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Extracorporeal Arteriovenous Ultrasound Measurement of Cardiac Output in Small Children

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ABSTRACT

Background: Technology for cardiac output (CO) and blood volume measurements has been developed based on blood dilution with a small bolus of physiologic body temperature saline, which, after transcardiopulmonary mixing, is detected with ultrasound sensors attached to an extracorporeal arteriovenous loop using existing central venous and peripheral arterial catheters. This study aims to compare the precision and agreement of this technology to measure cardiac output with a reference method, a perivascular flow probe placed around the aorta, in young children. The null hypothesis is that the methods are equivalent in precision, and there is no bias in the cardiac output measurements.

Methods: Forty-three children scheduled for cardiac surgery were included in this prospective single-center comparison study. After corrective cardiac surgery, five consecutive repeated cardiac output measurements were performed simultaneously by both methods.

Results: A total of 215 cardiac output measurements were compared in 43 children. The mean age of the children was 354 days (range, 30 to 1,303 days), and the mean weight was 7.1 kg (range, 2.7 to 13.6 kg). The precision assessed as two times the coefficient of error was 3.6% for the ultrasound method and 5.0% for the flow probe. Bias (mean $CO_{ultrasound}$ 1.28 l/min – mean $CO_{flow\ probe}$ 1.20 l/min) was 0.08 l/min, limits of agreement was ±0.32 l/min, and the percentage error was 26.6%.

Conclusions: The technology to measure cardiac output with ultrasound detection of blood dilution after a bolus injection of saline yields comparable precision as cardiac output measurements by a periaortic flow probe. The difference in accuracy in the measured cardiac output between the methods can be explained by the coronary blood flow, which is excluded in the cardiac output measurements by the periaortic flow probe.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- To date, there are not clinically practical, accurate, and precise noninvasive methods for measuring cardiac output in small children

What This Article Tells Us That Is New

- This study describes a noninvasive method by which ultrasound can be used in small children to determine cardiac output with good precision
- After surgery in 43 small children for repair of atrial or ventricular septal defects, cardiac output measurements performed using saline bolus injections and ultrasound detection of the expected blood dilution showed similar precision for measuring cardiac output as a cardiac outputs measured using periaortic flow probe

The clinical examination of a severely hemodynamically unstable child has obvious limitations and may give unreliable estimates of the overall hemodynamic status. The cause of arterial desaturation, degree of hypovolemia, and systemic hypoperfusion are parameters that may be particular difficult to evaluate because of compensatory mechanisms.[1–5] Easily adapted and safe monitoring devices with good reliability and reproducibility are needed to address these parameters, especially in children.[6–8]

An available invasive cardiac output (CO) measuring method, such as thermodilution technique, although applicable for adults, has size restrictions for use in young children and may cause a substantial risk of complications (bleeding, thrombosis, embolism, and arrythmia). Noninvasive methods are less accurate and precise in measuring CO in small children (electrical bioimpedance, carbon dioxide rebreathing, and Doppler methods), require high level of training (echocardiography), or are clinically impractical and time consuming (magnetic resonance imaging).[9,10]

A technology that uses ultrasound detection of blood dilution by means of a saline bolus injection and an extracorporeal arteriovenous loop between existing central venous and peripheral arterial lines has been developed for hemodynamic assessment in young children and neonates.[11] It is minimally invasive, because it uses existing catheters and does not require additional invasive procedures. It measures total CO, including coronary blood flow.

The hypothesis of the study is that blood dilution detected by ultrasound is comparable with the reference method, perivascular flow probe around aorta to determine

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cardiac output. The aim of the study was to estimate the precision of this technology in young children compared with CO measured by a perivascular flow probe around the aorta (reference method) through five simultaneously replicated CO measurements and to assess the agreement by quantifying the difference (bias) between the two methods.

Materials and Methods

Study Design and Subjects

Forty-seven children undergoing elective cardiac surgery for correction of atrial septal defect and/or ventricular septal defect were enrolled in the study. Inclusion criteria were informed written parental consent, weight of less than 15 kg, and atrial septal and/or ventricular septal defects. Because lack of repeatability of the CO measurement can interfere with the comparison of the two methods, it was important that the CO measurement and the stroke volume were fairly constant during the measurement. Exclusion criteria were, therefore, shunts (undiagnosed extracardiac or significant residual shunt after the surgical correction), perioperative arrythmias (supraventricular, nodal tachycardia, and atrioventricular heart block), and/or significant valvular regurgitations (aortic, mitral, tricuspid, and pulmonary valvular leaks). This study was approved and registered by the Ethics Committee of Lund University, Lund, Sweden (Dnr 2013636).

Cardiac Output Measurements

Calculation of CO by Use of Saline Blood Dilution Detected by Ultrasound Sensors (CO_{UD}). The technology is based on the premise that the ultrasound velocity of blood changes linearly with the level of blood dilution caused by injection of a specified bolus volume of body-temperature isotonic saline. The ultrasound velocity in blood is 1,560 to 1,585 m/s and decreases toward the ultrasound velocity of saline (1,530 m/s) after a bolus injection of saline. The device, developed by Transonic Systems Inc. (USA), uses an extracorporeal arteriovenous loop connected between existing arterial and central venous lines. The loop is connected to an external roller pump, which maintains a stable blood flow in the loop of 10 to 12 ml/min. The loop contains specific venous and arterial segments to which external ultrasound sensors fit. The sensors measure the ultrasound velocity and the blood flow at the out-flow and in-flow parts of the loop circuit.

A measurement session begins by entering the patient's weight, length, arterial blood pressure, central venous pressure, and heart rate into the device. The connection stopcock to the out- and in-flow segments of the arteriovenous loop, primed with 5 ml of body-temperature, heparinized isotonic saline, is opened. The roller pump starts, and a small amount of body-temperature physiologic isotonic saline (0.5 to 1.0 ml/kg) is injected at the out-flow segment of the loop on the venous side before the venous ultrasound sensor. The saline is warmed to 37°C body temperature by a bag warmer that is connected to the device. The volume and time of the injected saline is determined by the venous ultrasound sensor. The saline is completely mixed as the blood passes through the cardiopulmonary circulation and gives rise to a homogenous blood dilution on the arterial side. The final blood dilution that occurs in the systemic arterial circulation is detected by the arterial ultrasound sensor at the arterial in-flow segment of the loop, and an ultrasound velocity curve is generated (fig. 1).

Because the technology records the ultrasound velocity simultaneously at both the out-flow and in-flow segments of the loop at a constant blood flow rate, not only can the area under the curve be analyzed, but the time of occurrence and form of the dilution curve after it passes through the lungs and heart can be used to calculate total end-diastolic cardiac volume, central blood volume, and active blood volume and to determine and detect cardiac shunts.[12–17] CO is calculated by analyzing the area under curve based on the Stewart–Hamilton indicator dilution principle.[18–20]

CO Measurement with Perivascular Flow Probes (CO_{PVFP}). AU-series confidence perivascular flow probes (Transonic Systems Inc.) were used in this study. The flow probe is custom-designed to fit around vessels to measure blood flow in real time by ultrasound transit-time technology. Transit-time technology uses four crystals and wide-beam illumination to send ultrasonic signals back and forth across the vessel, alternately intersecting the blood in upstream and downstream directions. The flowmeter derives an accurate measure of the "transit time" it takes for the wave of ultrasound to travel from one transducer to the other. The difference between the upstream and downstream integrated transit times is a measure of true volume flow, not velocity.

The flow probes are available in different diameter sizes (8 to 24 mm) and can be used multiple times because they can undergo standard sterilization. The probes come ready to use and calibrated from the manufacturer with a certified length of use for more than 1 yr.

In our study, the flow probe was applied to the aorta approximately 1 cm distal to the origin of the coronary arteries (fig. 2). The flow probe was then connected to an Optima dual-channel HT363 Flow-QC meter (Transonic Systems Inc.). AureFlo diagnostic software (Transonic Systems Inc.) was used to visualize a good signal of pulsating aortic blood flow waveform and record CO. Transit-time ultrasound perivascular flow probes are considered the standard reference method for cardiac output estimation and have been verified in number of studies.[21,22]

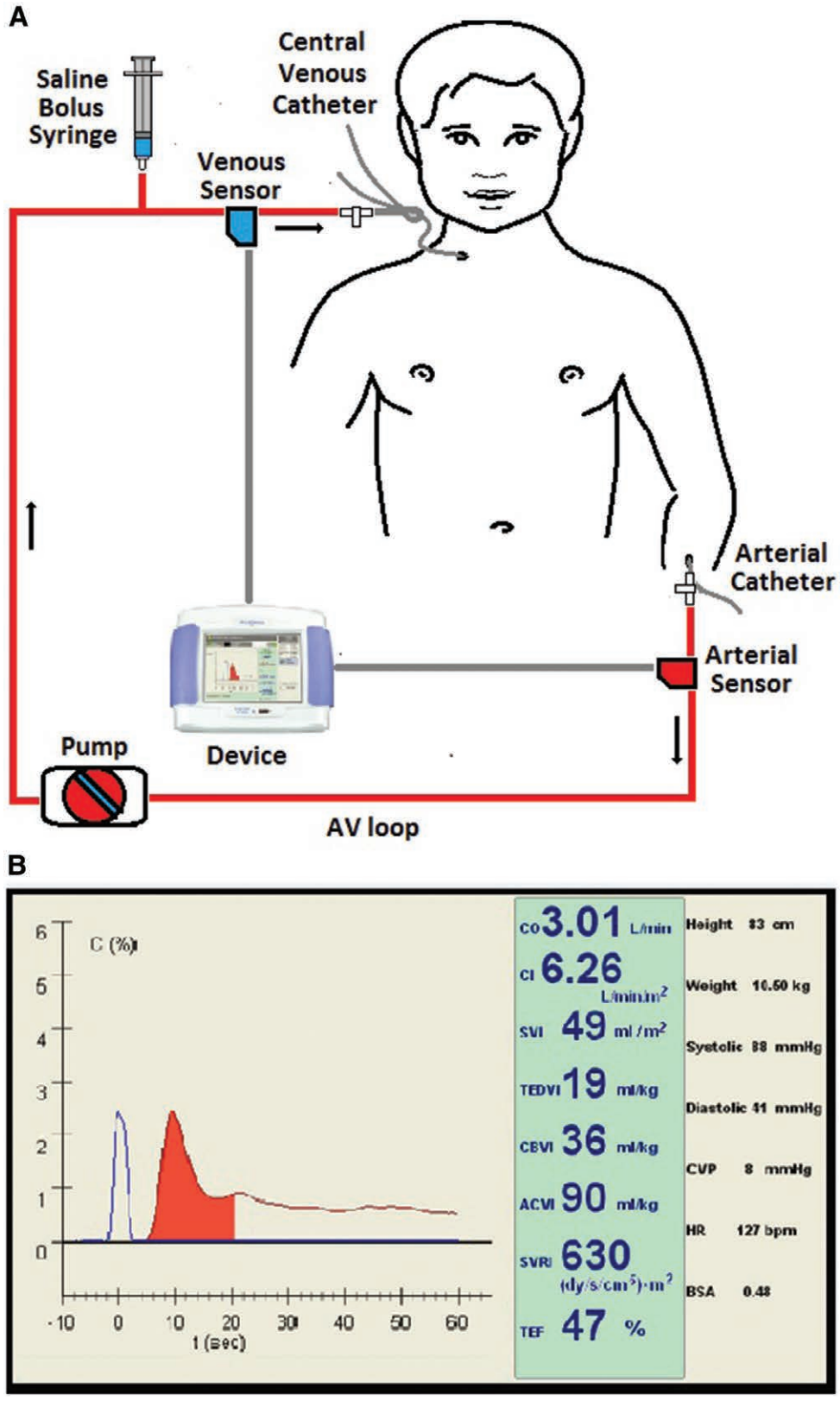

Fig. 1. Schematics (*A*) and monitor display (*B*) of the tested cardiac output (CO) measurement device. The y axis C (%) represents the percentage concentration of saline in the arterial blood while the x axis is time (seconds). ACVI, active circulation volume index; BSA, body surface area; CBVI, central blood volume index; CI, cardiac index; CVP, central venous pressure; HR, heart rate; SVI, stroke volume index; SVRI, systemic vascular resistance index; TEDVI, total end diastolic volume index; TEF, total ejection fraction.

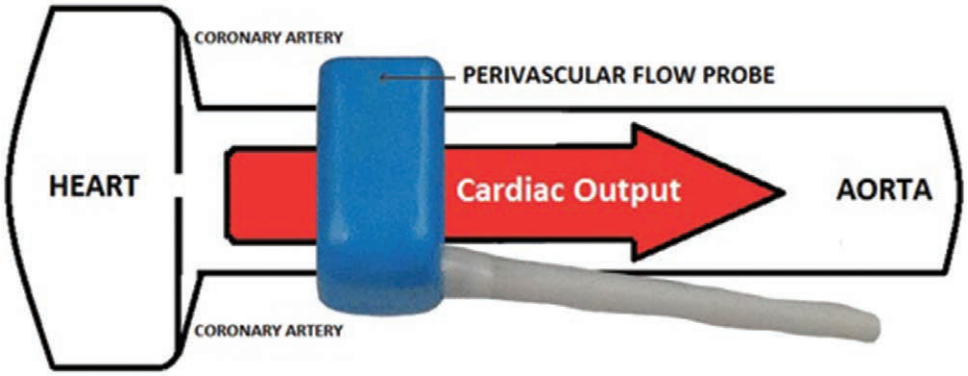

Fig. 2. Placement of the perivascular flow probe around aorta.

Experimental Protocol

Anesthesia was induced using fentanyl (5 μg/kg) and penthothal (5 mg/kg) and maintained with isoflurane (0.5 to 1.0%). Pancuronium (0.2 mg/kg) was given to facilitate intubation with a cuffed endotracheal tube. As is routine in children undergoing cardiac surgery, all subjects had a peripheral arterial catheter placed in the radial artery and a central venous catheter placed in the right internal jugular vein. The catheters were connected to the arteriovenous loop of the CO device and were primed with heparinized (2 units/ml) 37°C physiologic saline. Ultrasound sensors were placed on the venous and arterial segments of the arteriovenous loop before surgery. After surgical correction and weaning from cardiopulmonary bypass, transesophageal echocardiography was performed to exclude residual intracardiac shunts or valve regurgitations. When a stable sinus rhythm and normal body temperature were achieved, the surgeons applied the perivascular flow probe around the aorta, and measurements were initiated. Each measurement session consisted of five consecutively repeated CO measurements with injections of body temperature physiologic saline boluses and, simultaneously, five readings of aortic blood flow measured with the transit-time ultrasound periaortic flow probe.

Statistical Analysis

Statistical analysis was performed using Statistica version 12 (Statsoft, USA). No statistical power calculation was conducted before the study, because the bias and SD of the bias between the two methods were unknown, and the CI for the 95% limits of agreement was not possible to estimate. The sample size was based on previous experience with this design. All data are expressed as mean ± SD unless indicated otherwise.

The degree of variation of each technique was presented as the coefficient of error (CE) of average repeated measurements, calculated as ratio of the coefficient of variation (CV) divided with the square root of the number (n) of repeated measurements ($CE = CV/\sqrt{n}$). Precision of a technique is considered to be two times the coefficient of error as suggested by Cecconi *et al.*[23]

Bland–Altman analysis was used to estimate bias between the different techniques while accounting for the repeated measurements within each individual.[24] The mean difference (bias) between cardiac output with saline dilution and ultrasound detection (CO_{UD}) minus cardiac output with perivascular flow probe around aorta (CO_{PVFP}) was calculated and plotted against the average of the comparison ($CO_{UD} + CO_{PVFP}$)/2. The 95% limits of agreement were calculated as mean bias ± 1.96 × SD (SD of the bias). Limit of agreement analysis was performed to determine whether the two methods agreed sufficiently with each other so that one could replace the other. The 95% CI of the bias and the limits of agreement were determined after testing for normal distribution using Levene's test.[25]

According to Critchley and Critchley,[26] the percentage error (PE) was calculated as 1.96 × SD of the bias/mean cardiac output of the reference method × 100%.

$$PE = \frac{1.96 \times SDbias}{mean\,CO\,PVFP} \times (100\%)$$

Results

A total of 47 children were enrolled in the study. Four children were excluded before surgery: one because of hemodynamic instability; another because an ultrasound sensor came loose underneath the surgical drape; and two because the internal calibration date for the tested device had expired, and the monitor refused to accept data. This resulted in 43 children being included in the study, in which a total of 215 paired CO_{UD} and CO_{PVFP} measurements were performed (table 1). Mean age was 356 days (range, 30 to 1,303 days); mean weight was 7.1 kg (range, 2.7 to 13.6 kg); and mean

body surface area was 0.36 m^2 (range, 0.18 to 0.59 m^2). There were no missing data from the included children.

The mean CO_{UD} was 1.28 l/min (range, 0.46 to 2.98 l/min) and CO_{PVFP} 1.20 l/min (range, 0.42 to 2.70 l/min). Means and SDs were normally distributed. The coefficient of error for repeated CO_{UD} measurements was 1.8%, resulting in precision of 3.6% for CO_{UD}. Coefficient of error for CO_{PVFP} was 2.5%, resulting in precision of 5.0% for CO_{PVFP}.

Table 1. Simultaneously Measured Mean Cardiac Outputs by CO_{UD} and CO_{PVFP} (n = 5), Heart Rates, Blood Pressures, Central Venous Pressures, and Ejection Fractions in All 43 Children after Surgical Correction

Patient	CO_{UD}, l/min	CO_{PVFP}, l/min	HR, rate/min	SBP/DBP (MAP) mmHg	CVP, mmHg	EF, %
1	1.09	1.27	156	68/33 (47)	7	54
2	1.22	1.06	127	76/49 (57)	4	45
3	0.56	0.86	149	63/38 (47)	7	44
4	0.79	0.79	146	86/43 (58)	7	55
5	0.73	0.70	122	69/45 (54)	4	41
6	1.58	1.38	122	77/50 (55)	5	47
7	0.78	0.50	131	76/46 (57)	11	41
8	0.46	0.43	144	65/45 (54)	5	40
9	1.81	1.95	130	69/41 (50)	4	45
10	0.86	0.64	124	62/33 (43)	4	45
11	0.91	0.85	130	61/31 (39)	6	55
12	1.12	0.77	138	62/32 (41)	10	47
13	1.01	0.64	127	75/34 (45)	9	53
14	1.67	1.77	119	84/53 (66)	7	52
15	0.94	0.75	113	72/44 (55)	4	48
16	2.98	2.59	127	92/42 (58)	8	46
17	0.68	0.42	149	71/42 (53)	13	44
18	2.50	2.10	128	67/36 (46)	9	54
19	0.91	0.90	150	71/43 (50)	12	37
20	1.25	1.25	127	82/41 (54)	7	50
21	1.09	1.08	130	75/46 (54)	9	49
22	1.41	1.36	144	87/40 (55)	7	49
23	2.72	2.70	119	98/46 (64)	7	47
24	1.87	1.72	97	88/42 (60)	6	51
25	1.18	0.96	128	78/43 (56)	7	51
26	0.81	0.80	137	70/35 (49)	12	50
27	0.84	0.68	130	75/45 (58)	6	44
28	1.90	1.86	126	77/39 (51)	10	49
29	2.32	2.66	111	80/37 (51)	7	57
30	1.12	0.98	146	70/30 (42)	8	55
31	0.88	0.81	111	80/37 (51)	7	53
32	0.73	0.72	154	83/41 (54)	5	45
33	1.47	1.38	128	68/43 (52)	7	49
34	1.42	1.37	136	71/35 (48)	8	64
35	2.41	2.42	112	87/43 (59)	12	52
36	1.71	1.52	139	82/36 (52)	8	51
37	0.80	0.81	158	70/40 (54)	6	46
38	1.19	1.14	123	86/42 (57)	8	50
39	0.81	0.62	115	90/55 (67)	7	48
40	0.68	0.49	155	68/38 (47)	5	43
41	0.76	0.64	126	80/51 (61)	8	44
42	1.00	1.19	123	68/36 (48)	6	41
43	2.23	2.10	107	89/38 (52)	8	75

DBP, diastolic blood pressure; CO_{UD}, cardiac output with saline dilution and ultrasound detection; CO_{PVFP}, cardiac output with perivascular flow probe around aorta; CVP, central venous pressure; EF, ejection fraction; HR, heart rate; MAP, mean arterial blood pressure; SBP, systolic blood pressure.

Bland–Altman analysis (fig. 3) showed that the bias between CO_{UD} and CO_{PVFP} was 0.08 l/min (95% CI, 0.05 to 0.10), and the limits of agreement were −0.24 l/min (95% CI, −0.17 to −0.32) and 0.40 l/min (95% CI, 0.33 to 0.47). The percentage error between CO_{UD} and CO_{PVFP} was 26.6%.

Three patients had insignificant residual shunts after the surgical correction. No valvular regurgitations were observed that affected the results. There were no adverse effects in any patient related to measurements.

Discussion

In the present study, we found that repeated CO measurements by the tested method, which uses saline bolus injections and ultrasound detection of the expected blood dilution (CO_{UD}), showed a similar precision as our reference method, a perivascular flow probe around the aorta (CO_{PVFP}). We believe that CO measurement with a periaortic flow probe is the most accurate technique to be used for comparison studies using repeated CO measurements *in vivo*. There was a small but significant bias of the measured CO between CO_{UD} and CO_{PVFP} according to the Bland–Altman analysis of 0.08 l/min. This finding of a lower CO_{PVFP} compared with CO_{UD} is consistent with a coronary blood flow of approximately 4 to 10% of the measured CO, which agrees with suggestions from earlier publications.[27]

Earlier studies using perivascular flow probes in animals have applied the flow probe around the pulmonary artery as a measurement of total CO, which is also measured by CO_{UD}. This had been our intention, but we discovered that the peripulmonary flow probe tended to compress the right coronary vessels, resulting in a reduction of CO. This led us to abandon its use for the simultaneously repeated

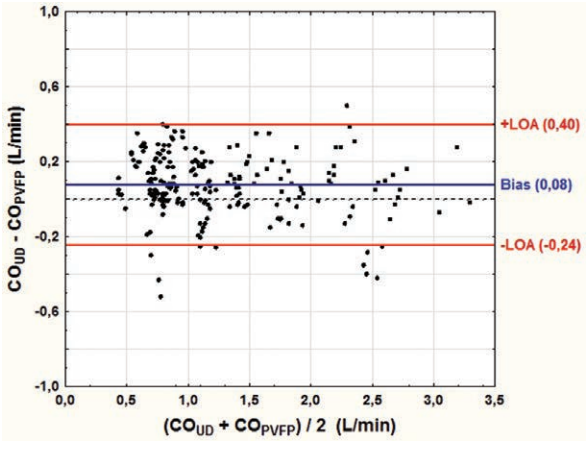

Fig. 3. Bland–Altman plot comparing different methods for cardiac output (CO) measurement, saline dilution and ultrasound detection (CO_{UD}), and perivascular flow probe (CO_{PVFP}). LOA, limits of agreement.

CO measurements and rely solely on the blood flow probe around the aorta, although the total CO missed the drain by the coronary blood flow.

There will always be a physiologic variability in CO caused by ventilation and cardiac filling, which result in various degree of imprecision during the CO measurements. The CO_{PVFP} analysis recorded beat-to-beat fluctuations in CO caused by the ventilation, changes in cardiac filling, and changes in coronary blood flow. This can be the reason for a slightly but not significantly higher coefficient of error (2.5%) compared with CO measured with CO_{UD} (1.8%). In addition, the dilution curve, which is used by the CO_{UD} to calculate CO, reflects a mean of several heart beats, which may give a more stable value. We suspected that five consecutive repeated injections of 0.5 to 1.0 ml/kg of saline could decrease the precision of the CO_{UD} analysis, because of a potential dilutional effect on the blood by multiple saline injections, but this did not affect the precision of our analysis. Because we conducted a trial with a high number (n = 5) of repeated measurements and did not remove any measurements, we believe that our analysis is accurate and indicates that the dilution of the blood with bolus doses of saline and detection by ultrasound sensors in a constant extracorporeal arteriovenous loop flow gives stable CO measurements compared with, for example, thermodilution, which still is regarded to be the gold standard for CO measurement in children and a reference method in validation studies.[28,29]

Although our analysis was negatively influenced by the bias caused by the coronary blood flow between CO_{UD} and CO_{PVFP}, our results show a percentage error of 26.6%, which is less than the 30% limit, that has been concluded by Critchley and Crithchley[26] as an acceptable limit of a new technique to be equivalent to the reference method.

One limitation to the tested technology is that the arterial blood pressure monitoring has to be closed during the CO measurement. The device, in its present form, only allows for intermittent but not continuous CO measurements as would be preferable for a monitoring device. In addition, one central venous line is occupied for the injection and the loop circulation during the measurement. However, there is no patient blood loss because all blood in the arteriovenous loop is flushed back into the circulation after measurements. Only small-volume (0.5 to 1.0 ml/kg) body-temperature saline boluses are needed to do the measurements, and there is no drop in heart rate as often is seen during measurements with a thermodilution catheter because of cold saline boluses.

In summary, the tested technology, which uses a saline bolus into the venous side and ultrasound sensors on an extracorporeal loop to detect the blood dilution both on the venous and arterial side for calculation of CO, has a precision comparable with the precision obtained by continuous CO measurement by a periaortic flow probe in young children. A Bland–Altman plot shows that the tested method detects a small expected bias between CO_{UD} and CO_{PVFP} caused by the coronary blood flow. It is easy to apply clinically in children with arterial and central venous catheters in place. The technology could potentially be a promising alternative as a reference method for comparison studies of CO in young children.

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Competing Interests

The authors declare no competing interests.

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References

1. Lemson J, Nusmeier A, van der Hoeven JG: Advanced hemodynamic monitoring in critically ill children. Pediatrics 2011; 128:560–71
2. Tibby SM, Hatherill M, Marsh MJ, Murdoch IA: Clinicians' abilities to estimate cardiac index in ventilated children and infants. Arch Dis Child 1997; 77:516–8
3. Egan JR, Festa M, Cole AD, Nunn GR, Gillis J, Winlaw DS: Clinical assessment of cardiac performance in infants and children following cardiac surgery. Intensive Care Med 2005; 31:568–73
4. Skowno JJ, Broadhead M: Cardiac output measurement in pediatric anesthesia. Paediatr Anaesth 2008; 18:1019–28
5. de Boode WP: Cardiac output monitoring in newborns. Early Hum Dev 2010; 86:143–8
6. Shephard JN, Brecker SJ, Evans TW: Bedside assessment of myocardial performance in the critically ill. Intensive Care Med 1994; 20:513–21

7. Le Manach Y, Collins GS: Disagreement between cardiac output measurement devices: Which device is the gold standard? Br J Anaesth 2016; 116:451–3
8. Suehiro K, Joosten A, Murphy LS, Desebbe O, Alexander B, Kim SH, Cannesson M: Accuracy and precision of minimally-invasive cardiac output monitoring in children: A systematic review and meta-analysis. J Clin Monit Comput 2016; 30:603–20
9. Darling E, Thuramalla N, Searles B: Validation of cardiac output measurement by ultrasound dilution technique with pulmonary artery thermodilution in a pediatric animal model. Pediatr Cardiol 2011; 32:585–9
10. Peyton PJ, Chong SW: Minimally invasive measurement of cardiac output during surgery and critical care: A meta-analysis of accuracy and precision. Anesthesiology 2010; 113:1220–35
11. Krivitski NM, Kislukhin VV, Thuramalla NV: Theory and *in vitro* validation of a new extracorporeal arteriovenous loop approach for hemodynamic assessment in pediatric and neonatal intensive care unit patients. Pediatr Crit Care Med 2008; 9:423–8
12. Crittendon I 3rd, Dreyer WJ, Decker JA, Kim JJ: Ultrasound dilution: An accurate means of determining cardiac output in children. Pediatr Crit Care Med 2012; 13:42–6
13. Vrancken SL, de Boode WP, Hopman JC, Looijen-Salamon MG, Liem KD, van Heijst AF: Influence of lung injury on cardiac output measurement using transpulmonary ultrasound dilution: A validation study in neonatal lambs. Br J Anaesth 2012; 109:870–8
14. Lindberg L, Johansson S, Perez-de-Sa V: Validation of an ultrasound dilution technology for cardiac output measurement and shunt detection in infants and children. Pediatr Crit Care Med 2014; 15:139–47
15. Saxena R, Krivitski N, Peacock K, Durward A, Simpson JM, Tibby SM: Accuracy of the transpulmonary ultrasound dilution method for detection of small anatomic shunts. J Clin Monit Comput 2015; 29:407–14
16. Vrancken SL, de Boode WP, Hopman JC, Singh SK, Liem KD, van Heijst AF: Cardiac output measurement with transpulmonary ultrasound dilution is feasible in the presence of a left-to-right shunt: A validation study in lambs. Br J Anaesth 2012; 108:409–16
17. Vrancken SL, van Heijst AF, Hopman JC, Liem KD, van der Hoeven JG, de Boode WP: Hemodynamic volumetry using transpulmonary ultrasound dilution (TPUD) technology in a neonatal animal model. J Clin Monit Comput 2015; 29:643–52
18. Stewart GN: Researches on the circulation time and on the influences which affect it. J Physiol 1897; 22:159–83
19. Hamilton WF, Moore JW, Kinsman JM, Spurling RG: Studies on the circulation. Am J Physiol 1932; 99: 534–51
20. Reuter DA, Huang C, Edrich T, Shernan SK, Eltzschig HK: Cardiac output monitoring using indicator-dilution techniques: Basics, limits, and perspectives. Anesth Analg 2010; 110:799–811
21. Dean DA, Jia CX, Cabreriza SE, D'Alessandro DA, Dickstein ML, Sardo MJ, Chalik N, Spotnitz HM: Validation study of a new transit time ultrasonic flow probe for continuous great vessel measurements. ASAIO J 1996; 42:M671–6
22. Botero M, Kirby D, Lobato EB, Staples ED, Gravenstein N: Measurement of cardiac output before and after cardiopulmonary bypass: Comparison among aortic transit-time ultrasound, thermodilution and noninvasive partial CO_2 rebreathing. J Cardiothorac Vasc Anesth 2004; 18:563–72
23. Cecconi M, Rhodes A, Poloniecki J, Della Rocca G, Grounds RM: Bench-to-bedside review: The importance of the precision of the reference technique in method comparison studies–with specific reference to the measurement of cardiac output. Crit Care 2009; 13:201
24. Bland JM, Altman DG: Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986; 1:307–10
25. Zou GY: Confidence interval estimation for the Bland–Altman limits of agreement with multiple observations per individual. Stat Methods Med Res 2013; 22:630–42
26. Critchley LA, Critchley JA: A meta-analysis of studies using bias and precision statistics to compare cardiac output measurement techniques. J Clin Monit Comput 1999; 15:85–91
27. The circulation during exercise: The coronary circulation and ischemic heart disease. Textbook of Medical Physiology, 9th edition. Edited by Guyton AC, Hall JE. Philadelphia, W.B. Saunders Company, 1996, pp 253–63
28. Stetz CW, Miller RG, Kelly GE, Raffin TA: Reliability of the thermodilution method in the determination of cardiac output in clinical practice. Am Rev Respir Dis 1982; 126:1001–4
29. Tibby S: Transpulmonary thermodilution: Finally, a gold standard for pediatric cardiac output measurement. Pediatr Crit Care Med 2008; 9:341–2