Clinical parameters to predict adverse outcomes in patients with parallel circulation with a Blalock-Taussig-Thomas shunt

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Research Article

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Abstract

Introduction

In patients with parallel circulation, early risk factor identification for adverse outcome can facilitate prevention. This retrospective study compares vital sign parameters, near infrared spectroscopy, central venous pressure, hemoglobin, serum lactate, and vasoinotrope score in the first 48 hours between those with parallel circulation with and without a composite adverse outcome after Blalock-Taussig-Thomas shunt placement.

Methods

Hemodynamic variables were collected at the following postoperative timepoints: admission to the cardiac intensive care unit, 6 hours, 12 hours, 24 hours, and 48 hours after. Outcomes of interest included cardiopulmonary arrest, need for extracorporeal membrane oxygenation, or inpatient mortality during the admission.

Results

Of the 39 neonates in the study, 10 experienced the composite outcome. Four variables had a receiver operator curve analysis area under the curve of > 0.60. The resulting risk score was as follows, with 1 point being assigned for a central venous pressure greater than 7.8, 1 point for a serum lactate greater than 1.8, renal oxygen extraction ratio of greater than 32, and vasoinotrope score of greater than 8.7. A score of 0 was associated with a 0% risk of the composite outcome, a score of 1 or 2 a 15% risk, and a score of 3 or 4 a 60% risk.

Conclusion

A combination of increased central venous pressure, increased serum lactate, increased renal oxygen extraction ratio, and increased vasoinotrope score are highly accurately associated with risk of cardiopulmonary arrest, need for extracorporeal membrane oxygenation, or inpatient mortality after a Blalock-Taussig-Thomas shunt in patients with parallel circulation.

Introduction

Congenital heart disease and associated cardiac surgeries are associated with increased morbidity and mortality. Parallel circulation, wherein the saturation of blood in the pulmonary and systemic circulations is equal, is associated with even greater risk due to the dependence of the arterial saturation on the systemic venous saturation as well as the interdependence of flow in the pulmonary and systemic circulations [1].
In those with parallel circulation, it is important to be vigilant for changes that may indicate increasing risk for cardiopulmonary arrest, as early detection can help facilitate early mitigation and prevention. Early detection requires identification of risk factors associated with cardiopulmonary arrest and subsequent monitoring of these identified risk factors [2–4]. Unfortunately, there is a paucity of data for such risk factors in children with specific congenital malformations of the heart or specific physiologies. This includes those with parallel circulation after Blalock-Taussig-Thomas shunt placement.

This study’s primary aim was to compare cerebral and renal oxygen extraction ratio in the first 48 hours between those with parallel circulation with and without a composite outcome of cardiopulmonary arrest, need for extracorporeal membrane oxygenation, and inpatient mortality after Blalock-Taussig-Thomas shunt placement. Secondary aims included comparing other hemodynamic and clinical variables between those with and without the composite outcome.

**Material And Methods**

**Study design**

This study was a single-center retrospective study including neonates with parallel circulation who underwent a Blalock-Taussig-Thomas shunt placement. Institutional review board approval was received for this study and the study is in concordance with the Helsinki declaration.

**Patient identification**

All neonates with parallel circulation who underwent a Blalock-Taussig-Thomas shunt placement between January 2013 and January 2022 were identified.

**Variables and timepoints of interest**

The following hemodynamic variables were collected: heart rate (beats per minute), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), central venous pressure (mmHg), respiratory rate (respirations per minute), pulse oximetry (%), and cerebral near infrared spectroscopy (%), renal near infrared spectroscopy (%). Hemoglobin and serum lactate were collected from arterial blood gases. Vasoinotrope score was also collected.

The following variables were calculated: cerebral oxygen extraction ratio and renal oxygen extraction ratio. The cerebral oxygen extraction ratio was calculated as: \( \frac{\text{pulse oximetry} - \text{cerebral near infrared spectroscopy}}{\text{pulse oximetry}} \). The renal oxygen extraction ratio was calculated as: \( \frac{\text{pulse oximetry} - \text{renal near infrared spectroscopy}}{\text{pulse oximetry}} \).

Data was collected or calculated immediately after admission to the cardiac intensive care unit after the Blalock-Taussig-Thomas shunt placement, 6 hours after, 12 hours after, 24 hours, after and 48 hours after. A smoothened average was then calculated for each collected and calculated variable.
Outcomes of interest included cardiopulmonary arrest, need for extracorporeal membrane oxygenation, or inpatient mortality at any point during the Blalock-Taussig-Thomas shunt admission. A composite outcome with the individual outcomes was developed. Thus, hemodynamic and clinical variables for the first 48 hours were used to model outcome for the entirety of the admission. This was done purposely as the first 48 hours is the period in which there is generally most hemodynamic instability.

**Statistical analyses**

Descriptive variables were described as absolute frequency and percentage while continuous variables were described as median and range. Patients were divided into two groups: those with and without the composite outcome. Variables of interest were compared between the two groups using a Fisher exact text for descriptive variables and a Mann-Whitney-U test for continuous variables.

Receiver operator curve analyses were conducted for all continuous variables to determine the accuracy of each in predicting the composite outcome. Those with an area under the curve of greater than 0.60 were then identified. For all variables with an area under the curve of greater than 0.60, an optimal cutoff point was identified using area from the diagonal line. Each of these identified variables with an area under the curve of greater than 0.60 was then converted into a binary variable based on the cutoff value. A score was then assigned using the presence of each binary variable. For instance, if four such variables were identified than the maximum score for the risk assessment tool was 4. This risk score was created to provide a risk assessment tool that could be simply calculated in a clinical situation.

A separate receiver operator curve analysis was conducted to determine the utility of this risk assessment tool in identifying those with the composite outcome.

**Results**

A total of 39 patients were included in the analyses. Of these, 10 (26%) experienced the composite outcome. There was no significant difference in gender or age at surgery.

By Mann-Whitney-U tests, significant differences were noted in central venous pressure, serum lactate, renal oxygen extraction ratio, and vasoinotrope score (Table 1). Central venous pressure was higher in those with the composite outcome, serum lactate was higher in those with the composite outcome, renal oxygen extraction ratio was higher in those with the composite outcome, and the vasoinotrope score was greater in those with the composite outcome.
Table 1
Comparison of average values over the course of the admission between those who did and did not experience the composite endpoint

<table>
<thead>
<tr>
<th></th>
<th>No composite endpoint</th>
<th>Composite endpoint</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at surgery (days)</td>
<td>6.0 (2.0 to 11.0)</td>
<td>5.5 (1.0 to 14.0)</td>
<td>0.33</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>159 (142 to 178)</td>
<td>164 (137 to 173)</td>
<td>0.94</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>81 (60 to 94)</td>
<td>67 (56 to 90)</td>
<td>0.08</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>36 (26 to 45)</td>
<td>39 (31 to 46)</td>
<td>0.17</td>
</tr>
<tr>
<td>Central venous pressure (mmHg)</td>
<td>7 (4 to 11)</td>
<td>8 (6 to 13)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hemoglobin (mg/dl)</td>
<td>14.0 (11.6 to 18.3)</td>
<td>13.7 (11.6 to 18.2)</td>
<td>0.82</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>1.5 (0.9 to 6.3)</td>
<td>2.2 (1.5 to 8.9)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Pulse oximetry (%)</td>
<td>85 (76 to 95)</td>
<td>85 (78 to 95)</td>
<td>0.53</td>
</tr>
<tr>
<td>Cerebral oxygen extraction ratio (%)</td>
<td>37 (19 to 56)</td>
<td>36 (20 to 52)</td>
<td>0.71</td>
</tr>
<tr>
<td>Renal oxygen extraction ratio (%)</td>
<td>21 (5 to 46)</td>
<td>33 (10 to 62)</td>
<td>0.04</td>
</tr>
<tr>
<td>Vasoinotrope score</td>
<td>5 (0 to 15)</td>
<td>10 (4 to 17)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

Table 2
Results of receiver operator curve analyses. Only variables with an area under the curve of greater than 0.60 are included

<table>
<thead>
<tr>
<th></th>
<th>Area under the curve</th>
<th>Cutoff value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum lactate (mmol/L)</td>
<td>0.81</td>
<td>1.8</td>
</tr>
<tr>
<td>Central venous pressure (mmHg)</td>
<td>0.71</td>
<td>7.8</td>
</tr>
<tr>
<td>Renal oxygen extraction ratio (%)</td>
<td>0.69</td>
<td>32</td>
</tr>
<tr>
<td>Vasoinotrope score</td>
<td>0.76</td>
<td>8.7</td>
</tr>
</tbody>
</table>

Receiver operator curve analyses demonstrated that central venous pressure (0.71), serum lactate (0.81), renal oxygen extraction ratio (0.69), and vasoinotrope score (0.76) had the highest areas under the curve. Optimal cutoff values were found to be less than 7.8 mmHg for central venous pressure, less than 1.8 mmol/L for serum lactate, less than 32 for renal oxygen extraction ratio, and less than 8.7 for vasoinotrope score.

Thus, the resulting risk score was as follows with 1 point being assigned for a central venous pressure greater than 7.8, 1 point for a serum lactate greater than 1.8, renal oxygen extraction ratio of greater than 32, and vasoinotrope score of greater than 8.7. The resulting score had an area under the curve of 0.84
with an optimal cutoff of 2.5. A score of 0 was associated with a 0% risk of the composite outcome, a score of 1 or 2 a 15% risk, and a score of 3 or 4 a 60% risk.

Discussion

This study demonstrates that smoothened averages for hemodynamic and clinical values in the first 48 hours after a Blalock-Taussig shunt in children with parallel circulation are associated with risk of cardiopulmonary arrest, need for extracorporeal membrane oxygenation, or inpatient mortality. More specifically, combination of a central venous pressure greater than 7.8 mmHg, a serum lactate greater than 1.8, a renal oxygen extraction ratio of greater than 32, and a vasoinotrope score greater than 8.7 were associated with increased risk.

Such a score can be helpful in identifying those at high risk and increasing situational awareness. Identification of patients at high risk for cardiopulmonary arrest can be helpful in intensive care units to assign cardiopulmonary resuscitation roles, prophylactically. Early identification of patients at high risk for cardiopulmonary arrest can also facilitate having certain medications at the bedside in case of clinical deterioration, specifically lower dose epinephrine. Such situation awareness and medication availability has been associated with decreases in cardiopulmonary arrests.

Previous studies have identified factors associated with cardiopulmonary arrest in critically ill children. Previous studies have demonstrated ST-segment variability, vasoinotrope score, higher inadequate oxygen delivery index, venous saturation, serum lactate, cerebral dysfunction by electroencephalography, a history of a previous cardiac arrest, specific cardiac lesions, and specific cardiac surgeries among others [3–16]. Risk factors for mortality have often mirrored the risk factors for cardiac arrest.

Compared to previous studies, the current study aimed to identify postoperative hemodynamics and routine clinical variables in a more static, binary approach so that the findings can be more easily applied at the bedside.

The cardiovascular system’s sole purpose is to ensure that adequate oxygen is delivered to other organs. Oxygen content is a function of arterial oxygen saturation, hemoglobin, and partial pressure of oxygen while. Cardiac output the quotient of oxygen consumption and the arteriovenous oxygen content difference. Systemic oxygen delivery is then the product of both oxygen content and cardiac output. Looking at systemic oxygen delivery broadly, arterial oxygen saturation, hemoglobin, partial pressure of oxygen, and venous oxygen saturation become the major components. From a more pragmatic standpoint, systemic oxygen delivery is proportional to the arteriovenous oxygen saturation difference [17]. From this it is not surprising that renal oxygen extraction ratio and serum lactate were found to be significantly associated with adverse outcomes in the current study, as both are markers of the adequacy of systemic oxygen delivery. Vasoinotrope score likely represents human action in response to the perceived inadequacy in systemic oxygen delivery. As for central venous pressure, central venous pressure does increase as a response to lower cardiac output, thus increased central venous pressure
preceding cardiorespiratory arrest may be an indicator of lower cardiac output and subsequently lower systemic oxygen delivery [18].

Also of note is that blood pressure was not found to be a predictor of adverse events. Blood pressure is the product of flow and systemic vascular resistance and thus increase in systemic vascular resistance alone can lead to increased blood pressure. When this happens, and flow is not increased, then cardiac output is not increased. Thus, if systemic vascular resistance is not being monitored, then blood pressure is not a good surrogate for cardiac output. Often, blood pressure is augmented by increasing systemic vascular resistance and not cardiac output, thus not increasing systemic oxygen delivery [19, 20]. In fact, increasing systemic vascular resistance may lead to no change or a decrease in the adequacy of systemic oxygen delivery [21, 22]. Low systemic vascular resistance with high cardiac output has been demonstrated as the physiologic state associated with the lowest likelihood to be associated with poor outcomes in parallel circulation [23]. Thus, interventions to decrease systemic vascular resistance and increase cardiac output lead to optimization of systemic oxygen delivery and clinical outcome [24–37]. In the current study, systemic oxygen delivery was quantified using the renal oxygen extraction ratio calculated using renal near infrared spectroscopy. Inferior caval vein saturations are also helpful in this regard as inferior caval vein saturation and renal near infrared spectroscopy correlate well [38–40].

While these data are clinically applicable and may be helpful in early identification of those at with parallel circulation with a high risk for cardiopulmonary arrest after Blalock-Taussig-Thomas shunt placement, they are not without their limitations. The exact cutoffs for variables defined here may be variable at different institutions due to institution specific nuances in management. However, the overall physiologic states that are more favorable shouldn’t change and it is unlikely that the absolute cutoffs are greatly different. The absolute frequency of the composite outcome was also relatively low which does limit the effect size that could be detected. Nonetheless, statistically significant differences were identified.

**Conclusion**

A combination of increased central venous pressure, increased serum lactate, increased renal oxygen extraction ratio, and increased vasoinotrope score are highly accurately associated with risk of cardiopulmonary arrest, need for extracorporeal membrane oxygenation, or inpatient mortality after a Blalock-Taussig-Thomas shunt in patients with parallel circulation.

**Declarations**

All authors contributed to the study conception and design. Material preparation and data collection were performed by Saloni Sheth. Data analysis was performed by Rohit S. Loomba. The manuscript was drafted by both Rohit S. Loomba and Saloni Sheth. All authors read and approved the final manuscript.
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The authors have no conflicts of interest to disclose.

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