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ORIGINAL ARTICLE

Comparison of Calculated with Measured Oxygen Consumption in Children Undergoing Cardiac Catheterization

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Abstract Our objective was to compare calculated (LaFarge) with measured oxygen consumption (VO_2) using the AS/3 TM Compact Airway Module M-CAiOVX (Datex-Ohmeda, Helsinki, Finland; AS/3 TM) in children without cardiac shunts in a prospective, observational study. VO_2 was determined at the end of the routine diagnostic and/or interventional catheterization. VO_2 was calculated according to the formula of LaFarge and Miettinen for each child and compared with the measured VO_2. Data were compared using simple regression and Bland Altman analysis. Fifty-two children aged from 0.5 to 16 years (median, 6.9 years) and weighing 3.4 to 59.4 kg (median, 22.9 kg) were investigated. Calculated VO_2 values ranged from 59.0 to 230.8 ml/min, and measured VO_2 values from 62.7 to 282.2 ml/min. Comparison of calculated versus measured VO_2 values revealed a significant correlation ($r = 0.90$, $p < 0.0001$). Bias and precision were 8.9 and 48.3 ml/min, respectively (95% limits of agreement: −39.4 to 57.2 ml/min). Comparison of calculated VO_2 in children older than 3 years ($n = 41$), as restricted to the formula, with measured VO_2, revealed a slightly reduced correlation ($r = 0.86$, $p < 0.0001$). Bias and precision were 10.0 and 52.5 ml/min, respectively (95% limits of agreement: –42.4 to 62.5 ml/min). We conclude that calculation of VO_2 by the LaFarge formula does not provide reliable values compared to measured values. In clinical routine, measured rather than calculated VO_2 values should be used for the estimation of cardiac output and related variables.

Keywords Oxygen consumption · LaFarge formula · Fick's principle · Cardiac catheterization · Children

Cardiac output (CO) measurement is part of the diagnostic evaluation in children with congenital and acquired heart disease undergoing cardiac catheterization [12]. Usually, calculation of CO according to Fick's principle [5] is widely used whenever thermodilution is not applicable. To date, the oxygen consumption (VO_2), needed to apply Fick's principle, is traditionally assumed with the help of empirical formulas, such as the LaFarge formula [9].

The application of cuffed tracheal tubes in children allows reliable sealing of the patients' tracheas for precise spirometry [13]. The availability of compact devices for the measurement of VO_2, as part of anesthesia equipment, permits the assessment of VO_2 in the cardiac catheterization laboratory under clinical routine conditions [7].

The aim of this prospective study was to compare VO_2 values calculated according to LaFarge with directly measured VO_2 in intubated pediatric patients undergoing cardiac catheterization and to analyze their implication for the calculation of CO by means of the Fick's principle.

Materials and Methods

Patients

With ethical review board approval and written parental consent, children aged from birth to 16 years undergoing elective diagnostic or interventional cardiac catheterization

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were included in the study. To allow CO calculation according to Fick's principle, only patients without intra- or extracardiac shunts were included. Patients with interventional occlusion of intracardiac shunts or persistent ductus arteriosus were included at the end of the procedure when persistence of a residual shunt could be excluded by contrast fluoroscopy or echocardiography.

Techniques

VO_2 was calculated according to LaFarge and Miettinen [9] for each child. This estimation of indexed rate of VO_2 was derived from a multivariate analysis of covariance in 879 patients with heart disease, aged from 3 to 40 years. Thereby, VO_2 related to body surface area (BSA) (VO_2/BSA; VO_2 index) is derived from the variables age and heart rate (HR), in two separate formulas for boys and girls (Table 1).

Direct measurement of VO_2 was performed with the AS/3 TM Compact Airway Module M-CAiOVX (Datex-Ohmeda, Helsinki, Finland), a compact module which is an integrated part of the S/5TM anesthesia monitor (Datex-Ohmeda). This combined airway gas and metabolic monitor analyzes CO_2, N_2O, O_2, volatile anesthetic agents, spirometry parameters, and gas exchange while continuously sampling 200 ± 20 ml/min airway gas from the connector (side-stream gas measurement). VO_2 is measured every minute from breath-to-breath oxygen concentration, which is analyzed by a fast differential paramagnetic oxygen analyzer, and spirometry using the so called D-lite flow sensor. The accuracy of VO_2 measurement is ±10% provided that inspiratory oxygen concentration is below 0.65 according to the manufacturer. Measurement is not valid if O_2–N_2O mixtures are used.

Experimental Setup

Cardiac catheterization was performed under general anesthesia with tracheal intubation. Induction of anesthesia (inhalational or intravenous) depended on patient's preference and medical conditions. Anesthesia was maintained with sevoflurane in oxygen/nitrous oxide (1:2) and muscle paralysis was obtained with atracurium. Cuffed tracheal tubes (Microcuff Endotracheal Tube Pediatric oral/nasal Magill [Kimberly-Clark, Zarentem, Belgium] and Lo-Contour Murphy Tracheal Tube oral/nasal [Mallinchrodt Medical, Athlone, Ireland]) were used to reliably seal the airway. Cuff pressure was controlled with an automated cuff tube manometer (Cuff Pressure Control; Tracoe, Neu-Isenburg, Germany) and kept at a maximum of $\leq$20 cm H_2O to avoid tracheal mucosal damage. Effectiveness of tracheal sealing was monitored by routine spirometry. Patients without effective sealing were excluded when expiratory tidal volumes differed from inspiratory tidal volume by more than 6%, which is the accuracy of spirometry as specified by the manufacturer. Pressure-controlled ventilation with standard respirator settings, starting with an inflation pressure of 15 cm H_2O, positive end expiratory pressure (PEEP) of 5 cm H_2O, and age-related respiratory rate, was adapted to achieve normocapnic ventilation during the procedure. Standard anesthesia monitoring consisted of pulsoximetry, electrocardiogram, noninvasive blood pressure measurement, rectal temperature, and relaxometry.

Table 1 Formulas for calculation of VO_2 in girls and boys according to LaFarge and Miettinen [9]

Patients	Formula
Male	VO_2/BSA [ml/min m^2] = 138.1 − 11.49 $\log_e$(age) + 0.378 HR
Female	VO_2/BSA [ml/min m^2] = 138.1 − 17.04 $\log_e$(age) + 0.378 HR

Note: BSA, body surface area as square meters; HR, heart rate as beats per minute. Age in years

VO_2 measurement and mixed venous blood sampling via the femoral vein for the calculation of CO was performed at the end of the routine diagnostic/interventional catheterization and after exclusion of residual cardiac shunts. All measurements were done under steady-state conditions without nitrous oxide and at an inspiratory oxygen concentration of about 30%.

Mixed venous and, if feasible, arterial, blood samples were taken and analyzed for oxygen concentration and hemoglobin value with the OSM3 Hemoximeter (Radiometer, Copenhagen, Denmark). Transcutanous oxygen saturation (S_pO_2) was used as a substitute for arterial oxygen saturation in patients without arterial catheterization. Measured VO_2, respiratory and hemodynamic parameters were recorded in each patient, during steady-state conditions.

Calculations and Statistics

Values for VO_2 and cardiac index (CI) derived from the LaFarge formula were compared with the measured values with simple linear regression and Bland Altman bias analysis [1]. For CO/CI the mean percentage error (2 SD divided by the mean) was calculated. A mean percentage error of <30% was considered to indicate acceptable disagreement between two methods of CO estimation [2].

Given that the LaFarge formula is only applicable to patients older than 3 years, calculations for VO_2 were repeated after exclusion of patients aged <3 years. In patients with a mixed venous oxygen saturation (S_vO_2) measurement of $\leq$85%, CO and CI calculation was performed according to Fick's principle, dividing VO_2 by the

Table 2 Demographic and measured physiological data ($n = 52$)

Demographic data, median (range)	
Male/female, *n*/*n*	25/27
Age, years	6.9 (0.5–16)
Weight, kg	22.9 (3.4–59.4)
Height, cm	120.5 (62–172)
Physiological data (mean ± SD)	
Hemoglobin (g/l)	111.2 ± 12.6
Heart rate (beats/min)	93.2 ± 19.1
Mean noninvasive blood pressure (mm Hg)	61.3 ± 8.6
Temperature (°C)	36.9 ± 0.6
Mixed venous oxygen saturation (%)	81.0 ± 6.7

Table 3 Interventional procedures and diagnoses

Procedure and cardiologic diagnosis	*n*
Occlusion of simple atrial septal defect (1 patient with combined occlusion of patent ductus arteriosus)	20
Occlusion of simple ventricular septal defect	9
Dilation and/or stenting of pulmonary valve/graft/artery and/or branch in complex congenital heart disease	13
Dilation and/or stenting of aortic valve or aortic arch/coarctation	2
Coil occlusion of pathologic pulmonary or coronary vessels	2
Diagnostic heart catheterization in hypertrophic obstructive cardiomyopathy, coarctation, pulmonary hypertension, or complex congenital heart disease	4

arteriovenous oxyen content difference across the pulmonary bed [5].

Demographic patient data, physiological variables, and measured/calculated VO$_2$, CO, and CI values are presented as range (median) and/or mean ± standard deviation, as appropriate.

Results

Fifty-two children (27 girls, 25 boys) aged from 0.5 to 16 years (median 6.9 years) and weighing 3.4 to 59.4 kg (median 22.9 kg) were investigated. Patient characteristics and physiological data are presented in Table 2. Diagnosis and procedures were distributed as reported in Table 3.

Mean measured and calculated VO$_2$ values were 138.0 ± 52.8 and 129.1 ± 41.5 ml/min, respectively. Comparison of calculated with measured VO$_2$ values revealed a significant correlation ($r = 0.90$, $p < 0.0001$) (Fig. 1). However, bias and precision were 8.9 and 48.3 ml/min, respectively (95% limits of agreement: −39.4 to 57.2 ml/min) (Fig. 2). After exclusion of all children younger than 3 years of age ($n = 41$), comparison of values for measured VO$_2$ and calculated VO$_2$ revealed a slightly reduced correlation ($r = 0.86$). Bias and precision were 10.0 and 52.5 ml/min, respectively (95% limits of agreement: −42.5 to 62.5 ml/min) (Table 4).

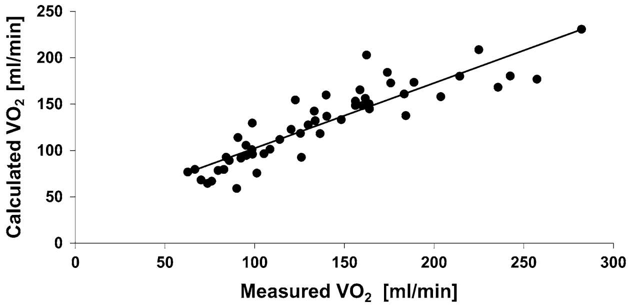

Fig. 1 Linear regression plot of measured and calculated VO$_2$ ($n = 52$, $r = 0.90$, $p < 0.0001$)

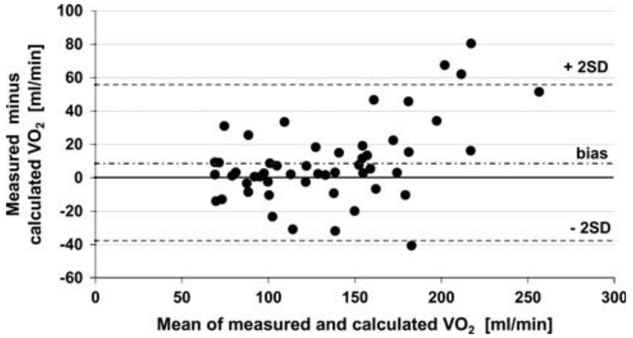

Fig. 2 Bland-Altman plot of measured and calculated VO$_2$ ($n = 52$; bias = 10 ml/min; 95% confidence limits, −42.5 to 62.5 ml/min)

Mean CO and CI derived from measured VO$_2$, in children >3 years of age with mixed venous SO$_2$ below 85% ($n = 27$), were 5.6 ± 2.7 l/min and 5.7 ± 1.7 l/min m^2. The corresponding CO/CI values derived from calculated VO$_2$ were 5.2 ± 2.2 l/min and 5.4 ± 1.7 l/min/m^2. Comparison of CI values from measured VO$_2$ with those derived from calculated VO$_2$ revealed a significant correlation ($r = 0.85$, $p < 0.0001$) (Fig. 3). Bias and precision were 0.26 and 1.85 l/min m^2 (95% limits of agreement: −1.6 to 2.1 l/min m^2) (Fig. 4), with a mean percentage error of 33.5%.

Discussion

The goal of this study was to compare VO$_2$ calculated by the LaFarge formula as commonly used in pediatric cardiology with VO$_2$ measured directly by a routinely applicable monitoring device and to evaluate its implications on derived CO values. The main finding was that VO$_2$ values calculated according to LaFarge differ significantly from measured VO$_2$ values, with an unacceptable mean

Table 4 Calculated and measured VO_2 values presented for all patients ($n = 52$) and for patients ≥3 years of age ($n = 41$)

	VO_2 (all patients, $n = 52$)		VO_2 (patients ≥3 years, $n = 41$)	
	Calculated VO_2	Measured VO_2	Calculated VO_2	Measured VO_2
Mean/SD (ml/min)	129.1/41.5	138.0/52.8	143.4/34.2	153.4/48.7
Median (ml/min)	130.8	131.5	144.9	148.3
Min/Max (ml/min)	59.0–230.8	62.7–282.2	91.7–230.8	84.1–282.2
R/p	0.90/0.0001		0.86/=0.0001	
Bias/precision	8.9/48.3 (ml/min)		10.0/52.5 (ml/min)	

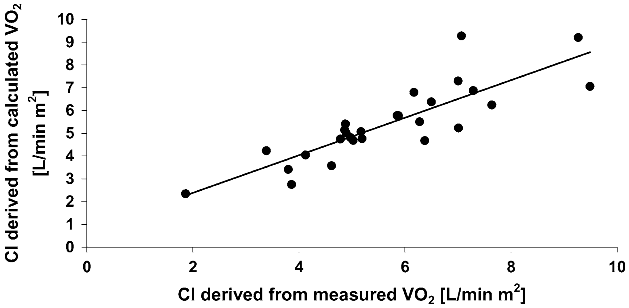

Fig. 3 Linear regression plot of cardiac index (CI) calculated according to Fick's principle: CI derived from measured and calculated VO_2 values in children older than 3 years with a mixed venous oxygen saturation ≤85% ($n = 27$, $r = 0.85$, $p < 0.0001$)

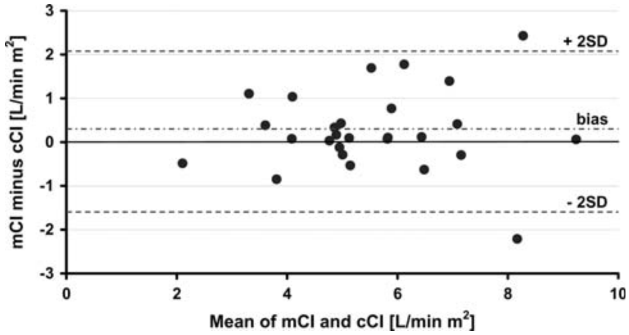

Fig. 4 Bland-Altman plot of cardiac index (CI) calculated according to Fick's principle: CI derived from measured (mCI) vs. calculated (cCI) VO_2 values in children older than 3 years with a mixed venous oxygen saturation <85% ($n = 27$; bias = 0.26 l/min m^2; 95% confidence limits, −1.6 to 2.1 l/min m^2)

percentage error of >30% for the calculation of CI values. The disagreement between calculated and measured VO_2 can be explained by problems inherent to any calculated method in principle: the only physiological parameter referring to the physiological state of the patient is heart rate, whereas depth of anesthesia, temperature, muscle tone, and other metabolic determinants are not considered when using the formula. The exclusion of children younger than 3 years did not show any improvement, so that the age range of our study population cannot explain the conflicting results of the two methods.

In the past, different studies comparing measured and assumed VO_2 in adult patients, using direct VO_2 measurement by collection of expiratory gas into a bag via mouthpiece and mass spectrometry of oxygen content, showed large unpredictable errors when using calculated values [8, 14]. Adult patients have generally not been sedated, whereas the reference formula was derived in mildly sedated patients, sometimes dozing but not unarousable [9]. Dehmer et al. found lower oxygen consumption in mildly sedated patients compared to unsedated patients, using Fick's principle to calculate VO_2 employing thermodilution CO values [3]. While studies in adult patients apply the LaFarge formula to an age range that differs from the original reference study group, thus making their results questionable, there have been few works in children [4, 11] supporting the unreliability of a VO_2 estimation calculated according to LaFarge. The application of different methods of VO_2 measurement by different study groups renders a systematic error depending on one monitoring device rather unlikely. The application of other formulas and estimated values from metabolic studies has led to similar disagreements with measured VO_2, in pediatric as well as adult patients [4, 8, 10, 11, 14].

Using Fick's principle, the disagreement of measured and calculated VO_2 is for arithmetic reasons conducted to CO and CI values when applying Fick's principle as shown in Fig. 4. Higher S_vO_2 values, leading to a small difference in arteriovenous oxygen content, result in a higher CO for a given VO_2 value. It is known that small inaccuracies in determination of mixed venous oxygen saturation from blood sampling and analysis may result in considerable differences when applying Fick's principle, particularly if the CO is high [6, 8]. Consequently, we excluded children with mixed venous SO_2 >85% at the time of VO_2 estimation to minimize this inaccuracy. Calculated CI values were still relatively high in some of our patients. This is likely because of the hyperdynamic circulatory state after occlusion of a pre-existing shunt, as the left and, especially, the right ventricle had been adapted to a higher output when atrial or ventricular septal defects were patent.

Based on our study results, VO_2 in cardiac patients should be measured rather than estimated by formula to obtain accurate calculated hemodynamic parameters. The technique of VO_2 measurement used in our study included tracheally intubated patients with a reliably sealed airway, which is not used at all cardiac catheterization facilities and, thus, is a limitation of this technique. As an alternative, fitting and sealing masks would allow application in nonsedated or only lightly sedated patients. But this is limited by patient compliance, which might not be achieved in children. A specific limitation of the device used in our study is that the fractional inspired oxygen concentration must be lower than 0.65, which would possibly exclude its application in critically ill patients.

The ease of applicability and the low cost of logistics and material, as opposed to the formerly used collection of the entire expiratory gas, support the recommendation to use measured VO_2 values in clinical routine. The module is small and light and requires, as an integrated module, no extra space at the anesthesia workstation. Education of staff concerning the use of cuff manometry and spirometry as well as the knowledge of contraindications such as high inspiratory oxygen concentration (≥ 0.65) and use of N_2O or air leakage (expiratory tidal volume differing from inspiratory tidal volume by more than 6%) is essential for exact VO_2 measurements. Reading of the VO_2 requires no further special skills such as the use of any routine monitor, so that inter- or intraobserver variability is not to be expected under steady-state conditions. The recording of VO_2 is not time-consuming but, rather, saves the time otherwise needed for calculations according to LaFarge or other formulas, with all their inherent inaccuracies. If cuffed tubes and spirometry are already used routinely, there are no further costs for single-use items, for example, the tubing for sampling is identical to the spirometry tubing, thus leaving the purchase of the module itself as the only inevitable expenditure.

In conclusion, estimation of VO_2 calculated by the LaFarge formula does not provide reliable values compared to measured values. In clinical practice measured rather than estimated VO_2 should be used for calculation of CO and related variables.

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