Analysis of Hemodynamics During Blood Transfusion Utilizing High-Fidelity Realtime Telemetry After the Arterial Switch Operation

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Abstract

Background

Red blood cell transfusions (pRBCTx) are given to many patients after congenital heart surgery to augment hemodynamics, but our current understanding is limited by hourly vital sign recordings. The goal of this study was to analyze hemodynamic parameters surrounding pRBCTx with high-fidelity, real-time telemetry monitoring.

Methods

This is a retrospective review of patients after the arterial switch operation receiving post-operative pRBCTx from 07/15/2020-07/15/2021. Continuous, 1-Hz vital sign data were analyzed in five-minute intervals up to six hours before, four hours during, and six hours after pRBCTx—up to 57,600 data points per pRBCTx. Oxygen delivery was assessed using pre- and post-pRBCTx laboratory data, hourly renal and cerebral near-infrared spectroscopy, sedation medication doses, and vasoactive-inotropic scores.

Results

Six patients, median age 8.5[IQR:5–22] days and weight 3.1[IQR:2.8–3.2]kg, underwent the arterial switch operation. There were 10 pRBCTx administered with a median dose of 10[IQR:10–15]mL/kg over 169[IQR:110–190]min; at median post-operative hour 36[IQR:10–40]. There was an increase in systolic and mean arterial blood pressures by 5-12.5% at three hours after pRBCTx, but returned to baseline at six hours. There were no changes in heart rate or oxygen saturations. Renal spectroscopy increased by 6.2% after pRBCTx. There were no changes in ventilation, sedation, vasoactive support, or laboratory variables related to oxygen delivery.

Conclusions

pRBCTx given to arterial switch operation patients increases arterial blood pressures three hours post-pRBCTx without evidence of sustained effects at six hours. High-fidelity real-time data can be used to better assess hemodynamic parameters after congenital heart surgery and provide nuanced, patient-specific care.

Introduction

Postoperative management of children with congenital heart disease (CHD) requires careful monitoring of hemodynamics and optimization of oxygen delivery (DO$_2$) through mechanical ventilation, vasoactive support, and management of volume status. Packed red blood cell transfusions (pRBCTx) are frequently utilized to augment DO$_2$ by increasing hemoglobin (Hb) and oxygen-carrying capacity, replacing blood loss, or increasing preload$^{1,2}$. However, unique CHD physiologies place patients at high risk of pRBCTx-specific adverse outcomes including: fluid overload, ventricular dysfunction, prolonged mechanical
ventilation, elevated vascular resistance, and immune sensitization\textsuperscript{1,3–5}. Use of pRBCTx is therefore provider-dependent and variable with minimal evidence-based guidelines for their use. In 2018, the Transfusion and Anemia Expertise Initiative published guidelines recommending pRBCTx with Hb < 7 g/dL after biventricular CHD repair and Hb ≥ 9 g/dL after staged single ventricle palliation based on moderate and weak-quality evidence, respectively\textsuperscript{5}. While they recommended considering the overall clinical context and not exclusively hemoglobin concentration, no specific hemodynamic parameters were outlined or recommended\textsuperscript{5}. Other publications investigating hemodynamic changes are limited to retrospective studies of \textit{hourly} vital signs and binary pre/post-pRBCTx data variables, which are prone to errors, omissions, and outliers\textsuperscript{1,6–11}. With Sickbay™ (Medical Informatics Corp, Houston, TX), a surveillance and analytics platform that collects high-fidelity, continuous hemodynamic data from routinely-used bedside devices\textsuperscript{12}, we can analyze \textit{second-to-second} changes in vital signs. This technology has been previously used to assess medical interventions such as intravenous acetaminophen or sotalol in CHD populations\textsuperscript{13–16}.

Accordingly, we sought to describe the real-time hemodynamic changes surrounding pRBCTx in patients with dextro-transposition of the great arteries (d-TGA) undergoing the arterial switch operation (ASO)\textsuperscript{17}. We chose the ASO cohort given their relative homogeneity in preoperative diagnosis, demographics, and perioperative clinical course to help minimize potential confounding variables\textsuperscript{18}. By analyzing the hemodynamic parameters surrounding pRBCTx, we may better understand pRBCTx effect on hemodynamics and DO\textsubscript{2}.

**Patients and Methods**

**Study Structure and Data Sources**

The study was approved by the Institutional Review Board at The University of Texas at Austin (STUDY00001279, approved 11/11/2021). This is a retrospective review of patients who underwent ASO and received a postoperative pRBCTx at Dell Children’s Medical Center from 07/15/2020-07/15/2021. Our cardiac care unit’s Philips\textsuperscript{®} telemetry monitors (Koninklijke Philips N.V., Amsterdam, Netherlands) display heart rate (HR) calculated from electrocardiogram leads, oxygen saturations from pulse oximetry (SpO\textsubscript{2}), and systolic, diastolic and mean arterial blood pressures (ABP-S, ABP-D, and ABP-M), which are captured by Sickbay™ at 1-Hz for future analysis. There were three categories of data collected: 1) Sickbay™ data were collected up to 6hr prior to pRBCTx, during pRBCTx (up to 4h), and 6hrs after pRBCTx, 2) binary pre-and-post-pRBCTx laboratory data within 4h of pRBCTx, with data closest to the start or end time used, 3) cerebral and renal near-infrared spectroscopy (NIRS), continuous infusion medication doses, and vasoactive-inotropic scores (VIS) were collected hourly from medical records up to 6hr before and 6hr after pRBCTx\textsuperscript{19}.

**Statistical analysis**
Descriptive statistics were used for clinical characteristics and labs. Continuous variables are reported as median [interquartile range (IQR)]. For hourly recorded data, the mean values over the 6hr pre-pRBCTx and post-pRBCTx for each patient were compiled, and a mean difference was calculated. Median pre-to-post-pRBCTx labs were compared using Wilcoxon signed-rank test.

Sickbay™ data were analyzed using previously published methods\textsuperscript{14, 15}. Data was cleaned by filtering out all pRBCTx/time pairs with missing data. The time axis for each pRBCTx was standardized so that time “0-min” corresponded to the recorded pRBCTx starting time. Pre-transfusion baselines were taken to be their average values prior to pRBCTx, excluding the 10 minutes leading up to the pRBCTx to account for possible error between documented and actual start time. A non-overlapping, five-minute moving average was applied to the time series for each event to filter out monitor “noise”. Hemodynamic variables in these intervals were converted into percentage changes relative to their pRBCTx-specific baseline. Aggregated hemodynamic data was then plotted along with 95% confidence intervals (95%CI). Additionally, to provide additional context, binary comparisons of baseline hemodynamic values one hour prior to pRBCTx compared to hemodynamic values at 3hr and 6hr after pRBCTx using paired Wilcoxon signed rank tests. All statistical analyses were performed using R and RStudio\textsuperscript{20}.

**Results**

**Patient Population and Clinical Course**

There were six patients who underwent ASO at median 8.5[IQR:5–22] days and 3.1[IQR:2.8–3.2]kg and received a total of 10 pRBCTx post-operatively (Table 1). One patient had prior pulmonary artery banding at day of life 4 at 3.4kg because of difficulty visualizing ventricular septal defects and challenging coronary anatomy. This allowed the patient to grow prior to ASO, which was performed at 3 months and 4.85kg. Median pRBCTx prescriptions were 10[IQR:10–15]mL/kg, over 169[IQR:110–190]min at median post-operative hour 36[IQR:10–40]. Indications for pRBCTx in caregiver notes included: four for hypotension, three for anemia (without delineated hemoglobin values), and three were not specified. There were no adverse events directly related to pRBCTx. All patients survived to discharge, with zero 30-day readmissions.
Table 1
Baseline Demographics and Transfusion Characteristics

<table>
<thead>
<tr>
<th>Factor</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age at surgery (days) [IQR]</td>
<td>8.5[5–22]</td>
</tr>
<tr>
<td>Median weight at surgery (kg) [IQR]</td>
<td>3.1[2.8–3.2]</td>
</tr>
<tr>
<td>Female (n)</td>
<td>2</td>
</tr>
<tr>
<td>Anatomic Diagnosis (n)</td>
<td>4</td>
</tr>
<tr>
<td>d-TGA with ventricular septal defect</td>
<td>2</td>
</tr>
<tr>
<td>d-TGA with intact ventricular septum</td>
<td></td>
</tr>
<tr>
<td>Median hospital length of stay (days) [IQR]</td>
<td>39[24–43]</td>
</tr>
<tr>
<td>Survival to discharge (n)</td>
<td>6</td>
</tr>
<tr>
<td>Median pRBCTx dose (mL/kg) [IQR]</td>
<td>10[10–15]</td>
</tr>
<tr>
<td>Median pRBCTx duration (min) [IQR]</td>
<td>169[110–190]</td>
</tr>
<tr>
<td>Median post-operative hour until pRBCTx [IQR]</td>
<td>36[10–40]</td>
</tr>
</tbody>
</table>

Key: IQR—interquartile range; pRBCTx—packed red blood cell transfusion

Hemodynamic Analysis

One of 10 transfusions was excluded from high-frequency hemodynamic analysis due to data error that was secondary to faulty collection-device linkage to Sickbay™ storage. Hemodynamic data represented up to 57,600 continuous data points (1 data point per second over a maximum of 16hr) per vital sign per pRBCTx. Figure 1 displays aggregated mean change in HR and SpO₂ and Fig. 2 displays the aggregate change in ABP-S, ABP-D, and ABP-M over time for all pRBCTx events. After pRBCTx initiation, all three ABP parameters crossed 95%CI at ~3hr by 7-12.5%, with return to established baseline by 6hr. HR trended downward gradually after pRBCTx, though never crossing 95%CI. To determine if these trends were statistically different, comparison of baseline hemodynamic values were compared to those at 3hr and 6hr. At 3hr, there was a 5.1 ± 2.2% (p = 0.039) increase in ABP-S and 5.4 ± 2.1% (p = 0.039) increase in ABP-M, but no changes in HR, ABP-D, or SpO2 at 3hr and no changes in any hemodynamic parameters compared to baseline at 6hr after pRBCTx (Table 3). Concurrently, there were no changes in ventilator support, continuous sedating infusion, and vasoactive support before and after pRBCTx (Table 2).
Table 2
Pre- and Post-Transfusion Laboratory Values, Peripheral Oxygenation, Ventilation, and Vasoactive Support

<table>
<thead>
<tr>
<th>Lab value</th>
<th>Pre-Transfusion (median [IQR])</th>
<th>Post-Transfusion (median [IQR])</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>10.4[9–11]</td>
<td>12[11.6–12.3]</td>
<td>0.021</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>31.5[26.5–33.4]</td>
<td>35.5[34.6–36.6]</td>
<td>0.027</td>
</tr>
<tr>
<td>$P_aCO_2$ (mmHg)</td>
<td>37.7[35.8–40.1]</td>
<td>37.4[36.0–42.5]</td>
<td>0.383</td>
</tr>
<tr>
<td>$P_aO_2$ (mmHg)</td>
<td>130.3[124.4–157.6]</td>
<td>125[82.7–144.3]</td>
<td>0.25</td>
</tr>
<tr>
<td>$HCO_3^-$ (mEq/L)</td>
<td>22.1[20.7–22.8]</td>
<td>21.9[21.3–22.5]</td>
<td>0.78</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>1.24[1.16–1.34]</td>
<td>1.38[1.11–1.90]</td>
<td>0.74</td>
</tr>
<tr>
<td>Factor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Near-infrared spectroscopy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal (%)</td>
<td>67.4</td>
<td>73.6</td>
<td>0.039</td>
</tr>
<tr>
<td>Cerebral (%)</td>
<td>66.3</td>
<td>72.3</td>
<td>0.055</td>
</tr>
<tr>
<td>Ventilator</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$FiO_2$ (%)</td>
<td>43.1</td>
<td>39</td>
<td>0.353</td>
</tr>
<tr>
<td>Tidal volume (mL)</td>
<td>29</td>
<td>28.1</td>
<td>0.181</td>
</tr>
<tr>
<td>PEEP (cmH$_2$O)</td>
<td>5</td>
<td>5</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexmedetomidine (mcg/kg/min)</td>
<td>0.3</td>
<td>0.3</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Epinephrine*100 (mcg/kg/min)</td>
<td>2.9</td>
<td>2.8</td>
<td>0.834</td>
</tr>
<tr>
<td>Vasopressin*10000 (units/kg/min)</td>
<td>1.2</td>
<td>1.2</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Calcium chloride (mEq/mL/min)</td>
<td>6.8</td>
<td>6.3</td>
<td>0.59</td>
</tr>
<tr>
<td>Vasoactive-Inotrope Score</td>
<td>4.3</td>
<td>4.2</td>
<td>0.722</td>
</tr>
</tbody>
</table>
### Table 3
Comparisons of Hemodynamic Parameters at Baseline, + 3 Hours, and + 6 Hours After Red Blood Cell Transfusion*

<table>
<thead>
<tr>
<th>Measure</th>
<th>Baseline (mean ± SD)</th>
<th>3 Hours (mean ± SD)</th>
<th>% Change at 3 Hours (% ± SE)</th>
<th>p value</th>
<th>6 Hours (mean ± SD)</th>
<th>% Change at 6 Hours (% ± SE)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>137.5 ± 6.3</td>
<td>136.0 ± 6.9</td>
<td>-1.3 ± 1.1%</td>
<td>0.38</td>
<td>132.3 ± 7.4</td>
<td>-5.1 ± 2.6%</td>
<td>0.2</td>
</tr>
<tr>
<td>ABP-S (mmHg)</td>
<td>80.1 ± 5.2</td>
<td>83.8 ± 5.0</td>
<td>5.1 ± 2.2%</td>
<td>0.039</td>
<td>79.1 ± 4.6</td>
<td>-2 ± 4.5%</td>
<td>0.38</td>
</tr>
<tr>
<td>ABP-D (mmHg)</td>
<td>41.0 ± 2.7</td>
<td>43.1 ± 3.1</td>
<td>5.2 ± 2.4%</td>
<td>0.078</td>
<td>42.7 ± 3.5</td>
<td>-1.3 ± 4.3%</td>
<td>0.64</td>
</tr>
<tr>
<td>ABP-M (mmHg)</td>
<td>56.8 ± 3.6</td>
<td>59.7 ± 3.6</td>
<td>5.4 ± 2.1%</td>
<td>0.039</td>
<td>58.6 ± 3.8</td>
<td>0.5 ± 4.1%</td>
<td>0.84</td>
</tr>
<tr>
<td>SpO₂ (%)</td>
<td>99.4 ± 0.3</td>
<td>99.3 ± 0.33</td>
<td>-0.1 ± 0.3%</td>
<td>0.67</td>
<td>99.3 ± 0.2</td>
<td>-0.2 ± 0.3%</td>
<td>0.8</td>
</tr>
</tbody>
</table>

*p-values are computed from a paired Wilcoxon signed rank test, comparing change at 3 hours to baseline and 6 hours to baseline, respectively. Key: ABP-S/D/M—arterial blood pressure-systolic/diastolic/mean; HR—heart rate; SD—standard deviation, SE—standard error; SpO₂—oxygen saturations

### Markers of DO₂

Pre-to-post-pRBCTx labs demonstrated an increase in median Hb from 10.4[IQR: 9–11] to 12[IQR: 11.6–12.3] (p = 0.021) and median hematocrit from 31.5[IQR: 26.5–33.4] to 35.5[IQR: 34.6–36.6] (p = 0.027), but there were no differences in arterial blood gas markers of DO₂, such as pH, PaO₂, or lactate (Table 2). Hourly renal and cerebral NIRS, a surrogate marker of end-organ oxygen extraction and venous saturations, are plotted in Fig. 3. Renal NIRS showed an overall increasing trajectory, with an average increase of 6.2% (from 67.4% before pRBCTx to 73.6% after pRBCTx, p = 0.039). Cerebral NIRS had a similar increase in saturations by 6%, but did not amount to statistical significance (p = 0.055).

### Comment

To the authors’ knowledge, this represents the first attempt to analyze the hemodynamic parameters of CHD patients during pRBCTx using high-frequency telemetry. Utilizing the Sickbay™ platform, physiologic vital signs were continuously captured as data points and waveforms (approximately 1-Hz), which allowed for analysis of more than 50,000 data points per vital sign per pRBCTx. This pilot study found an initial increase in ABPs of 5-12.5% from baseline at roughly 3hr after pRBCTx with a subsequent return to baseline at 6hr. This data, which requires further study, can help create nuanced, patient-specific care paths and better understand the hemodynamic changes that may occur surrounding pRBCTx.
pRBCTx is utilized frequently in patients after congenital heart surgery for a variety of reasons such as anemia, volume resuscitation, and blood pressure augmentation; however, there are few guidelines to help clinicians determine when to transfuse. Understanding the effects of pRBCTx from a hemodynamic perspective may help provide justification for pRBCTx. With high-frequency, real-time hemodynamic data, we demonstrate a declining HR trend relative to baseline and at least initial improvement in ABPs at 3hr after pRBCTx. These trends, along with improvement in peripheral NIRS by 6%, and in the absence of clinically significant changes in VIS or ventilator support, may represent improvements in cardiac output and decrease in cardiac metabolic demand, but would require further verification.

A term neonate status post ASO with ABP-M of 35-40mmHg, a 5-12.5% increase would correspond to a 2-5mmHg improvement, providing a considerable increase in overall perfusion pressure. The ability to augment hemodynamics directly after pRBCTx—perhaps instead of interventions such as increasing vasoactive or ventilator support—could have clinical implications for many CHD patients. Especially for those who cannot tolerate high FiO$_2$ or vasoactive infusion doses, pRBCTx may offer another therapeutic option for augmentation of vascular pressure and DO$_2$.

However, as reported above, the hemodynamic changes observed were not sustained at 6hr post-pRBCTx on either continuous Sickbay™ analysis or binary comparison to baseline and did not affect VIS or respiratory support. With the time-limited acute effects seen in this study combined with previous evidence showing no differences in overall outcomes between “restrictive” and “liberal” pRBCTx thresholds, this helps provide evidence for patient-specific transfusion goals instead of set hemoglobin/hematocrit levels$^{3–6, 21}$. Limiting pRBCTx exposure has been shown to increase overall survival and decrease immune sensitization, so the decision to transfuse should be tailored to the patient’s specific needs$^3, 5$.

There were limitations to this study, as we retrospectively analyzed a relatively small number of pRBCTx at a single center. The small sample size necessitates further validation of our results, despite robust hemodynamic data in a relatively homogeneous and hemodynamically stable population. In the analyzed time windows, there may be variables influencing patient hemodynamics outside of those studied. The defined time window may not correspond to a clinical belief of a sustained response to pRBCTx. NIRS and vasoactive infusion doses were hourly data instead of at the same high-frequency vital sign data. Additionally, while we chose the ASO cohort given its relative patient homogeneity, this limits the generalizability of these results to other CHD populations$^{15}$. pRBCTx decision-making was at the treatment team discretion, the rationale for which was not always documented. Our approach to analysis of the Sickbay™ data also was limited by a lack of clinical correlation: we presumed significant “high” and “low” pressure waveform deflections to be non-physiologic changes secondary to “artifact” from patient or provider manipulation.

**Conclusions**
In this pilot study investigating high-fidelity, real-time hemodynamic parameters surrounding pRBCTx in CHD, pRBCTx resulted in short-term increases in ABP-M and ABP-S by 5–12% relative to baseline after ASO without significant changes in vasoactive or ventilatory support. Future studies with a larger number of patients are needed to determine if these findings are generalizable to other patients after ASO or other CHD patients. Through high-frequency hemodynamic analysis we may better understand the hemodynamic effects during pRBCTx or other interventions to allow for precise quantification and patient-specific treatment after congenital cardiac surgery.

**Abbreviations**

95%CI—95% confidence interval

ABP-S/D/M—arterial blood pressure-systolic/diastolic/mean

ASO—arterial switch operation

CHD—congenital heart disease

d-TGA—dextro-transposition of the great arteries

IQR—interquartile range

NIRS—near-infrared spectroscopy

pRBCTx—packed red blood cell transfusion

VIS—vasoactive inotropic score

**Declarations**

None of the authors have competing interests to report.

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**Informed consent:** This study was approved under the auspice of the Institutional Review Board at The University of Texas at Austin (STUDY00001279, approved on 11/11/2021)

**Meeting Presentation:** The abstract from this work was presented at the Pediatric Cardiac Intensive Care Society Annual Meeting, Miami, FL, December 15-18, 2022.

**Acknowledgements:** Supported in part by the National Science Foundation under Grant No. DMS-2144933.

**References**


Figures
Figure 1

Sickbay™ Aggregate Percent Change from Baseline – HR (1a) and SpO₂ (1b). The central line represents the aggregate percent change from baseline of all nine red blood cell transfusion using 1 data point per second per red blood cell transfusion with the surrounding grey area representing the 95% confidence interval. HR trends began declining at 3hr after red blood cell transfusion but never eclipse 95% confidence interval. Key: HR—heart rate; SpO₂—oxygen saturations
Figure 2

Sickbay™ Aggregate Percent Change from Baseline – ABP-S (2a), ABP-D (2b), and ABP-M (2c). The central line represents the aggregate percent change from baseline of all nine pRBCTx using 1 data point per second per red blood cell transfusion with the surrounding grey area representing the 95% confidence interval. The 95% confidence interval is eclipsed at roughly 3hr after red blood cell transfusion corresponding to 7-12.5% increase from baseline with decrease to original baseline at 6hr. Key: ABP-D—
diastolic arterial blood pressure; ABP-M—mean arterial blood pressure; ABP-S—systolic arterial blood pressure

Figure 3
Cerebral and Renal NIRS Over Time. Lines correspond to hourly data from each of the red blood cell transfusion events included in final analysis. Key: NIRS—near-infrared spectroscopy