. *Clin Cardiol.* 1982;5:436-40.
8. Dubois D, Dubois E. Clinical calorimetry. A formula to estimate the approximate surface area if height and weight are known. *Arch Intern Med.* 1916;17:863-71.
9. Tissot S, Delafosse B, Bertrand O, Bouffard Y, Viale JP, Annat G. Clinical validation of the Deltatrac monitoring system in mechanically ventilated patients. *Intensive Care Med.* 1995;21:149-53.
10. Takala J, Keinänen O, Väisänen P, Kari A. Measurements of gas exchange in intensiv care; laboratory and clinical validation of a new device. *Crit Care Med.* 1980;18:638-44.
11. Browning JA, Lindberg SE, Turney SZ, et al. The effects of a fluctuating FiO2 on metabolic measurements in mechanically ventilated patients. *Crit Care Med.* 1982;10:82-5.
12. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurements. *Lancet.* 1986;1:307-10.
13. Wolf A, Pollman MJ, Trindade PT, et al. Use of assumed versus measured oxygen consumption for the determination of cardiac consumption using the Fick principle. *Cathet Cardiovasc Diagn.* 1998;43:372-80.
14. Gorlin R, Gorlin G. Hydraulic formula for calculation of area of stenotic mitral valve, other cardiac valves and central circulatory shunts. *Am Heart J.* 1951;41:1-29.
15. Sandler H, Dodge H, Hay R, et al. Quantitation of valvular insufficiency in man by angiocardiography. *Am Heart J.* 1963;65:501-13.
16. Gentles TL, Mayer JE, Gauvreau K, et al. Fontan operation in five hundred consecutive patients: factors influencing early and late outcome. *J Thorac Cardiovasc Surg.* 1997;114:376-91.
17. Gentles TL, Mayer JE, Gauvreau K, et al. Functional outcome after Fontan operation: factors influencing late outcome. *J Thorac Cardiovasc Surg.* 1997;114:392-403.
18. Shanahan CL, Wilson NJ, Gentles TL, Skinner JR. The influence of measured versus assumed uptake of oxygen in assessing pulmonary vascular resistance in patients with a bidirectional Glenn anastomosis. *Cardiol Young.* 2003;13:137-42.
19. Laitinen PO, Räsänen J. Measured versus predicted oxygen consumption in children with congenital heart disease. *Heart.* 1998;80:601-5.