Cardiac index monitoring by pulse contour analysis and thermodilution after pediatric cardiac surgery

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Objectives: To validate a new device (PiCCO system; Pulsion Medical Systems, Munich, Germany), we compared cardiac index derived from transpulmonary thermodilution and from pulse contour analysis in pediatric patients after surgery for congenital heart disease. We performed a prospective clinical study in a pediatric cardiac intensive care unit of a university hospital.

Methods: Twenty-four patients who had had cardiac surgery for congenital heart disease (median age 4.2 years, range 1.4-15.2 years) were investigated in the first 24 hours after admission to the intensive care unit. A 3F thermodilution catheter was inserted in the femoral artery. Intracardiac shunts were excluded by echocardiography intraoperatively or postoperatively. Cardiac index derived from pulse contour analysis was documented in each patient 1, 4, 8, 12, 16, 20, and 24 hours after admission to the intensive care unit. Subsequently, a set of three measurements of thermodilution cardiac indices derived by injections into a central venous line was performed and calculated by the PiCCO system.

Results: The mean bias between cardiac indices derived by thermodilution and those derived by pulse contour analysis over all data points was 0.05 (SD 0.4) $L \cdot min \cdot m^{-2}$ (95% confidence interval 0.01-0.10). A strong correlation between thermodilution and contour analysis cardiac indices was calculated (Pearson correlation coefficient $r = 0.93$; coefficient of determination $r^2 = 0.86$).

Conclusions: Pulse contour analysis is a suitable method to monitor cardiac index over a wide range of indices after surgery for congenital heart disease in pediatric patients. Pulse contour analysis allows online monitoring of cardiac index. The PiCCO device can be recalibrated with the integrated transpulmonary thermodilution within a short time frame.

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Monitoring of cardiac index (CI) after surgery for congenital heart disease is an important method to optimize medical management.

Thermodilution with a pulmonary artery catheter (PAC) is commonly used in adult patients to measure CI. However, PACs are not without risks, and their use is limited in pediatric patients with congenital heart disease because of patients' size or aberrant anatomy. Therefore, the management of these patients is commonly based on indirect parameters like central venous pressure, mixed venous oxygen saturation, and arterial waveform appearance as indicators of CI after surgery for congenital heart disease.

A newer alternative technology to monitor CI is the transpulmonary thermodilution method (TDCI),[1] enabling CI measurement by injecting cold saline into a central venous line and monitoring the blood temperature in a central artery. The validity and accuracy of this method have been documented in different patient populations and settings.[2-5]

The analysis of the contour of arterial waveforms is another new technology using algorithms to assess stroke volume and therefore CI. The principal advantage

Abbreviations and Acronyms
CI = cardiac index
CO = cardiac output
PAC = pulmonary artery catheter
PCCI = cardiac index derived from pulse contour analysis
TDCI = cardiac index derived from transpulmonary thermodilution

of this method is that it provides a continuous measurement of CI without the need of performing thermodilutions for every measurement. This pulse contour analysis has been recently introduced.[6-8] The technology uses the principle that the area under the curve of a central arterial waveform correlates with the stroke volume. This correlation can be calculated after obtaining the CI through a calibrating technology. The PiCCO system (Pulsion Medical Systems, Munich, Germany) incorporates TDCI as well as the pulse contour analyzing technology (PCCI) to measure CI. It uses TDCI for initial and periodic calibrations. The validity of this technique has been demonstrated in adult patients, showing a good correlation with PACs or other methods of CI monitoring.[8-10] However, in children the PCCI in postoperative management has not been validated sufficiently. This subgroup of pediatric patients might benefit from CI monitoring because there are no good alternatives available for measuring CI in them.

This study investigated the validity of this technology in the postoperative management of pediatric patients undergoing corrective surgery for congenital heart disease.

We evaluated the relationship between the CI derived from TDCI versus the CI derived from PCCI in the first 24 hours after surgery.

Materials and Methods

Patient Selection

With the approval of the institutional research and ethics committee and after informed written consent by the patients' guardians had been obtained, 24 patients undergoing corrective operations for congenital heart disease were enrolled in this prospective study. The types of cardiac malformations are shown in Table 1. Only patients with a body weight greater than 10 kg were included to avoid vascular complications of the limbs.

Because thermodilution is not reliable in patients with persisting intracardiac shunting after surgery because of indicator recirculation,[11] patients with intracardiac shunts were excluded by transesophageal or transthoracic echocardiography.

Ages ranged from 1.4 to 15.2 years, median 4.2 years, and body weights ranged from 10.6 to 35.6 kg, median 16.5 kg.

Interventions

For thermodilution injections we used the central venous line that was inserted routinely in the jugular vein in each patient. In addition a 3F catheter with a thermistor at the tip (PiCCO system) was inserted in the femoral artery during the preoperative conditioning of the patient, enabling the determination of both arterial blood pressure and changes of blood temperature for the thermodilution-based calculation of CI.

Data acquisition began after the initial calibration of the device performing a set of three thermodilution measurements with a bolus of cold saline into the central venous line (5-15 mL depending on the patient's weight). In each patient 1, 4, 8, 12, 16, 20, and 24 hours after admission to the intensive care unit the current PCCI value at the monitor of the device was documented. Subsequently, another set of three TDCI measurements was performed and the mean was calculated by the PiCCO system. This mean TDCI value was compared with the PCCI value documented before, forming 1 data point.

The PiCCO system operates in such a way that every time a thermodilution injection is performed, the pulse contour analysis is automatically and immediately self-calibrating with the new value of TDCI. Because of this self-calibrating process, we used the PCCI value documented immediately before such a calibration for the comparison with TDCI.

We obtained 7 data points in each patient and a total of 168 data points by this procedure.

Data Analysis

Data were analyzed with StatView 4 and SAS 9.1 (SAS Institute, Inc, Cary, NC). Statistical analysis of accuracy of PCCI in comparison with TDCI was performed by the method of Bland and Altman[12] and by calculating mean bias and limits of agreement (bias $\pm$ 2 SD) between TDCI and PCCI. In addition, the Pearson correlation coefficient and a linear regression were calculated, including the coefficient of determination r^2. The difference between TDCI and PCCI was further investigated by a paired t test.

Analyses were performed on the basis of all available measurements (7 time points $\times$ 24 patients) and on the basis of the 24 individual means.

The sample size of 24 patients was motivated by the following: A paired t test with a 5% significance level was performed to prove equivalence between TDCI and PCCI, using an equivalent limit of 10% and a power of 90%. At the planning stage there was uncertainty on the standard deviation of the difference between TDCI and PCCI. Therefore, a preliminary estimate of this parameter was made after the first 14 patients. The resulting power using 14 patients was already found to be 99%. To reach a sample size similar to other studies in this area, it was decided to increase the sample size to 24 patients. All power calculations were performed with the software nQuery Advisor 4.0 (Statistical Solutions, Cork, Ireland).

The inferential statistical and power calculations have been performed by an institutional statistical expert.

Results

TDCI measurements showed values between 1.86 and 7.04 $L \cdot min^{-1} \cdot m^2$, representing a wide range of hemodynamic conditions in the investigated postoperative period. The mean standard deviation for three repeated measure-

TABLE 1. Characteristics of investigated patients

Patient No.	Age (y)	Diagnosis	Operation
1	3	DORV, LVOTO, VSD, CoA	Closure of residual VSD + LVOTO resection after Rastelli operation
2	5	PAVSD	ASD patch closure + closure of mitral valve cleft
3	5.4	Pulmonary atresia. IVS, RV hypoplasia	Total cavopulmonary connection with extracardiac conduit
4	3	TGA, LVOTO	Rastelli operation with RV-PA trunk allograft
5	6.4	PS	Pulmonary valve commisurotomy, patch arterioplasty of PA trunk
6	4.1	ASD	ASD suture
7	5.2	PS	Replacement of pulmonary valve
8	2.8	PAVSD	ASD patch closure + closure of mitral valve cleft
9	1.4	DORV Fallot type, RVOTO	Rastelli operation with RV-PA trunk allograft
10	9.3	Dextrocardia, DORV, LV hypoplasia	Total cavopulmonary connection with extracardiac conduit
11	5.8	PAVSD	ASD patch closure + closure of mitral valve cleft
12	3.3	TGA, VSD, LVOTO	Rastelli operation
13	2.4	TOF, PDA	Replacement of RV-PA conduit after correcting operation
14	3.1	LVOTO, AS after CoA repair	Replacement of aortic valve
15	1.8	TOF	RVOT patch, patch arterioplasty of PA trunk
16	11.7	AS	Ross operation
17	2.5	TAC A1	Change of RV-PA conduit
18	3.9	TAC A1	Aortic valve replacement + RV-PA conduit
19	2.4	Subvalvular AS	Resection of subvalvular membrane + subvalvular myectomy
20	2.9	DORV, L-MAG, subvalvular RVOTO, PFO, PDA	Total cavopulmonary connection with extracardiac conduit
21	2.4	TOF	RVOTO resection + VSD patch closure
22	6.9	PAVSD	ASD patch closure + closure of mitral valve cleft
23	15.2	PAVSD, MR, TR	Replacement of mitral valve and valvuloplasty of tricuspid valve after PAVSD correction
24	4.6	CoA	CoA resection and end-to-end anastomosis

AS, Aortic valve stenosis; *ASD*, atrial septal defect; *CoA*, coarctation of the aorta; *DORV*, double-outlet right ventricle; *IVS*, intact ventricle septum; *LV*, left ventricle; *LVOTO*, left ventricular outflow tract obstruction; L-*MAG*, levo-malposition of the great arteries; *MR*, mitral regurgitation; *PA*, pulmonary artery; *PAVSD*, partial atrioventricular septal defect; *PDA*, persisting ductus arteriosus; *PFO*, persisting foramen ovale; *PS*, pulmonary stenosis; *RVOTO*, right ventricular outflow tract obstruction; *RV*, right ventricle; *TAC*, truncus arteriosus communis; *TGA*, transposition of the great arteries; *TOF*, tetralogy of Fallot; *TR*, tricuspid regurgitation; *VSD*, ventricular septal defect.

ments of TDCI was 5.2 %, showing a variation in CI in each individual injection similar to that seen with PACs.

The mean bias between TDCI and PCCI over all data points was 0.05 (SD 0.4) $L \cdot min^{-1} \cdot m^2$ (95% confidence interval 0.01-0.10). The maximum bias was 1.33 $L \cdot min^{-1} \cdot m^2$, in a data point where the corresponding TDCI was 5.04 $L \cdot min^{-1} \cdot m^2$, leading to a relative maximum bias of 26%.

The mean bias and limits of agreement between TDCI and PCCI corresponding to the 7 separate times of comparison are shown in Table 2.

As seen in Figure 1, there was a good correlation between TDCI and PCCI. The Pearson coefficient of correlation r between all data points of TDCI versus PCCI was 0.93; the coefficient of determination r^2 was 0.86. The Pearson coefficient of correlation r on the basis of the 24 individual means between TDCI versus PCCI was 0.99, and the coefficient of determination r^2 was 0.98. The linear regression equation was PCCI = 0.90 TDCI + 0.33.

The Bland–Altman plot in Figure 2 shows the mean bias and limits of agreement of PCCI compared with TDCI.

Discussion

Our study showed that pulse contour analysis with the PiCCO system is a feasible method to monitor CI constantly and online in pediatric patients after cardiac surgery.

TABLE 2. Accuracy of PCCI compared with TDCI during different points of time after surgery for congenital heart disease

Time after admission to ICU (h)	Mean bias ± SD	r^2	No. of patients
1	0.18 ± 0.39	0.83	24
4	0.15 ± 0.47	0.85	24
8	0.02 ± 0.35	0.90	24
12	0.04 ± 0.44	0.86	24
16	−0.04 ± 0.37	0.90	24
20	−0.01 ± 0.38	0.90	24
24	0.03 ± 0.38	0.86	24

Mean bias = TDCI − PCCI; r^2 = coefficient of determination. *ICU*, Intensive care unit; *SD*, standard deviation.

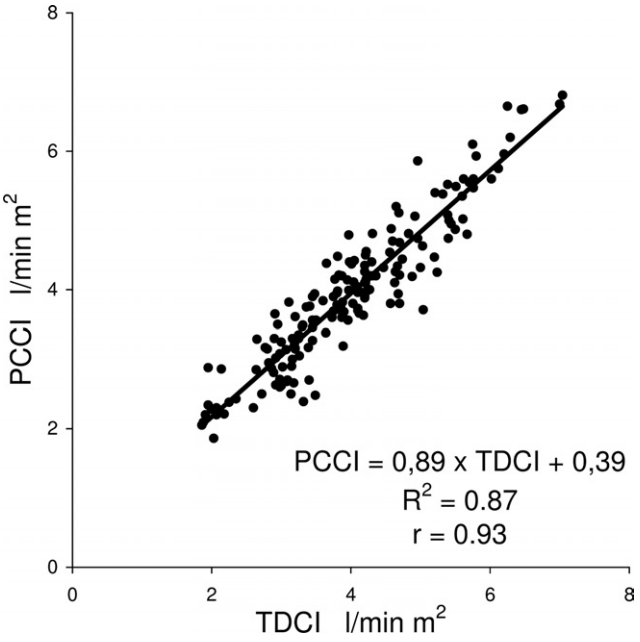

Figure 1. Comparative plot showing the correlation of TDCI and PCCI.

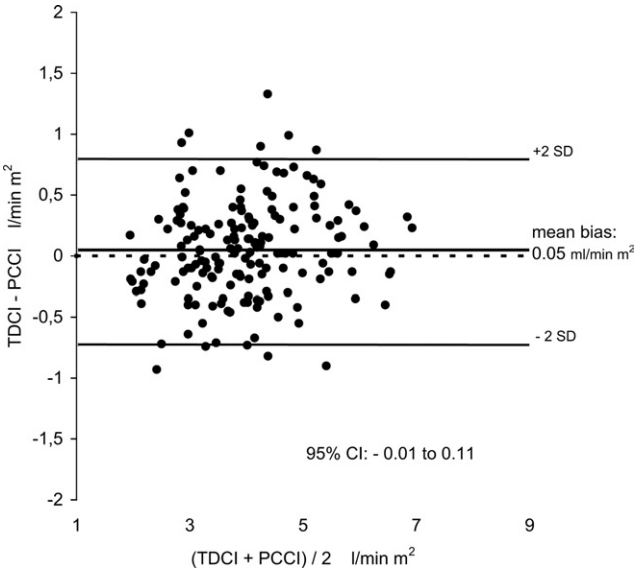

Figure 2. Bland–Altman plot showing the comparison of TDCI and PCCI, expressed by mean bias and limits of agreement and 95% confidence interval *(CI). SD,* Standard deviation.

Although this technology has been evaluated in different clinical settings, such as coronary artery bypass surgery and noncardiac surgery, as well as in intensive care unit settings,[9,13-16] these studies were all performed in adult patients.

PCCI monitoring is less invasive than PAC-derived CI and only one small cannula in the femoral artery is needed. Thus, the use of pulse contour technology after surgery for congenital heart disease may be even more beneficial because it offers an online monitoring of CI to estimate cardiac function and tissue perfusion, enabling optimization of postoperative management.

Our study was performed to look at the accuracy of PCCI using the PiCCO system in this special group of pediatric patients with congenital heart disease. PCCI was compared with TDCI, a method widely evaluated in different populations and settings.[2-5] TDCI was considered as the reference method to measure CI in this study.

Our results showed that the difference between PCCI and TDCI values does not exceed the limits of clinical utility.

Our findings are in contrast with other studies of pulse contour analysis using cardiac output (CO) that describe a wide spectrum of measured bias and agreement between pulse contour CO and transpulmonary thermodilution or thermodilution via PAC.

However, one must be aware that interindividual differences were quite substantial in the investigated populations. In addition, some of the studies were performed using CO instead of CI, including the restriction of comparability. We used CI because use of CO values without indexing them to body surface area introduces the potential for relevant statistical error when comparing data of smaller children with data of larger patients.

Compared with other studies, there was a difference of the registration of PCCI. Gödje and associates[9,14] calculated a mean of one PCCI value assessed immediately before and one after recalibration. The PCCI value after thermodilution was then recalibrated. They compared this mean PCCI value with the TDCI value of the corresponding thermodilution. Instead of this, we used the PCCI value immediately before the calibration for comparison with TDCI without a recent recalibration, because this reflects the common clinical practice of looking at a monitor and using the observed parameter for decision making. Zöllner,[15] Rauch,[16] and their collegues compared PAC-derived CO for comparison with pulse contour–derived CO. Interestingly, the agreement ranges in those two groups are considerably larger than those derived by Gödje and associates[9] or Mahajan and coworkers[17] using TDCI.

In addition, the complicated physiology of congenital lesions, especially intracardiac shunting or Fontan-type circulation with altered lung perfusion in our patients, might be responsible for the discrepancy with data from others.

Mahajan and colleageus[17] investigated also a pediatric population in different settings: 191 data points of PCCI versus TDCI were compared, including 61 points in a prebypass period (46 data points in shunted patients and 15 in

nonshunted patients). Therefore, at least 46 data points in patients with intracardiac shunts were included. This intracardiac shunting might explain the different limits of agreement between PCCI and TDCI. However, no intraoperative or postoperative ultrasound investigation was mentioned controlling the shunt situation after operation.

In our study, relevant disagreement was observed in only a few data points of PCCI versus TDCI.

Focusing at the mean bias between TDCI and PCCI corresponding to the 7 separate times of comparison, as shown in Table 2, it appears that 1 or 4 hours after the admission to the ICU the mean bias was more relevant than at the later times of comparison. In this first postoperative period, essential changes in the hemodynamic state of the patient might explain this observation.

The maximum bias was 1.33 $L \cdot min^{-1} \cdot m^2$ in a data point where the corresponding TDCI was 5.04 $L \cdot min^{-1} \cdot m^2$, leading to a relative maximum bias of 26%. This data point was measured in a patient after closure of an atrial septal defect and suture of a mitral valve cleft, 4 hours after admission to the intensive care unit and the first calibration of the PiCCO system. Between these 2 time points the patient obtained a larger amount of volume infusion, raising the central venous pressure from 2 to 8 mm Hg. The change of preload and peripheral vasoconstriction will influence the arterial waveform appearance essentially and might have caused the discrepancy between PCCI and TDCI values.

Six data points with a bias between PCCI and TDCI from 0.75 to 1.05 $L \cdot min^{-1} \cdot m^2$ were observed shortly after extubation and reduction of analgosedative medication. Active inspiration could explain a relevant change of preload and lung perfusion. The awake status of the patient influences heart rate and CI. These mechanisms will alter both vascular resistance and arterial waveform substantially. In consequence, a recalibration of PiCCO is necessary.

However, the PiCCO system provides a reliable ability of online CI monitoring. The difference between PCCI and TDCI values does not exceed the limits of clinical utility, if you consider essential therapeutic alterations.

The widely evaluated method of TDCI enables CI to be determined within a short time frame of about 2 minutes including a recalibration of PCCI.

Conclusions

In summary, we demonstrated a sufficient agreement between PCCI and TDCI in our group of pediatric patients after surgery for congenital heart disease since pulse contour analysis enables the constant and online monitoring of CI.

We recommend this method for optimal hemodynamic monitoring, particularly in pediatric patients after surgery for congenital heart disease.

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