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ORIGINAL ARTICLE

Transpulmonary Thermodilution in Neonates Undergoing Arterial Switch Surgery

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Abstract Measurement of the global end-diastolic volume index (GEDI) by transpulmonary thermodilution (TPTD) has become a useful technique for measuring preload in adults. This study aimed to investigate the hemodynamic changes in neonates during the postoperative period after arterial switch surgery. Over a 13-month period, the postoperative data of 12 neonates with transposition of the great arteries were retrospectively investigated. Arterial and central venous blood pressures were monitored, Cardiac index (CI), stroke volume index (SVI), systemic vascular resistance index (SVRI), GEDI, and extravascular lung water index (ELWI) were measured by thermodilution. The CI was significantly correlated with the SVRI only in the closed chest condition ($r = -0.92$; $P < 0.001$). The CI and SVI values were significantly lower and the ELWI and SVRI values significantly higher in both the open and closed chest conditions than the postextubation values. The relationship between change in GEDI and change in CI was stronger in the open chest condition ($r = 0.93$; $P < 0.006$) than in the closed chest condition ($r = 0.75$; $P = 0.055$). However, the latter just missed statistical significance. According to the findings, TPTD seems to be a useful tool for assessing cardiac function after neonatal arterial switch surgery. Establishment of normal values will be essential for proper guidance of therapy for this population using volumetric parameters.

Keywords Cardiac output · Hemodynamics · Pediatrics · Thermodilution

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Volumetric parameter-guided therapy leads to a reduced and shortened need to use vasopressors, catecholamines, mechanical ventilation, and intensive care unit (ICU) therapy for patients undergoing cardiac surgery [6]. For pediatric populations, particularly patients with congenital heart disease, hemodynamic status usually is estimated by clinical assessment, continuous pressure recording, pulse oximetry, core–peripheral temperature difference, and echocardiography [18, 26].

Ten years ago, Wernovsky et al. [27] described a series of neonates undergoing arterial switch operations in whom cardiac output was measured intermittently during the early postoperative period without any serious complications, but this technique has not attained widespread use. The current strategies in pediatric heart surgery have led the majority of patients to undergo corrective surgical procedures before the age of 12 months and one-third of patients to undergo procedures before the age of 30 days [9]. Newly developed catheters have made continuous cardiac output monitoring possible for this age group of patients [4, 25].

In neonates, pathophysiologic and compensatory mechanisms of circulatory failure are considerably different from those in adults [17]. We hypothesized that simply

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adapting adult experiences and normal ranges for this population would lead to false interpretations.

The chief aims of this study were to investigate the postoperative hemodynamic changes in neonates undergoing arterial switch operations and to determine the hemodynamic parameters that most strongly influence cardiac output in the early postoperative period.

Methods

This study retrospectively evaluated 12 infants 7–28 days old. The data were initially collected as part of a prospective study performed to examine the relationship between N-terminal natriuretic peptides and cardiac output during a 24-month period. This prospective study was approved by the local ethics committee, and parental informed consent was obtained for each patient. The selected patients had transposition of the great arteries, and each of them underwent an arterial switch operation (an anatomic correction).

The attending cardiologist reported each patient's preoperative history, echocardiogram results, and catheterization data. Procedure and intraoperative data were collected by review of the surgical notes and anesthesia reports. Hemodynamic status was assessed with routinely monitored parameters (arterial blood pressure, central venous pressure, peripheral oxygen saturation, two-channel electrocardiogram). Cardiac output, stroke volume (SV), stroke volume variation, and systemic vascular resistance (SVR) were continuously monitored by pulse contour analysis (PiCCO system v 4.12; Pulsion Medical Systems, Munich, Germany; Philips CMS System, Andover, MA; Endower, Massachusetts), and additional measurements were made by transpulmonary thermodilution (TPTD).

For the thermodilution procedure, a 3-Fr thermistor-tipped arterial catheter (PV 2013L07 Pulsiocath; Pulsion Medical Systems) was inserted into the femoral artery of the patients after induction of anesthesia. The TPTD enabled intermittent calculation of several cardiac function parameters such as global ejection fraction and cardiac function index, as well as thoracic fluid volumes including global end-diastolic volume, intrathoracic blood volume, and extravascular lung water. Indexes of the measured hemodynamic parameters including cardiac index (CI), stroke volume index (SVI), systemic vascular resistance index (SVRI), global end-diastolic volume index (GEDI), intrathoracic blood volume index (ITBI), and extravascular lung water index (ELWI) were calculated after body surface area had been estimated from body height and weight.

Measurements were taken after termination of the cardiopulmonary bypass (T_0), then four times daily during the postoperative period. Measurements also were taken in cases of severe circulatory changes. Measurements of TPTD were carried out in duplicate or triplicate by placing 3 ml of cold injectate into the right internal jugular vein through a double-lumen catheter. The average of the measurements performed at the same time point was used for statistical analysis. After extubation, we attempted at least two TPTD measurements.

Catheters were removed when patients were ready for discharge from the intensive care unit (ICU) and in cases of possible catheter-related infection (1 patient). Plans also were made to remove catheters in cases of limb ischemia, but none of our patients experienced that complication. Participation in this study caused no delay in discharge from the ICU, including potential delays from catheter-related complications.

Statistical Analysis

Results were calculated as means ± standard deviations. Continuous parameters were compared using Student's *t* test and analysis of variance (ANOVA) with post hoc Bonferroni correction. The correlations between the variables were assessed by Pearson correlation and linear regression analysis. The correlations of the change in parameters between two consecutive measurements (d) also were calculated and analyzed. To avoid violating the test assumption of independent measurements, Pearson's test and linear regression analysis were applied after the mean of the parameters for each subject had been calculated [1]. All P values less than 0.05 were considered significant. For statistical evaluation, SPSS for Windows 11.5.0 (SPSS Inc., Chicago, IL, USA) was used.

Results

The main perioperative parameters of the patients are shown in Table 1. All the patients underwent anatomic corrections for transposition of the great arteries. One patient also underwent ventricular septal defect closure. Two-thirds of the patients had delayed sternal closure, and their operations were significantly longer ($P = 0.009$). The median duration of the open chest condition was 20.5 h (interquartile range, 0–46.5 h). Each baby was successfully extubated at the first attempt, and the study mortality rate was 0. As noted earlier, none of the patients experienced limb ischemia.

Most hemodynamic parameters improved throughout the postoperative period (Table 2). After sternal closure, the CI and SVI measurements were significantly higher the SVRI, heart rate, and ELWI measurements significantly lower than the open chest measurements. Significant differences in CI, SVI, heart rate, global ejection fraction, and

Table 1 Main perioperative parameters of the patients

Patient no.	Diagnosis	Age (days)	Weight (kg)	Operation	Operation time (min)	CPB time (min)	Cross-clamp time (min)	Delay in sternal closure (h)	Time of extubation (h)
1	TGA	7	3.9	Arterial switch	275	210	111	21	95
2	TGA, VSD	8	3.4	Arterial switch, VSD closure	245	204	135	21	70
3	TGA	9	3.2	Arterial switch	240	146	85	20	96
4	TGA	10	3.3	Arterial switch	210	142	83	0	79
5	TGA	10	3.6	Arterial switch	255	183	121	43	141
6	TGA	10	3.6	Arterial switch	210	120	81	0	121
7	TGA	10	4.9	Arterial switch	230	151	95	0	57
8	TGA	11	3.6	Arterial switch	225	148	93	69	145
9	TGA	11	3.6	Arterial switch	265	157	111	71	199
10	TGA	14	3.9	Arterial switch	150	146	101	0	94
11	TGA	15	3.0	Arterial switch	230	132	92	50	121
12	TGA	28	4.2	Arterial switch	240	113	78	18	151

CPB cardiopulmonary bypass, *TGA* transposition of the great arteries, *VSD* ventricular septum defect

Table 2 Hemodynamic parameters in the postoperative period

	Open chest (1) ($n = 47$)	Closed chest (2) $n = 91$)	After extubation (3) ($n = 7$)	ANOVA (P value)	1 vs. 2 (P value)	1 vs. 3 (P value)	2 vs. 3 (P value)
CI (l/min/m^2)	2.1 ± 0.6	3.1 ± 1.1	4.0 ± 0.6	<0.001	<0.001	<0.001	0.005
SVI (ml/m^2)	15.5 ± 3.3	22.7 ± 7.5	33.1 ± 4.3	<0.001	<0.001	<0.001	<0.001
MAP (mmHg)	57 ± 10	61 ± 9	68 ± 7	0.002	0.10	0.003	0.059
SVRI (dyn × s/cm^5/m^2)	1639 ± 243	1411 ± 396	1150 ± 295	<0.001	0.005	<0.001	0.067
HR (bpm)	165 ± 17	145 ± 18	128 ± 8	<0.001	<0.001	<0.001	0.003
GEF (%)	22.3 ± 11.3	25.6 ± 6.0	35.8 ± 8.0	<0.001	0.16	<0.001	0.002
SVV (%)	11.3 ± 4.0	11.2 ± 3.9	15.6 ± 4.8	0.003	1	0.005	0.002
PPV (%)	12.8 ± 5.1	12.2 ± 4.7	13.5 ± 6.5	0.68			
GEDI (ml/m^2)	298 ± 120	355 ± 123	404 ± 103	0.016	0.05	0.06	0.76
ITBI (ml/m^2)	398 ± 134	454 ± 147	489 ± 125	0.067			
ELWI (ml/kg)	37.3 ± 6.6	32.4 ± 8.5	20.2 ± 7.0	<0.001	0.021	<0.001	0.002
PVPI	7.7 ± 1.6	6.5 ± 2.1	6.9 ± 1.7	0.037	0.032	0.95	1

Data are expressed as mean ± standard deviation. Data are shown for the open and closed chest conditions and after extubation. The ANOVA test and the post hoc Bonferroni test were applied

ANOVA analysis of variance, *CI* cardiac index, *SVI* stroke volume index, *MAP* mean arterial pressure, *SVRI* systemic vascular resistance index, *HR* heart rate, *bpm* beats per minute, *GEF* global ejection fraction, *SVV* stroke volume variation, *PPV* pulse pressure variation, *GEDI* global end-diastolic index, *ITBI* intrathoracic blood volume index, *ELWI* extravascular lung water index, *PVPI* pulmonary vascular permeability index

ELWI before and after extubation also were observed. The skin temperature and the core–peripheral temperature difference also improved significantly after sternal closure (Table 3).

Table 4 shows the correlations of the change in parameters between two consecutive measurements. The change in CI showed a significantly positive correlation with the change in GEDI, whereas these correlations just missed statistical significance during closed chest conditions ($P = 0.055$). In the open chest condition, the change in GEDI was correlated with the change in ELWI. In the closed chest condition, the change in SVRI was inversely correlated with the change in GEDI.

Discussion

We found that the change in the GEDI and ITBI showed stronger correlation with the change in cardiac output during the closed chest condition than during the open

Table 3 Clinical parameters in the postoperative period

	Open chest (1) ($n = 47$)	Closed chest (2) ($n = 91$)	After extubation (3) ($n = 7$)	ANOVA (P value)	1 vs. 2 (P value)	1 vs. 3 (P value)	2 vs. 3 (P value)
Hematocrit (%)	35 ± 4	35 ± 3	33 ± 0	0.66			
Skin temperature (°C)	32.6 ± 1.8	34.5 ± 1.3	35.5 ± 1.3	<0.001	<0.001	<0.001	0.22
Core–peripheral temperature difference (°C)	4.0 ± 1.8	2.1 ± 1.3	1.1 ± 1.3	0.002	<0.001	<0.001	0.22
PaO_2 (mmHg)	154 ± 56	107 ± 38	106 ± 41	<0.001	<0.001	0.026	1
FiO_2	0.58 ± 0.14	0.56 ± 0.10	0.46 ± 0.07	0.065			
PaO_2/FiO_2 (mmHg)	282 ± 139	204 ± 91	264 ± 44	0.001	0.01	1	0.71

Data are expressed as mean ± standard deviation. Data are shown for the open and closed chest conditions and after extubation. The ANOVA test and the post hoc Bonferroni test were applied

ANOVA analysis of variance, PaO_2 arterial oxygen tension, FiO_2 fraction of inspired oxygen

Table 4 Correlation of the change in hemodynamic parameters

	Change in the parameters			
	Open chest		Closed chest	
	r value	*P* value	*r* value	*P* value
ΔCI-ΔSVI	0.88	0.022	0.96	<0.001
ΔCI-ΔSVRI	−0.45	0.38	−0.92	<0.001
ΔCI-ΔGEDI	0.93	0.006	0.75	0.055
ΔCI-ΔITBI	0.86	0.028	0.75	0.054
ΔELWI-ΔPVPI	0.58	0.42	0.91	0.012
ΔELWI-ΔGEDI	0.88	0.048	0.62	0.14

Correlations of the change in parameters between two consecutive measurements in the open and closed chest conditions are shown

CI cardiac index, *SVI* stroke volume index, *SVRI* systemic vascular resistance index, *GEDI* global end-diastolic index, *ITBI* intrathoracic blood volume index, *ELWI* extravascular lung water index, *PVPI* pulmonary-vascular permeability index

chest condition. Compared with postextubation levels, the CI and SVI were significantly lower and the heart rate and ELWI significantly higher in both the open and closed chest conditions. The measured values differed from the adult values previously reported by the manufacturer.

Continuous postoperative assessment of pediatric patients still is based on heart rate, pressure values, poorly validated clinical signs, and intermittent bedside echocardiographic measurements [26]. Compared with PiCCO values, clinical assessments underestimate CI and overestimate GEDI and SVRI [3]. Capillary refill times and core–peripheral temperature differences predict vascular resistance inaccurately. Moreover, hypothermia and vasoactive medications strongly influence the accuracy of these measurements [3, 26]. The "snapshot" view of echocardiography also is inadequate for continuous assessment of cardiac status in the immediate postoperative period. Moreover, it is operator dependent, requiring skilled staff.

The TPTD technique has been validated [25], and application of this method has spread in pediatric intensive care. However, normal values for pediatric patients under special conditions are not yet known [22].

One strength of our study was its relatively homogeneous study population. We considered the values measured after extubation to be "normal" for this population because patients with adequate breathing were stable from a cardiorespiratory standpoint. For these patients, the CI and especially the SVI values were at the lower limit of the normal pediatric and adult values provided by the manufacturer [4, 10, 21, 24].

Previous studies in experimental and clinical settings also have reported lower GEDI and ITBI values and a higher ELWI value for pediatric patients [4, 10, 19–21]. However, the age of the populations under study has ranged from infants to children, and the underlying cardiac diseases have been heterogeneous.

Based on our findings, we assume that low GEDI and high ELWI values should instead be attributed to an age-related difference, not to special characteristics of pediatric patients or a false software algorithm [13]. Neonates seem to have a higher tolerance to ELWI.

The physiology of circulation in neonates and infants is markedly different from that of adults [17]. Whereas the normal CI is 3 to 5 l/min/m^2 in both adult and pediatric patients, the normal stroke volume is 5 ml in neonates and 10 ml in 6-month-old infants, which means that the SVI in this population is 25 to 35% lower than that of adults [7, 15]. Therefore, children are able to achieve the same CI only with a 20 to 30% faster heart rate.

In the case of incipient low cardiac output, the mean arterial pressure still will be in the normal range because compensatory mechanisms in pediatric heart failure are accompanied by increases in heart rate or systemic vascular resistance [8], as observed in our study. Therefore, pressure monitoring in the absence of volume measurements may not be sufficiently informative [23].

Preload is a main determinant of cardiac output. Thus, measuring and optimizing the filling volume is essential in the treatment of cardiac failure. In adult [5] and pediatric studies [11, 21], central venous or pulmonary artery wedge pressure have correlated poorly with cardiac output, whereas GEDI and ITBI have strongly correlated with cardiac output.

In contrast, Cecchetti et al. [2] found that these relationships were apparent only for patients with hemorrhagic and cardiogenic shock [2]. The weaker association between the change in GEDI and the change in CI values in the closed chest condition can be explained by the previous finding that stroke volume does not increase if the baseline GEDI value is already high [14]. Additionally, we have found that increases in the GEDI value are associated with increases in the ELWI value in the open chest condition. This finding can be attributed to the fact that absolute hypovolemia is relatively uncommon in neonates and aggressive volume administration can lead to myocardial dysfunction and edema, particularly after cardiac surgery with cardiopulmonary bypass [9, 16]. The improvement in the hemodynamic parameters is entirely expected as the myocardium recovers.

The power of this study was limited by its limited enrollment. However, the study still makes a contribution by analyzing TPTD measurements in a homogeneous patient population including age, type of congenital heart disease, and method of corrective surgery. The applied statistical analysis avoided violating the test assumption of independent measurements. Further assessments of different cardiac anomalies in various age groups are warranted [12].

In summary, our findings have shown that the normal values of hemodynamic parameters in neonates after cardiac surgery with cardiopulmonary bypass are different from those of adults and other pediatric patients. Additionally, the values and the correlation of certain parameters also differed in the open and closed chest conditions and after extubation.

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