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Clinical validation of cardiac output measurements using femoral artery thermodilution with direct Fick in ventilated children and infants

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Abstract *Objective*: To validate clinically cardiac output (CO) measurements using femoral artery thermodilution in ventilated children and infants by comparison with CO estimated from the Fick equation via a metabolic monitor.
Design: Prospective, comparison study.
Setting: Paediatric intensive care unit of a university hospital.
Patients: 24 ventilated infants and children, aged 0.3 to 175 months (median age 19 months).
Interventions: Oxygen consumption measurements were made and averaged over a 5-min period, at the end of which arterial and mixed venous blood samples were taken and oxygen saturations measured by co-oximetry, with CO being calculated using the Fick equation. Over this 5-min period, five sets of femoral arterial thermodilution (FATD) measurements were made and averaged. One comparison of CO values was made per patient.
Results: Mean Fick CO was 2.55 l/min (range 0.24 to 8.71 l/min) and mean FATD CO was 2.51 l/min (range 0.28–7.96 l/min). The mean bias was 0.03 l/min (95% confidence interval –0.07 to 0.14 l/min), with limits of agreement of –0.45 to 0.52 l/min. When indexed to body surface area, the mean Fick cardiac index became 3.51 l/min per m^2 (1.52–6.98 l/min per m^2) and mean FATD 3.49 l/min per m^2 (1.74–6.84 l/min per m^2). The mean bias was 0.02 l/min per m^2 (95% confidence interval –0.11 to 0.15 l/min per m^2) with limits of agreement of –0.57 to 0.61 l/min per m^2. The mean FATD coefficient of variation was 5.8% (SEM 0.5%).
Conclusions: FATD compares favourably with Fick derived CO estimates in infants and children and may represent an advance in haemodynamic monitoring of critically ill children.

Key words Thermodilution · Fick principle · Cardiac output · Infants · Children

Introduction

Finding a reliable bedside technique for measurement of cardiac output (CO) in the paediatric population remains elusive, especially in those weighing less than 10 kg. A variety of methods are available [1, 2], but most have limitations when used in the intensive care unit (ICU) environment, such as technical constraints, cost and variability, along with the difficulties of obtaining and the complications of central vascular access in very young patients [3]. As a result, in the United Kingdom, invasive CO monitoring is not commonly employed in the paediatric ICU. In a recent survey of 24 paediatric ICUs containing more than four beds, only one-third had access to thermodilution (TD) for CO measurement, with only 40 pulmonary artery catheters being used in the year surveyed [4]. With recent publications questioning the benefits of pulmonary artery cath-

Table 1 Patient characteristics (*BSA* body surface area, *Db* dobutamine, *D* dopamine, *A* adrenaline, *NA* noradrenaline, *VSD* ventricular septal defect, *ASD* atrial septal defect, *TAPVD* total anomalous pulmonary venous drainage, *RVOTO* right ventricular outflow tract obstruction, *AVSD* atrioventricular septal defect, *PDA* patent ductus arteriosus, *TOF* tetralogy of Fallot, *ARDS* acute respiratory distress syndrome

Patient	Age (months)	BSA (m^2)	Weight (kg)	Inotropes (μg/kg per min)	$VO_{2measured}$ (ml/min per m^2)	Mean CI (l/min per m^2)	Diagnoses
1	0.3	0.16	2.5	Db 5	72.5	1.63	Truncus arteriosus repair
2	3	0.19	2.6	nil	103.2	1.91	VSD / ASD repair
3	0.5	0.20	3.0	D 4, Db 5	116.0	1.77	TAPVD repair
4	1	0.21	3.0	D 3, Db 5	106.2	2.51	Arterial switch
5	1	0.21	3.2	nil	107.2	2.37	VSD, RVOTO repair
6	4	0.28	4.6	D 3	156.8	2.18	AVSD repair
7	5	0.28	5	nil	151.8	3.81	VSD repair
8	5	0.29	5	nil	204.5	3.37	VSD repair
9	4	0.29	5.5	nil	205.2	3.10	VSD / PDA repair
10	8	0.32	6.3	D 4	115.6	2.45	TOF repair
11	7	0.36	7	nil	213.1	3.47	TOF repair
12	29	0.41	10.3	nil	253.7	5.20	Ross procedure
13	9	0.42	9.2	D 10	172.6	2.31	Rastelli procedure
14	31	0.49	11	D 3	187.6	4.02	AVSD repair
15	40	0.61	13	Db 5	204.9	3.72	VSD repair
16	95	0.81	20	nil	158.0	6.66	VSD repair
17	73	0.94	22	D 15, A 0.75, NA 0.2	202.1	3.87	Staphylococcal sepsis
18	115	0.94	28	nil	151.1	3.77	Ross procedure
19	94	0.98	27	nil	148.0	2.60	Ross procedure
20	48	1.02	34	nil	154.9	6.65	nephrotic synd / ARDS
21	135	1.22	36	nil	166.4	3.47	Ross procedure
22	133	1.28	37	nil	148.4	3.19	Ross procedure
23	172	1.50	50	Db 10	166.7	5.56	cardiomyopathy / ARDS
24	175	1.66	60	D 3, NA 0.33	198.8	4.36	Staphylococcal sepsis

eterisation [5], usage may become even more infrequent in paediatrics.

The purpose of this study was to validate in ventilated patients a relatively new innovation in CO measurement in paediatrics – namely, femoral artery thermodilution (FATD). This technique compares favourably with pulmonary artery thermodilution (PATD) in older children [6] but has yet to be validated over a wider range of age, weight and cardiac indices. We chose to use CO measurements using the Fick principle via indirect calorimetry using a monitor with constant internal flow [7, 8] as our "gold-standard" because of the 10–20% documented variation with PA TD [9, 10], along with the difficulties in PATD catheter placement in the very young.

Patients and methods

Patients

The study protocol was approved by the Guy's Hospital Research Ethics Committee, and written informed consent obtained from the patients' parents or legal guardians.

Twenty-four ventilated patients were studied, median age 19 months (range 0.3–175 months), median weight 9.8 kg (range 2.5–60 kg) and median body surface area 0.42 m^2 (range 0.16–1.66 m^2). Diagnoses and inotropic support are outlined in Table 1. All patients were sedated with morphine (10–40 μg/kg per h) and paralysed with vecuronium (50–100 μg/kg per h). All but four patients had a surgically placed single lumen pulmonary artery catheter; in patients 17, 20, 23 and 24, 5.5 Fr pulmonary artery catheters (Abbott Laboratories, North Chicago, US) were inserted via the left subclavian vein, with correct placement confirmed by chest roentgenogram. Absence of intracardiac shunting was confirmed by colour Doppler echocardiography.

Mechanical ventilation was volume controlled (10–15 ml/kg tidal volumes) using Servo 900C ventilators (Siemans-Elema Systems, Solna, Sweden). No patient required a fractional inspired oxygen (FIO_2) greater than 0.50.

Protocol

One set of FATD and oxygen consumption (VO_2) measurements were made per patient, when they were haemodynamically stable and when postcardiac bypass rewarming was complete, defined as a core-peripheral temperature gap of ≤ 1 °C.

Measurement VO_2 and calculation of CO

VO_2 was measured by indirect calorimetry using the Deltatrac 11 Metabolic Monitor (Datex, Helsinki, Finland). Uncuffed nasotracheal tubes were used and were substituted for a cuffed tube of the same size if an air leak of > 5% was present, defined as (inspiratory volume – expiratory volume) × 100/inspiratory volume. There were no episodes of postextubation stridor. The machine was calibrated prior to measurement on each patient in accordance with the manufacturer's instructions.

VO_2 was measured each minute for 5 consecutive min (while the FATD measurements were being made) and then averaged. At the end of this period, arterial and mixed venous blood samples were taken for calculation of their respective oxygen contents, with oxygen saturations being measured by co-oximetry (682 Co-oximeter, Instrumentation Laboratory).
CO was calculated from the Fick equation:

$CO = VO_2/(CaO_2–CvO_2)$

where $CaO_2 = (1.36 \times Hb \times SaO_2) + (PaO_2 \times 0.003)$
and $CvO_2 = (1.36 \times Hb \times SvO_2) + (PvO_2 \times 0.003)$.

Hb: haemoglobin concentration (g/l), CaO_2, CvO_2: arterial and mixed venous oxygen contents (ml/l), SaO_2, SvO_2: arterial and mixed venous oxygen saturations, and PaO_2, PvO_2: partial pressure of dissolved arterial and mixed venous oxygen (torr).

FATD

A 1.3-Fr thermistor (COLD Z-021, Pulsion Medical Systems, Munich, Germany) was introduced into the femoral artery via a 22G cannula equipped with a haemostatic valve. The line was kept patent by infusion of heparinised saline (1 unit/ml) at 1 ml/h via a side arm. Five consecutive FATD measurements were made using central venous injectates of cold (less than 10 °C) 5% dextrose of appropriate volume for patients' weights (1.5 ml + 0.15 ml/kg). CO was calculated by the Stewart-Hamilton method. There were no line-related complications.

Statistical methods

To quantify the degree of agreement between the two techniques, the mean bias (with 95% confidence interval) and limits of agreement (mean bias ± 1.96 × standard deviation of the differences) were calculated in the manner outlined by Bland and Altman [11]. Analysis of linear regression was also performed for historical completeness. Repeatability of COLD CO measurement was quantified using the coefficient of variation [12].

Results

The mean Fick CO was 2.55 l/min (range 0.24–8.71 l/min), and mean FATD CO was 2.51 l/min (range 0.28–7.96 l/min). Fick-derived measurements were, on average, slightly higher, with a mean bias of 0.03 l/min (95% confidence interval –0.07 to 0.14 l/min), and limits of agreement –0.45 to 0.52 l/min. The mean FATD CO coefficient of variation was 5.8% (SEM 0.5%). The regression equation for these variables was: $y = 1.0494x–0.0847$, $r^2 = 0.9921$, $p < 0.0001$ (see Fig. 1).

When indexed to body surface area, mean Fick cardiac index (CI) was 3.51 l/min per m^2, (range 1.52–6.98 l/min per m^2), and FATD CI was 3.49 l/min per m^2 (range 1.74–6.84 l/min per m^2), mean bias 0.02 l/min per m^2 (95% confidence interval –0.11 to 0.15) with limits of agreement –0.57 to 0.61 l/min per m^2.

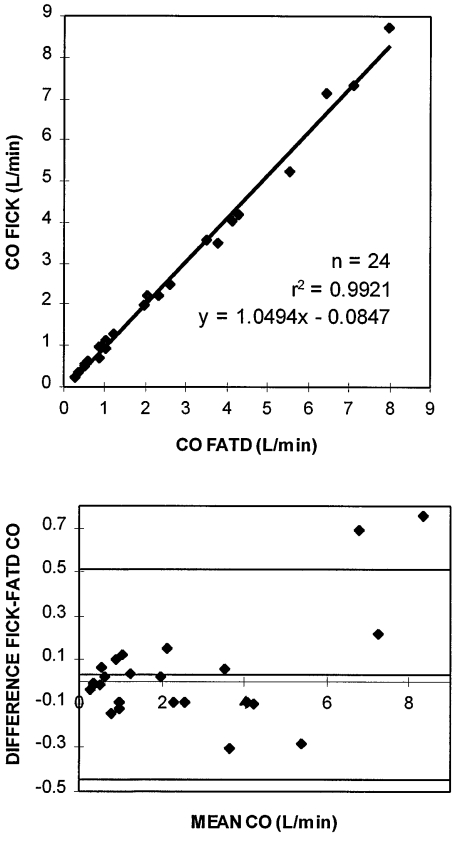

Fig. 1 **a** Linear regression diagram of Fick-derived CO versus femoral artery thermodilution *FATD* CO for all patients. **b** Bland-Altman plot showing mean bias (0.03 l/min) and limits of agreement.(–0.45 to 0.52 l/min) for Fick-derived and FATD CO. Note how the scatter of results increases as CO increases

A subgroup analysis was performed on 19 patients less than 30 kg in weight. For this group, the mean Fick CO was 1.56 l/min (range 0.24–5.25 l/min), with a mean FATD CO of 1.60 l/min (range 0.28–5.54 l/min). Here, Fick-derived measurements were lower with a mean bias of –0.03 l/min (95% confidence interval –0.09 to 0.03 l/min), and limits of agreement –0.28 to 0.21 l/min. The mean FATD CO coefficient of variation was 5.7% (SEM 0.5%). The regression equation for these variables was $y = 0.9531x + 0.0416$, $r^2 = 0.994$, $p < 0.0001$ (see Fig. 2).

Discussion

To our knowledge, this is the first study validating femoral artery/transpulmonary thermodilution in the paediatric population over such a wide range of weight, age and cardiac output. Two previous studies have compared Fick-derived CO with PATD in infants and children [13, 14]. Our results compare favourably with those

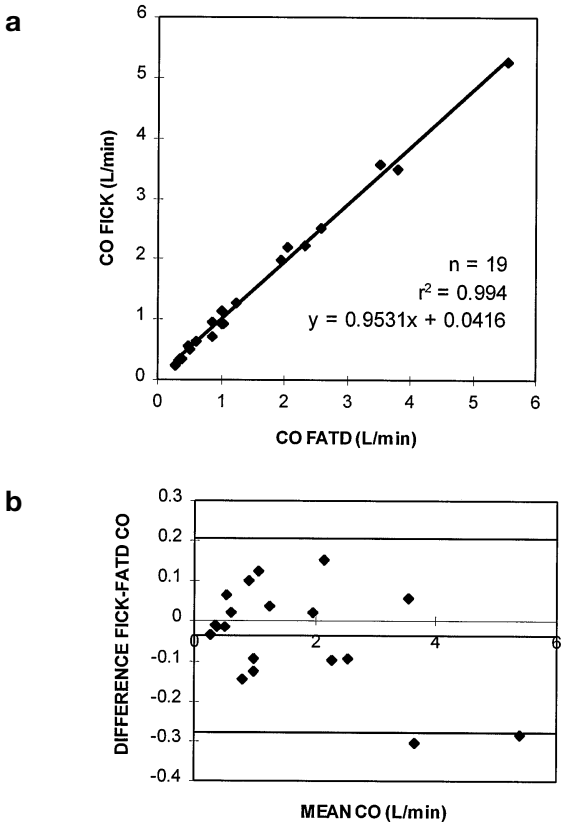

Fig. 2 a Linear regression diagram of Fick-derived CO versus femoral artery thermodilution *FATD* CO for patients weighing < 30 kg. **b** Bland-Altman plot showing mean bias (–0.03 l/min) and limits of agreement.(–0.28 to 0.21 l/min) for Fick-derived and FATD CO in patients < 30 kg

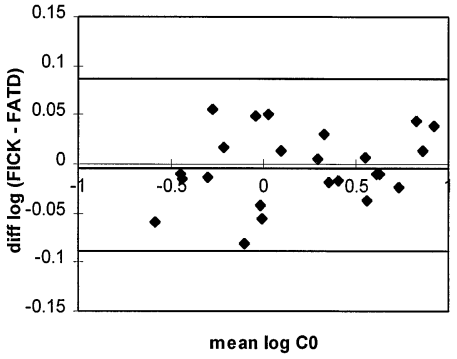

Fig. 3 Log transformation of data from Fig. 1 b. The limits of agreement are –0.07496 to 0.06931, with corresponding antilog values of 0.8415 and 1.1730. Thus, the FATD measurement may differ from the Fick measurement by –16% to +17% for 95% of the recordings

obtained by Chang et al. [13] (CI mean bias –0.01 ± 1.08 l/min per m^2 vs 0.02 ± 0.59 l/min per m^2) and Wippermann et al. [14] (CO mean bias –0.05 ± 0.32 l/min vs 0.03 ± 0.48 l/min).

It can be seen from Fig. 1 that the scatter of differences increases as CO increases. Log transforming these data (Fig. 3) abolishes this scatter, which implies that the degree of difference is proportional to the CO. Back transforming the logarithmic limits of agreement [11] reveals that, for 95% of measurements FATD CO will be between –16% and + 17% of Fick CO.

Sources of error in calculation of CO from the Fick principle were kept to a minimum by avoiding air leaks through the use of cuffed endotracheal tubes where necessary [15], avoidance of VO_2 measurement at higher FIO_2 levels [16, 17] and use of co-oximetry to measure oxygen saturations. It can be assumed that the mean bias and precision for the Deltatrac monitor over the range of VO_2 studied will be –3.2% (± 23%) [8].

It would appear that FATD using the COLD system offers several advantages over traditional PATD:

1. *Ease of insertion*. The femoral artery is a readily accessible site in all age groups. We have used this method in patients weighing as little as 2.0 kg without access problems. Also, because of the femoral approach, the problems associated with pulmonary artery cannulation via a large neck/chest vessel do not apply [18, 19].
2. *Low complication rate*. Although no episodes of vascular compromise were noted, this must be interpreted with caution owing to a relatively small sample size and the fact that no catheters were left in situ for longer than 36 h. We would advise meticulous attention to limb perfusion with monitoring of pedal pulses and limb temperature.
3. *Reproducibility.* A mean coefficient of variation of 5.8% compares favourably with that obtained in most traditional PATD studies [20, 21]. No measurements were excluded in this calculation in comparison to the common clinical practice of excluding PATD measurements that fall outside of 10% of the mean. Also, because of the longer mean transit time, there is no need to time injections with the ventilator cycle.
4. *Less potential for fluid overload*. The volume of the injectate is governed by the patient's weight – for example, a 5 kg infant would require an injectate volume of 2.3 ml.

The limitations of this measuring technique are similar to those of PATD – namely, the presence of left-to-right or right-to-left shunts, severe valvular regurgitation, arrhythmias and variations in heart rate. Although rapid injection of cold saline can transiently slow the heart rate by more than 10% in approximately 20% of deter-

minations [22], the error in estimation of CO by FATD can be expected to be less than that of PATD owing to the longer transit time.

Despite these limitations, we believe the ability to measure CO accurately in all paediatric age groups via a relatively simple bedside technique represents a significant advance in haemodynamic monitoring of the critically ill child.

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