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Original Article

Core to toe temperature gradient during early post cardiac surgery period does not correlate with cardiac output in pediatric population

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ABSTRACT :

Hypothesis: Core to toe temperature gradient measured during early post-operative phase will not correlate with oxygen extraction ratio, a surrogate marker for Cardiac Output.

Materials and Method: This is a prospective observational study in pediatric cardiac intensive care unit, at Hamad General Hospital, Doha Qatar. Patients who underwent biventricular repair on cardio-pulmonary bypass were included. At hour 1, 4, 8 and 12 post surgery, core to toe temperature gradient was recorded. At similar time intervals, Oxygen extraction ratio (OER) was calculated using formula SaO2 – SvO2/ SaO2 x 100, where SaO2 is systemic arterial saturations and SvO2 is mixed venous (central) saturations.

Results: There were total of 99 patients enrolled in the study. The median age was 10.93 months (range 1.93 -176.7 months). Male: Female ratio was 1.1:1. At each of 1,4, 8 and 12 hours, Pearson's pairwise correlation coefficient (r) was calculated between oxygen extraction ratio and core-toe temperature gradient. The associated confidence interval, coefficient of determination (r2) and p-value are: [1-hour: r =0.0565 (-0.1512 to 0.2595), r2=0.0032 p=0.5 [4-hour: r = 0.2094 (0.0024 to 0.3992), r2=0.0439, p=0.047], [8-hour: r = 0.2113 (0.0079 to 0.3979), r2=0.0446, p= 0.042], [12 hour: r =0.2776 (0.0672 to 0.4643), r2=0.0771, p = 0.010]. There was no correlation between the core to toe temperature gradient and oxygen extraction ratio at the first hour mark and a weak correlation was observed at the 4 hour, 8 hour and 12 hour mark.

Conclusions: The core to toe temperature gradient does not correlate with the oxygen extraction ratio (surrogate marker of cardiac output) during the early post-operative phase in pediatric patients following cardiac surgery under cardiopulmonary bypass. There are multiple factors effecting this relationship and need further studies.

Keywords : Core toe temperature gradient, oxygen extraction ratio; peripheral perfusion, cardiac output, congenital heart defects, cardiopulmonary bypass, serum lactate, skin temperature, rectal temperature

Introduction:

Peripheral temperature has been used as a tool for assessing hydration status and cardiovascular reserve in critically sick children for a long time.[1] Continuous metabolic activities in the body generate heat which is dissipated to the atmosphere in order to maintain homeostasis. One of the effective ways of heat dissipation is by promoting skin perfusion causing heat to be eliminated to the atmosphere by conduction, convection and radiation. Whenever there is a fall in cardiac output, humoral responses will prioritize blood flow to vital organs like kidney and brain at the expense of skin, subcutaneous tissue and muscles. In a low cardiac output situation, the continuous heat generation at the core and the fall in skin temperature therefore significantly results in widening of core-toe temperature gradient. Medial side of the great toe has been used as a preferred site of monitoring skin temperature.[2] Normal skin temperature, measured objectively using a standard skin probe lies between 33 and 34 degree Celsius (°C), whereas core temperature typically ranges between 36.5 and 37.5 °C. Peripheral perfusion is considered to be adequate if the temperature difference between the core and the skin is < 3 to 4°C. [3, 4]

Serial measurement of mixed venous oxygen saturation is useful in the care of critically ill patients and it is regarded as an index of cardiac output and overall tissue perfusion [5, 6]. Venous saturation obtained from superior venae cava (SVC) is considered as a surrogate of mixed venous saturation in many intensive care settings [7,8,9] and it represents the end result of both oxygen delivery and consumption at the tissue level.

Oxygen Extraction Ratio (OER) is the fractional uptake of oxygen from the capillary bed. It is derived as the ratio of oxygen uptake to oxygen delivery. The final derived formula for calculation of OER is = (SaO_2 – SvO_2/ SaO_2) x 100 where SaO_2 is systemic

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arterial saturations and SvO2 is superior venae cave saturation. The normal value of oxygen extraction ratio is 22 -32 % .[10]

The uptake of oxygen from the microcirculation is a set point that is maintained by adjusting the extraction ratio to match changes in oxygen delivery. If central venous saturation falls below 60% a decrease in oxygen delivery and/or an increase in oxygen consumption should be suspected. When central venous saturation falls below 40%, the body's ability to compensate is limited, and oxygen is relatively unavailable for use by the tissues.

Core to toe temperature gradient has been shown to be an easy, valuable, and inexpensive monitor of tissue perfusion in critically ill adults and children and also following cardiac surgery. [11,12] However, a large number of studies especially from pediatric intensive care literature have strongly questioned the value of core to toe temperature gradient as a marker of cardiac output. [2, 13] Most of these studies have used thermo dilution techniques and Doppler echocardiography for measuring cardiac output to correlate it with core to toe temperature gradient. [2, 13, 14] Thermo dilution technique in pediatric patients has its own limitations and requires to have presence of pulmonary artery catheter.[15, 16] Doppler echo technique is not accurate in patients with congenital heart defects due to marked variation in the size of left ventricular outflow tract compared to age and sex matched controls and it has significant performer dependency [17, 18]. In pediatric cardiac surgical patients, Doppler echo therefore does not reliably represent absolute cardiac output values. [17] Oxygen extraction ratio is the fractional uptake of oxygen from the capillary bed and therefore is a surrogate of cardiac output at tissue level. It is easily calculated from routine monitoring indices of a postoperative cardiac patient.

We therefore hypothesize that core to toe temperature gradient measured in early post-operative phase will not correlate with oxygen extraction ratio measured at the same time intervals.

In order to validate or invalidate core to toe temperature gradient as a marker of cardiac output, we used the principle of mixed venous saturation rather than other measures for assessment of cardiac output including thermodilution / doppler technique.

Material and Methods:

Longitudinal observational study conducted in the pediatric cardiac intensive care unit (PICU). This study was approved by the Institutional Review Board at Hamad Medical Corporation Doha, Qatar.

Pediatric patients with congenital heart defects who had biventricular repair under cardiopulmonary bypass were included. Patients who had single ventricle physiology, patients who could have heat loss by other mechanisms like open chest, active cooling, peritoneal dialysis and patients on extra corporeal life support were excluded.

Following induction of anesthesia, a radial or femoral arterial cannula was introduced for sampling arterial blood and monitoring during surgery. Central venous access was obtained using triple lumen venous catheter placed in the right internal jugular vein and its position was confirmed to be at the junction of SVC (superior vena cava) and right atrium by a chest X-ray.

Core temperature was measured using temperature probe (Philips: 21075A, $\pm 0.1^0$C) placed in the rectum and peripheral (skin) temperature was measured using a standard skin temperature probe (Philips: 21091A, $\pm 0.1^0$ C) applied at the medial side of the great toe. Core to toe temperature gradient is the difference between rectal temperature and the skin temperature. Arterial and venous blood gases were analyzed using Roche-Omni-S COBAS B221 which was calibrated on daily basis. In case a femoral arterial cannula was inserted, the skin temperature probe was put on great toe on the side opposite to the arterial cannula (to avoid underestimation of skin temperature due to the vasospasm likely to develop on the side of insertion of arterial cannula). Ambient temperature was maintained at 22 °C. Patients were covered with a cotton blanket to minimize heat loss by convection or radiation and they were not actively warmed under a warmer following surgery.

The data recorded included cardiopulmonary bypass time, aortic cross clamp time, inotropes and/or vasodilators used, arterial blood gas, venous blood gas, core temperature, toe temperature, serum lactate and base excess at 1, 4, 8 and 12 hours mark after admission to PICU.

Pearson's (pairwise) correlation (including 95% CIs (confidence intervals), coefficients of determination

and p-value were used to describe the correlation between the outcome variables. The statistics package JMP, version 8.1 (SAS Institute, USA) was used for all analyses. Scatterplots were produced between the principal outcome variables using the scientific graphics package ORIGIN v8.1 (Microcal Inc); Origin was also used to produce all other graphs. P value < 0.05 was considered statistically significant.

Results:

We enrolled total of 99 patients. The median age of patients was 10.93 months (range 1.93-176.7 months) and the mean age was 38.8 months. Male: Female ratio was 1.1. The mean bypass time, cross clamp time was 88.23+/- 46.6 minutes and 53.62+/- 33.67 minutes respectively. Diagnosis and associated anomalies are described in Table-1.

Table 1 : Primary heart defect and associated abnormalities

Basic pathology	Number	Other associated lesions
VSD (ventricular septal defect)	24	DCRV-2, Down Syndrome- 2
TOF (Tetrology of Fallot)	21	Down Syndrome 3
ASD (Atrial septal defect)	18	
AVCD (Atrioventricular canal defect)	11	Down Syndrome 8
DORV(Double outlet right ventricle)	3	
PAVCD (Partial AVCD)	5	
PS (pulmonary stenosis)	3	
ASD, PDA (Patent ductus arteriosus)	2	
ASD, VSD, PDA	2	
Supra valvar aortic stenosis	2	William Syndrome -1
TAPVD(total anomalous pulmonary venous drainage)	2	
PAPVD (partial anomalous pulmonary venous drainage)	2	
Multiple VSD	1	
d-transposition of great arteries	1	
Truncus arteriosus	1	
Shone complex	1	

Relationship between core to toe temperature gradient and oxygen extraction ratio was correlated using Pearson's (pairwise) correlation coefficient. At each of one, four, eight and twelve hours, Pearson's pairwise correlation coefficient was calculated between oxygen extraction ratio and core-toe temperature gradient, along with its associated confidence interval, coefficient of determination and p-value. There was no correlation between the core to toe temperature gradient and oxygen extraction ratio at the first hour mark and a weak correlation was observed at the 4 hour, 8 hour and 12 hour mark as described in Table 2.

Table 2: Correlation between core-toe temperature gradient and oxygen extraction ratio at 1, 4, 8 and 12 hour

Time	Sample (N)	r, CI	r 2	P value
1 hour	N=91	r = 0.0565 (-0.1512-0.2595)	2=0.0032,	p=0.5944
4-hour	N=90	r = 0.2094 (0.0024-0.3992)	r2=0.0439	p=0.0476
8-hour	N=93	r = 0.2113 (0.0079-0.3979)	r2=0.0446	p=0.0421
12-hour	N=84	r = 0.2776 (0.0672-0.4643)	r2=0.0771	p=0.0106

N = Sample size, r =correlation coefficient, CI= confidence interval r2 = coefficient of determination.

Patients were divided in to 4 groups based on the post-operative use of vasoactive drugs. The main purpose of this classification into 4 groups was to reduce the confounding effect due to medication use. Group 1(N=36) included patients who received neither adrenergic drugs nor milrinone, group 2(N=30) received only milrinone, group 3(N=28) received both adrenergic drugs and milrinone/phentolamine and the group4 (N=5) included only those who received adrenergic drugs. The adrenergic drug used was adrenaline in majority of the patients.

Pearson's pairwise correlation coefficient was calculated for each group between core to toe temperature gradient oxygen extraction ratio at 1, 4, 8 and 12 hours mark, along with its associated confidence interval, coefficient of determination and

p-value (Table 3) (figure 1). There was no statistically significant correlation between core to toe temperature gradient and oxygen extraction ratio in between the groups. Note that group 4 correlations (N=5) was not done because sample-size was too small for meaningful subgroup analysis.

A multiple linear regression analysis of age, bypass time, cross clamp time, lactate and base excess level did not show any compounding effect on the correlation between core to toe temperature gradient and oxygen extraction ratio.

Table 3: Correlation between core-toe temperature gradient and oxygen extraction ratio at 1,4,8 and 12 hours among the subgroups

	1 hour	4 hour	8 hour	12 hour
Group 1	N=33 r=0.04, (-0.30, 0.38) r 2=0.0018,P=0.81	N=30 r=-0.098, (-0.44, 0.27) r2=0.0096, p=0.6065	N=33 r= .239, (-0.11,0.53) r2=0.0573 p=0.1798	N=26 r=0.25, (-0.14, 0.58) r2=0.0648 p=0.2093
Group 2	N=26 r=0.08, (-0.31, 0.45) r2=0.0068 p=0.6889	N=29 r=-0.29, (-0.08, 0.59) r2=0.0845, p=0.1260	N=21 r= 0.14 (-0.24, 0.48) r2=0.0182, p=0.4718	N=28 r=0.30, (-0.07, 0.60) r2=0.0921 p=0.1165
Group 3	N=27 r= -0.33 (-0.63, 0.05) r2=0.1090 p=0.0927	N=26 r= 0.13, (-0.26, 0.49) r2=0.0180 p=0.5136	N=26 r= 0.19, (-0.21, 0.53) r2=0.0363, p=0.3513	N=25 r= 0.34,(-0.05, 0.65) r2=0.1260 p=0.0904

N = Sample size, r =correlation coefficient, CI= confidence interval r2 = coefficient of determination

At the same time, there was no statistically significant correlation between core to toe temperature gradient and serum lactate level and base excess level at 1, 4, 8 and 12 hour mark (secondary outcomes of the study).

Discussion:

A patient with warm extremities generally gives an assurance of better hemodynamic status than a patient with cold extremities. Use of peripheral temperature and core to peripheral skin temperature gradient has been used as a guide to assess circulatory status in clinical practice. [2,11,19] Following pediatric cardiac surgery, sophisticated monitoring devices like continuous central venous saturation monitoring and near infra-red spectroscopy are being increasingly used in intensive care units. However, skin temperature is still being used by many as an indirect indicator of cardiac output.[20, 21] Several studies especially from pediatric intensive care have questioned the value of core-toe temperature gradient as a marker of cardiac output. [3, 13, 14, 22]

The presence of cold skin on its own is nonspecific and may have many other causes. Many factors can affect peripheral temperature and hence the core-peripheral temperature gradient. Peripheral vasoconstriction can occur as a response to cold environment, hypovolemia or pain.[14] More over during early post-operative phase after cardio-pulmonary bypass, most patients have increased vascular tone that leads to decreased perfusion to peripheral tissue and decreased skin temperature.[24] In pediatric population, no strong correlations between core to toe temperature gradient and cardiovascular status have been reported from various studies. [3, 13, 14] We believe that core to toe temperature gradient correlation with cardiac output is very weak during early post-operative phase due to above mentioned multiple factors.

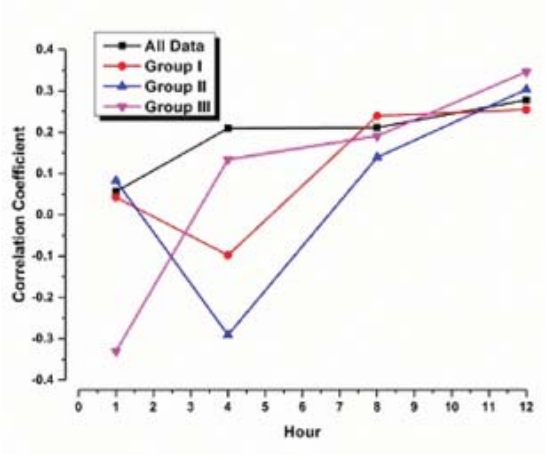

Figure 1: Comparison of correlation coefficients among subgroups and total patients at 1, 4, 8 and 12 hours.

In our study we observed no correlation between core to toe temperature gradient and oxygen extraction ratio at 1hour mark and a weak correlation at 4,8 and 12 hours marks in a relatively homogeneous cohort of patients and this is observed when the subjects are considered as a single cohort.

In post cardiac surgical patients, a variety of factors can alter skin temperature and core- toe temperature gradient. Hypothermia induced during cardiopulmonary bypass followed by subsequent rewarming results in a heat debt and the creation of large temperature gradient between the body's core and peripheries because the deeper tissues rewarm first. [24] Secondly non-physiological blood flow during cardiopulmonary bypass itself induces a generalized vaso-constrictive state and its effect can continue during the post-operative period.[24] Thirdly, use of vasoactive drugs following cardiac surgery can affect peripheral temperature and hence core- toe temperature gradient. Finally, reliability of core-toe temperature gradient is also affected by post perfusion syndrome seen in post cardiac surgical patients which is characterized by low systemic vascular resistance, increased cardiac output, and hypotension [25]

We believe that following the use of cardiopulmonary bypass, multiple factors come into play that have got an impact on peripheral circulation and hence on thermoregulatory mechanisms, thus making core-toe temperature gradient an unreliable marker of cardiac output during the initial 12 hours after surgery. However, since our study is limited to the initial 12hours after surgery, we couldn't demonstrate how the correlation between oxygen extraction ratio and core-toe temperature gradient progressed beyond the initial 12 hours.

In contrast to other studies, we have tried to minimize the confounding effect of vasoactive agents on peripheral circulation, by categorizing the patients in to 4 different groups (Group 1, 2,3 & 4). However, we couldn't demonstrate any statistical significance during the entire study period among the subgroups.

Many studies have demonstrated a weak correlation between core- toe temperature gradient and cardiac output in children following congenital heart surgery. Ryan et al studied the correlation between core-peripheral temperature gradient and cardiac index measured by thermodilution technique in pediatric cardiac surgical patients. Their conclusions were similar to ours demonstrating only a weak correlation between core-peripheral temperature gradient and cardiac index ($r = –0.28$, $P < .001$), and systemic vascular resistance index ($r = 0.38$, $P < 0.01$).[14] Tibby et al studied great toe and rectal temperature measurement and compared it with cardiac output measured by thermo-dilution method in a group of post cardiac surgery and septic patients. They observed that core-peripheral temperature gradient correlated poorly with cardiac index and systemic vascular resistance index in postoperative cardiac surgical patients.[18] Murdoch et al, compared core-peripheral temperature gradient with cardiac output which was measured using thermo dilution method and found that core-peripheral temperature gradient does not reflect cardiac index.[13] Seki et al studied pediatric and adult patients following cardiac surgery. They measured temperature over patella, ankle, great toe, rectum and axilla to measure core-peripheral temperature gradient and used indicator dilution technique to measure cardiac output. Weak correlation was seen between skin temperature and cardiac output ($r = 0.41$).[20] However, their use of thermo-dilution technique to measure cardiac output necessitates the use of pulmonary artery catheters and has limitations in patients with tricuspid regurgitation. [15, 16]

Butt et al studied 136 patients comparing core-peripheral temperature gradient core-peripheral temperature gradient with cardiac index measured by doppler echocardiogram. They found that cardiac index does not correlate with core-peripheral temperature gradient, hence absolute peripheral temperature or core-peripheral temperature gradient should not be used as an index of cardiac output or systemic vascular resistance in children.[3] They used phenoxybenzamine liberally in their patients and did not categorize patients according to the use of vasoactive drugs there by allowing confounding factors to influence their results. Furthermore, their use of doppler technique to measure cardiac output in pediatric population is less accurate due to marked performer dependency and variation in the size of left ventricular outflow tract compared to age and sex matched controls [17, 18]

There are some studies that have been done in pediatric and mixed groups of adult and pediatric patients support the use of core- toe temperature gradient as a marker of cardiac output. Schey et al studied skin temperature and core-peripheral temperature gradient with cardiac output measured by thermodilution technique and reported that core-peripheral temperature gradient as a noninvasive marker of cardiac output and perfusion in adult post cardiac surgical patients.[26] Kirklin et al after studying pediatric patients following cardiac surgery reported that skin temperature of the foot (by subjective assessment) and pedal pulses reflect adequacy of cardiac output and they used indicator dilution technique to measure the cardiac output. [27]
Based on our study core-toe temperature gradient is not a reliable marker of cardiac output in the first 12 hours after cardiac surgery.

Limitation of the Study: Our patient cohort included only two ventricle physiology patients following surgery, and one of the exclusion criteria in our study was those patients with open chest and patients on peritoneal dialysis. We believe, in doing so; we have excluded a group of patients who are hemodynamically unstable, and theoretically those patients may have higher oxygen extraction ratio which is significant enough to have its impact on peripheral temperature dynamics. After excluding those high-risk patients i.e. patients on peritoneal dialysis and patients with open chest, most of our included patients in the study had cardiac output in normal range. In other words, fall in cardiac output leading to peripheral temperature variation was minimal in the study population which might have affected the co-relation between core to peripheral temperature gradient and OER.
Our study was also limited to the initial 12 hours following surgery; hence we cannot assess how this correlation was progressed after 12 hours.

Conclusion:

The core to toe temperature gradient does not co-relate with the oxygen extraction ratio during the early post-operative phase in pediatric patients following surgery under cardiopulmonary bypass. There are multiple factors effecting this relationship and need further studies.

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Conflict of Interest: None
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