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PII: S2666-2736(23)00228-0
DOI: https://doi.org/10.1016/j.xjon.2023.08.013
Reference: XJON 859

To appear in: JTCVS Open

Received Date: 4 May 2023
Accepted Date: 18 August 2023

Please cite this article as: Patel K, Dan Y, Kunselman AR, Clark JB, Myers JL, Ündar A, The Effects of Pulsatile vs. Non-Pulsatile Flow on Cerebral Pulsatility Index, Mean Flow Velocity at the Middle Cerebral Artery, Regional Cerebral Oxygen Saturation, Cerebral Gaseous Microemboli Counts, and Short-term Clinical Outcomes in Congenital Heart Surgery Patients, JTCVS Open (2023), doi: https://doi.org/10.1016/j.xjon.2023.08.013.

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Impact of Perfusion Modalities on Cerebral Hemodynamics and Clinical Outcomes in Pediatric Congenital Heart Surgery Patients

This retrospective review included 284 consecutive pediatric patients undergoing congenital cardiac surgery with CPB support utilizing only 8/10/12 Fr arterial cannulae.

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<td>Intubation Time (hours) (median [IQR - 75% percentile])</td>
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Although the pulsatility index was better maintained in the pulsatile group, mean cerebral blood flow velocity, regional cerebral oxygen saturation levels, GME counts, and clinical outcomes were statistically similar with the “non-pulsatile” group. These findings suggest that while pulsatile perfusion represents a safe modality for CPB support, its use may not translate into demonstrably superior short-term clinical outcomes.
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Krishna Patel, BS1,2*, Yongwook Dan, MD1,2*, Allen R. Kunselman, MA1,3, Joseph B. Clark, MD1,2, John L. Myers, MD1,2 Akif Ündar, PhD1,2,4

*Krishna Patel and Yongwook Dan contributed equally to this work.

Penn State Hershey Pediatric Cardiovascular Research Center, Departments of Pediatrics1, Surgery2, Public Health Sciences3, and Biomedical Engineering4, Penn State College of Medicine, Penn State Health Children’s Hospital, Hershey, PA, USA.

Conflict of Interest (COI) Statement: The author(s) declare no financial disclosures/conflicts of interest regarding the authorship and/or publication of this article.

Funding Statement: This project was supported by several seed funds from the Pediatric Cardiovascular Research Center at the Penn State Health Children’s Hospital and Penn State College of Medicine.
Glossary of Abbreviations

CPB: cardiopulmonary bypass

GME: gaseous microemboli

ICU: intensive care unit

LOS: length of stay

MAP: mean arterial pressure

MCA: middle cerebral artery

MFV: mean flow velocity

MUF: modified ultrafiltration

NIRS: near-infrared spectroscopy

PI: pulsatility index

rSO₂: regional cerebral oxygen saturation

STAT: Society of Thoracic Surgeons European Association for Cardio-Thoracic Surgery

Congenital Heart Surgery

TCD: transcranial doppler

VAVD: vacuum-assisted venous drainage

XC: cross-clamp
Central Picture Legend

Central Message
Pulsatile flow during pediatric cardiopulmonary bypass does not demonstrate superior clinical outcomes over non-pulsatile flow for patients with similar characteristics.

Perspective Statement
While pulsatile flow during cardiopulmonary bypass may offer more physiologic perfusion, definitive evidence is lacking that this advantage translates to improved postoperative outcomes compared to non-pulsatile flow. This study evaluates the impact of perfusion modalities on cerebral hemodynamics and clinical outcomes in pediatric congenital cardiac surgery patients.
Structured Abstract

Objective: The objective of this retrospective review was to evaluate whether pulsatile flow improves cerebral hemodynamics and clinical outcomes in pediatric congenital cardiac surgery patients.

Methods: This retrospective study included 284 pediatric patients undergoing congenital cardiac surgery with cardiopulmonary bypass (CPB) support utilizing non-pulsatile (n=152) or pulsatile (n=132) flow. Intraoperative cerebral gaseous microemboli (GME) counts, pulsatility index, and mean blood flow velocity at the right middle cerebral artery were assessed using transcranial Doppler ultrasound. Clinical outcomes were compared between groups.

Results: Patient demographics and CPB characteristics between groups were similar. While the pulsatility index during aortic cross-clamping was consistently higher in the pulsatile group (p<0.05), a significant degree of pulsatility was also observed in the non-pulsatile group. No significant differences in mean cerebral blood flow velocity, regional cerebral oxygen saturation, or GME counts were observed between the perfusion modality groups. Clinical outcomes including intubation duration, intensive care unit and hospital length of stay, and mortality within 180 days were similar between groups.

Conclusions: Although the pulsatility index was greater in the pulsatile group, other measures of intraoperative cerebral perfusion and short-term outcomes were similar to the non-pulsatile group. These findings suggest that while pulsatile perfusion represents a safe modality for CPB support, its use may not translate into detectably superior clinical outcomes.

Word Count: 212
Keywords:

Congenital heart surgery, cardiopulmonary bypass, pulsatility index, cerebral hemodynamics, gaseous microemboli, pulsatile flow, clinical outcomes
Graphical Abstract:

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Introduction

Significant progress has been made over the decades toward decreasing the morbidity and mortality experienced by congenital heart surgery patients (1). However, there remains substantial variability in outcomes due to a multitude of potential factors including sequelae arising from cardiopulmonary bypass (CPB) support (2). One major persistent source of morbidity after congenital heart surgery is neurologic injury (3-7). Suboptimal preoperative cerebral hemodynamics, including abnormal cerebral blood flow and cerebral oxygen extraction, may be a significant contributor within this patient population (8). In addition, different intraoperative CPB techniques and equipment may lead to the delivery of substantial amounts of gaseous microemboli (GME) to the brain, in addition to impaired cerebral hemodynamics (9-12). Therefore, continuous monitoring of cerebral perfusion in the intraoperative setting has been utilized by many programs to identify and attempt to mitigate potential causes of brain injury. Transcranial Doppler (TCD) is one such tool which can provide non-invasive and real-time measurements of cerebral blood flow velocity, emboli counts, and pulsatility index (PI) in the middle cerebral artery (MCA) and has been routinely utilized in all pediatric CPB operations at our institution for nearly 20 years (9,13).

There is no definitive evidence that supports the superiority of pulsatile flow over non-pulsatile flow during CPB in improving postoperative outcomes in congenital heart surgery patients. More importantly, the safety of pulsatile perfusion using 8Fr, 10Fr, and 12Fr arterial cannulas on cerebral hemodynamics has yet to be documented.

This retrospective study used several unique approaches and quantification techniques to demonstrate the safety of pulsatile and non-pulsatile perfusion using 8Fr, 10Fr, and 12Fr arterial cannulas. We utilized TCD intraoperatively to: (a) calculate the PI and quantify the pulsatility of flow in the MCA; (b) continuously monitor cerebral hemodynamics by measuring cerebral blood
flow velocity at the MCA; (c) record the GME counts delivered to the MCA in real time; (d) and quantify different modalities of perfusion waveforms on the arterial line of the CPB circuitry using a custom-made TCD probe housing unit.

The objective of this retrospective review was to evaluate the impact of pulsatile perfusion on cerebral blood flow velocities, GME counts, cerebral PI at the MCA, and clinical outcomes in pediatric congenital heart surgery patients when compared to non-pulsatile perfusion, while demonstrating its safety in 8Fr, 10Fr and 12Fr arterial cannulas. We hypothesized that pulsatile perfusion would significantly improve cerebral hemodynamics and clinical outcomes.

Methods:

Experimental design:

This retrospective review utilized institutional data from the Pediatric Cardiovascular Research Center at the Penn State Health Children’s Hospital and Penn State College of Medicine. The study protocol was last approved by the Institutional Review Board (IRB) on 07/13/2023 at Penn State College of Medicine (IRB No. PRAMS030476EP). Three hundred and eight-five patients who had a completed intraoperative neuromonitoring research data sheet between January 2009 and February 2014 were included in the analysis. Although 154 patients were included in the pulsatile group and 231 patients in the non-pulsatile group as surgeons’ preferences at the time of surgery, surgeons have blinded which patients have had a complete multi-modality neuromonitoring research datasheet for further analysis. We included an average of 75 patients (30 in the pulsatile and 45 in the non-pulsatile group) per year with a completed intraoperative multi-modality neuromonitoring research datasheet. Only three patients out of 385 were excluded due to incomplete or missing data sheets.
In the initial analysis of 382 patients, patients’ demographical data were significantly different between the groups, so it was impossible to make a meaningful comparison. Since our study focused on perfusion modalities, inclusion criteria in terms of arterial cannula sizes of 8Fr (n=51 (33.6%) in the NP, and n=45 (34.1%) in the P group), 10Fr (n=53 (34.9%) in NP, and n=52 (39.4%) in the P group), and 12Fr (n=48 (31.6% in the NP and n=35 (26.5%) in the P group) allowed us to create homogeneous groups for direct and meaningful comparison. The exclusion criteria included 98 pediatric patients (79 patients from NP group) (<18 years) with the following cannula sizes (6Fr = 16pts; 14Fr = 24 pts; 16Fr = 28pts; 18Fr = 22 pts; 20Fr = 7 pts; and 22Fr = 1 pt). The final cohort of consecutive patients who met all selection criteria (n = 284) was divided into two groups based on the perfusion modality used during CPB (non-pulsatile vs. pulsatile).

**Supplemental Methods:**

Each perfusion modality group was further subdivided based on mortality risk, which was calculated using the STAT 2020 Mortality Score and Categories (14). Patients in STAT mortality categories 1-3 were allotted to the “low/middle-risk” group, and patients in STAT mortality categories 4-5 were allotted to the “high-risk” group.

**Pulsatile flow settings:**

Patients in the pulsatile perfusion group underwent surgery with the following pump settings: 10% of the base flow, 20% of the pump head start point, and 80% of the pump head stop target. The pump rate was determined based on the patient’s weight: >15 kg = 90 beats/min; 7 to 15 kg = 100 beats/min; and <6.9 kg = 120 beats/min. Specific details regarding anesthesia and perfusion protocols were published previously (15) and are included in the Supplemental Methods.

**TCD:**
Intraoperative GME counts, PI measurements, and cerebral mean flow velocities (MFV) were measured at the right MCA and in the arterial line using a TCD (Pioneer TC8080; Nicolet Biomedical Inc., Madison, WI). The TCD device was placed anterior to the external auditory meatus and cephalad to the zygoma inside the right temporal window to collect information at the right MCA. PI was calculated using the difference between the maximum systolic blood flow velocity (Vmax) and the minimum diastolic (Vmin) blood flow velocity over the mean blood flow velocity (Vmean) (16).

\[
\text{PI} = \frac{V_{\text{max}} - V_{\text{min}}}{V_{\text{mean}}}
\]

Simultaneous M-mode and spectrogram readings were obtained using a 2-MHz transducer, and an insonation depth of 25-50 mm was utilized for assessment.

The mean flow velocity (MFV) was calculated by adding the End Diastolic Velocity (EDV) to one third of the difference between Peak Systolic Velocity (PSV) and EDV.

\[
\text{MFV} = \text{EDV} + \frac{1}{3} (\text{PSV} - \text{EDV})
\]

Near-Infrared Spectroscopy:

Near-infrared spectroscopy (NIRS) using an INVOS 5100B monitor (Somanetics, Troy, MI) was performed to assess regional cerebral oxygen saturation (rSO2). This device utilizes two near-infrared wavelengths of 730 nm and 805 nm to quantify the proportion of oxyhemoglobin to deoxyhemoglobin. Pediatric SomaSensors (Somanetics) were placed caudal to the level of the hairline on both the right and left side of the forehead following induction of anesthesia. During instances where spatial limitations prohibited the use of bilateral sensors, a single sensor was used for neuromonitoring. The rSO2 was measured by the NIRS machine at 5 second intervals. Intraoperative PI, mean flow velocity, and rSO2 measurements were collected at each of the
following time points: baseline pre-incision; initiation of CPB before aortic cross-clamp; 5, 20, 40, and 60 minutes after aortic cross-clamp; and cessation of CPB.

**Demographics and CPB Characteristics**

Patient demographics such as gender, age, weight, and height were collected. Additionally, CPB characteristics such as STAT mortality score, CPB time, perfusion modality, aortic cross-clamp time, pump flow index, arterial line pressure, vacuum-assisted venous drainage (VAVD) level, ultrafiltration, modified ultrafiltration (MUF), urine output during CPB, GME counts at the right MCA, and arterial cannula sizes were included in the study. Clinical outcomes assessed included intubation duration, intensive care unit (ICU) length of stay (LOS), hospital LOS, and short-term mortality within 180 days. PI in the right MCA and in the arterial line, mean flow velocity in the right MCA, and rSO₂ at various time points during CPB were also compared between non-pulsatile and pulsatile groups.

**Statistical analysis**

Unpaired t-tests were used to compare continuous demographic/characteristic and clinical outcome variables (e.g., age, weight, CPB time, aortic cross-clamp time, pump flow index, intubation time) between perfusion modalities. In the event the distributions did not meet parametric assumptions (e.g., normality), Wilcoxon rank-sum tests were used to compare these continuous variables (i.e., intubation time, ICU length of stay, and hospital length of stay) between perfusion modalities. Chi-square tests, or Fisher’s exact tests if the expected cell counts were small, were used to compare categorical demographic/characteristic and clinical outcome variables (e.g., gender and mortality within 180 days) between perfusion modalities. Pearson’s correlation coefficients were used to assess the strength of bivariate associations at various time points with respect to temperatures, PI - MCA, PI - arterial line, MFV – MCA, MAP, and NIRS – left cortical
hemisphere. Linear mixed effects models were used for continuous variables measured repeatedly over time (e.g., PI - MCA, PI - arterial line, MFV – MCA, MAP, and NIRS – left cortical hemisphere) to compare perfusion modalities at each time point. The linear mixed model accounts for the within-subject and between-subject variability inherent in repeated measurement designs. All hypotheses were two-sided and all analyses were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC).

Results:

Demographics and CPB Characteristics:

Patient demographics for overall non-pulsatile and pulsatile cohorts are reported in Table 1. There were no differences noted in overall demographics between the perfusion modality groups. A comparison of CPB characteristics between non-pulsatile and pulsatile cohorts is reported in Table 2. No significant differences were noted in CPB time, aortic cross-clamp time, pump flow index, VAVD levels, ultrafiltration volume, MUF volume, urine output during CPB, and distribution of arterial cannula size usage. Arterial line pressures were statistically higher in the non-pulsatile group (non-pulsatile 126.9 ± 3.0 mmHg vs. pulsatile 115.8 ± 1.9 mmHg, p=0.003). Non-pulsatile patients had a statistically similar number of GME counts delivered to the right MCA during CPB when compared to pulsatile patients (non-pulsatile 337 ± 74 vs. pulsatile 176 ± 47, p=0.079).

Pulsatility Index in the MCA and in the Arterial Line:

Figures 1 and 2 display PI measurements recorded at the right MCA (Fig. 1) and in the arterial line (Fig. 2) at various timepoints for each perfusion modality group stratified by arterial cannula sizes. PI in the arterial line was consistently higher in the pulsatile group compared to the non-pulsatile group during aortic cross-clamping for all arterial cannula sizes. PI at the right MCA
was significantly higher in the pulsatility group during aortic cross-clamping for the 8 Fr and 10 Fr arterial cannula groups. However, no differences could be noted in the PI between the perfusion modality groups for the 12 Fr arterial cannula. It was also noted that PI at the right MCA decreased significantly during CPB from baseline values for both pulsatile and non-pulsatile groups for all arterial cannula sizes. As expected, this decline was more pronounced in the non-pulsatile group. Additionally, PI in the right MCA returned to baseline values after CPB was terminated in both pulsatile and non-pulsatile groups for all arterial cannula sizes.

**Mean Flow Velocities:**

Figure 3 depicts the MFV recorded at the right MCA at various timepoints for each perfusion modality group stratified by arterial cannula sizes. MFV decreased in both perfusion modality groups during aortic cross-clamping compared to baseline values in patients using 8 Fr arterial cannulas. However, it was noted that MFV were maintained closer to baselines values in 10 and 12 Fr arterial cannula sizes during aortic cross-clamping. No significant differences in MFV between non-pulsatile and pulsatile groups during and after CPB for all arterial cannula sizes were noted.

**Regional Cerebral Oxygen Saturation:**

Figure 4 displays the rSO₂ in the left cortical hemisphere and the mean arterial pressure at various timepoints for both non-pulsatile and pulsatile groups. Mean arterial pressures decreased significantly during CPB and returned to values greater than baseline values once CPB was terminated for both perfusion modalities. However, no significant differences were observed in mean arterial pressures between the perfusion modality groups. Additionally, no differences in rSO₂ could be identified between the non-pulsatile and pulsatile perfusion groups.

**Correlation Coefficients among cerebral parameters and temperature:**
Pulsatility Index in the MCA does not have any relation with rSO\(_2\) levels but has weak relations (0.25 < r < 0.50, and p < 0.05) with MFV – MCA at several experimental stages (Supplemental Table 1). The PI-MCA has weak to moderate relations (0.5 < r < 0.75, p < 0.05) with the PI in the arterial line, but no relations with the mean arterial pressures (Supplemental Table 2).

The temperature has moderate reverse relations with the rSO\(_2\) levels, particularly with the 8Fr arterial cannula subgroup at all experimental stages during CPB. The temperature has weak relations with MFV – MCA but no relations with PI – MCA and PI in the arterial line. Temperature also had weak relations with the mean arterial pressures after aortic clamping. All detailed correlations at each experimental stage are presented in Supplementary Tables 3 and 4.

**Clinical Outcomes for Non-pulsatile vs. Pulsatile Patients:**

Clinical outcomes for each perfusion modality group are reported in Table 3. Patients in the non-pulsatile and pulsatile groups had similar intubation times (non-pulsatile 9.6 (6.3, 30.9) hours vs. pulsatile 9.4 (6.4, 28.4) hours, p=0.712), ICU LOS (non-pulsatile 2.8 (1.3, 5.5) days and pulsatile 2.0 (1.2, 4.0) days, p = 0.103) and hospital LOS (non-pulsatile 5.3 (3.4, 8.0) days vs. pulsatile 4.5 (3.4, 8.0) days, p=0.195). Additionally, no significant differences in mortality rates within 180 days were noted between the groups. The number and causes of mortalities within 180 days of operation based on STAT mortality categories are presented in Supplemental Table 5. The Number of Patients Utilizing Deep Hypothermic Circulatory Arrest, Antegrade Cerebral Perfusion, and Types of Operations are displayed in Supplemental Table 6.

**Supplemental Results based on STAT Risk-Stratification Analysis: Demographics and CPB Characteristics:**
Demographics, CPB characteristics, and GME counts for risk-stratified non-pulsatile and pulsatile patients are displayed in Supplemental Table 7. In the high-risk mortality group (STAT 4-5), patients with non-pulsatile perfusion demonstrated higher baseline mortality scores, aortic cross-clamp times, and CPB times. However, in the low/middle-risk mortality group (STAT 1-3), baseline mortality scores and CPB times were statistically similar between the non-pulsatile and pulsatile groups, whereas aortic cross-clamp times were shorter in the non-pulsatile group. Additionally, no statistical differences were noted in the GME counts between non-pulsatile and pulsatile perfusion in any mortality risk groups.

Supplemental Clinical Outcomes for Risk-Stratified Non-pulsatile vs. Pulsatile Patients:

Clinical outcomes for risk-stratified non-pulsatile and pulsatile patients are depicted in Supplemental Table 8. No differences in any clinical outcomes were identified between the perfusion groups in low/middle-risk patients. Analysis of clinical outcomes revealed similar intubation times (non-pulsatile 53.3 (28.4, 151.9) hours vs. pulsatile 28.6 (7.0, 68.4) hours, p=0.119), and ICU LOS (non-pulsatile 8.6 (2.9, 23.5) days vs. pulsatile 3.1 (1.9, 4.9) days, p=<0.060), and more extended hospital LOS (non-pulsatile 16.6 (11.7, 44.0) hours vs. pulsatile 7.3 (4.3, 11.6) days, p=0.014) in high-risk patients using non-pulsatile perfusion compared to high-risk patients using pulsatile perfusion. Additionally, no differences in mortality were observed between pulsatile and non-pulsatile perfusion in both risk groups.

Discussion

In this retrospective study, we made the following observations comparing cerebral hemodynamics and short-term clinical outcomes related to non-pulsatile and pulsatile flow. First, although the PI was significantly better maintained in the arterial line of the CPB circuit and the MCA in the pulsatile group when compared to the non-pulsatile group, a significant degree of
Pulsatility was also generated under conventional non-pulsatile perfusion. Second, pulsatile flow was not associated with any adverse effects regarding GME counts and arterial line pressures of the CPB circuitry. Third, cerebral blood flow velocity at the MCA and rSO$_2$ levels were similar between perfusion groups. Last, contrary to our initial hypothesis, intubation time, ICU LOS, hospital LOS, and mortality within 180 days were statistically similar between the two groups.

**PI:**

The PI was calculated as the difference between the maximum systolic blood flow velocity ($V_{max}$) and the minimum diastolic ($V_{min}$) blood flow velocity divided by the mean blood flow velocity ($V_{mean}$). Under 100% non-pulsatile flow conditions, the difference between systolic and diastolic blood flow velocities would be "0", and the pulsatility index would be zero. In our study, however, the pulsatility index during non-pulsatile CPB was between 0.4 to 0.6 in the right MCA (Baseline (pre-CPB) PI was 1.5) (Figure 1) and between 0.7 and 0.9 in the arterial line (Figure 2). These results clearly demonstrate that roller pumps under non-pulsatile flow are unable to generate 100% non-pulsatile flow with 8, 10, and 12 Fr arterial cannula for congenital heart surgery patients. Therefore, we acknowledge that our study compared two different pulsatile modalities rather than purely non-pulsatile vs. pulsatile perfusion. Nevertheless, the TCD is an excellent tool to not only monitor cerebral hemodynamics and gaseous microemboli counts, but also quantify perfusion modalities in the MCA and in the arterial line of the CPB circuitry for congenital heart surgery patients. While the observation of pulsatility under non-pulsatile settings is a limitation of the current study, this finding may represent a serendipitous, unintended consequence of the long-term efforts toward CPB circuit optimization and evolution which now provide highly efficient and effective levels of circulatory support.
Patients in the pulsatile group have a statistically similar number of GME counts delivered to the right MCA during CPB compared to non-pulsatile patients (176 ± 47 vs. 337 ± 74, p=0.079). Arterial line pressures were statistically lower in the pulsatile group, but this statistical difference may not be clinically relevant. These results demonstrate that pulsatile flow is safe for use during CPB procedures in congenital heart surgery patients.

In addition, we used an empiric approach to determine the pulsatility settings for this study. We used identical heart-lung machines for pulsatile and non-pulsatile perfusions. Therefore, the use of pulsatile perfusion does not lead to additional cost. Pulsatility frequency, pulsatility width, and base flow parameters were determined for this clinical study based on our previous in-vitro and in-vivo experiments, as well as pilot clinical trials (13, 17-19). We have already documented that the pulsatile flow settings of this study had no adverse outcomes in microemboli counts in the arterial line and MCA and plasma-free hemoglobin levels after CPB in our previous randomized clinical trial for pediatric congenital heart surgery patients, including neonates and infants (15).

**Mean Blood Flow Velocity, \( rSO_2 \), and Short-term Clinical Outcomes:**

Cerebral perfusion and other clinical outcomes were similar between groups, including MFV in the right MCA and \( rSO_2 \) in the left cortical hemisphere before, during, and after CPB, intubation time, ICU LOS, and hospital LOS. To assess for other possible differences between subgroups, we further analyzed the data using STAT 2020 procedural-based mortality scores and categories (14). In the low-middle risk patients (STAT 1-3), pulsatile (n=121) and non-pulsatile (n=135) groups had an identical mortality score of 0.22 ± 0.01 (Supplemental Table 1). However, the high-risk (STAT 4-5) patients in the non-pulsatile (n=17) group had statistically higher mortality scores than patients in the pulsatile (n=11) group (1.8 ± 0.2 vs. 1.2 ± 0.2, p<0.05). Thus,
the significantly higher mortality scores may be the reason for higher intubation time, ICU, and hospital length of stay in the non-pulsatile group observed in this study (supplemental Table 2).

Contrary to our initial hypothesis, there were no benefits of pulsatile perfusion in terms of short-term clinical outcomes in our study. The majority of patients were included in the low-middle risk (n=256) than high-risk (n=28) category (n=28). This may be the major reason the groups had no significant differences due to lower risk categories subjected to less injury. In addition, perfusion modalities may have little or no impact on primary clinical outcomes regarding intubation durations, ICU LOS, and hospital LOS selected for this study.

Conclusions

Intraoperative TCD, both non-invasive and real-time, helped gather unique data on cerebral blood flow velocity and gaseous microemboli counts at the middle cerebral artery of congenital heart surgery patients during CPB procedures. To precisely quantify different perfusion modalities for a direct comparison, TCD flow probes can be used to record the pulsatility index at the middle cerebral artery and in the arterial line of the CPB circuitry. In this retrospective study, a significant degree of pulsatility, as calculated by the pulsatility index, was generated at the middle cerebral artery and the arterial line under both pulsatile and "non-pulsatile" perfusion. Therefore, this study compared low vs. high pulsatility rather than purely pulsatile vs. non-pulsatile flow. Without a TCD device and flow probes, it would not be possible to quantify precisely pulsatile and "non-pulsatile" modalities in terms of pulsatility index.

The results of this study indicate that while pulsatile perfusion is a safe modality for CPB support, its use may not translate into demonstrably superior short-term clinical outcomes (Figure
Further studies with multicenter data comparing non-pulsatile and pulsatile flow are necessary to provide a more conclusive answer.
References:


Tables:

**Table 1. Demographics for Pulsatile vs. Non-pulsatile Neonatal/Pediatric Patients Utilizing 8, 10, and 12 Fr Arterial Cannulae (Mean ± SEM)**

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<tr>
<td>Age (months)</td>
<td>17.5 ± 1.8</td>
<td>13.5 ± 1.5</td>
<td>0.09</td>
</tr>
<tr>
<td>Neonates, n (%)</td>
<td>20 (13.2%)</td>
<td>21 (15.9%)</td>
<td></td>
</tr>
<tr>
<td>Pediatric, n (%)</td>
<td>132 (86.8%)</td>
<td>111 (84.1%)</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>8.4 ± 0.4</td>
<td>7.7 ± 0.5</td>
<td>0.27</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>70.9 ± 1.6</td>
<td>67.5 ± 1.6</td>
<td>0.14</td>
</tr>
<tr>
<td>STAT Mortality Category</td>
<td>0.40 ± 0.05</td>
<td>0.31 ± 0.03</td>
<td>0.14</td>
</tr>
<tr>
<td>Mortality Category 1, n (%)</td>
<td>88 (57.9%)</td>
<td>74 (56.1%)</td>
<td></td>
</tr>
<tr>
<td>Mortality Category 2, n (%)</td>
<td>36 (23.7%)</td>
<td>39 (29.5%)</td>
<td></td>
</tr>
<tr>
<td>Mortality Category 3, n (%)</td>
<td>11 (7.2%)</td>
<td>8 (6.1%)</td>
<td></td>
</tr>
<tr>
<td>Mortality Category 4, n (%)</td>
<td>8 (5.3%)</td>
<td>10 (7.6%)</td>
<td></td>
</tr>
<tr>
<td>Mortality Category 5, n (%)</td>
<td>9 (5.9%)</td>
<td>1 (0.8%)</td>
<td></td>
</tr>
</tbody>
</table>

SEM = standard error of mean

STAT = Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery

Congenital Heart Surgery
Table 2. Characteristics of CPB for Pulsatile vs. Non-pulsatile Neonatal/Pediatric Patients Utilizing 8, 10, and 12 Fr Arterial Cannulae (Mean ± SEM)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Non-pulsatile</th>
<th>Pulsatile</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiopulmonary Bypass Time (min)</td>
<td>116.1 ± 5.0</td>
<td>111.2 ± 4.0</td>
<td>0.45</td>
</tr>
<tr>
<td>Aortic Cross-Clamp Time (min)</td>
<td>68.3 ± 3.2</td>
<td>73.8 ± 2.9</td>
<td>0.21</td>
</tr>
<tr>
<td>Pump Flow Index (L/m²/min)</td>
<td>2.4 ± 0.0</td>
<td>2.4 ± 0.0</td>
<td>0.40</td>
</tr>
<tr>
<td>Arterial Line Pressure (mmHg)</td>
<td>126.9 ± 3.0</td>
<td>115.8 ± 1.9</td>
<td>0.003</td>
</tr>
<tr>
<td>VAVD (mmHg)</td>
<td>-16.8 ± 0.7</td>
<td>-16.5 ± 0.8</td>
<td>0.81</td>
</tr>
<tr>
<td>Ultrafiltration (mL/kg)</td>
<td>22.0 ± 2.2</td>
<td>26.2 ± 2.9</td>
<td>0.25</td>
</tr>
<tr>
<td>Modified Ultrafiltration (mL/kg)</td>
<td>107.5 ± 6.0</td>
<td>107.1 ± 4.6</td>
<td>0.96</td>
</tr>
<tr>
<td>Urine Output During CPB (mL/kg/hr)</td>
<td>5.0 ± 0.4</td>
<td>4.2 ± 0.4</td>
<td>0.21</td>
</tr>
<tr>
<td>GME Counts – Right MCA</td>
<td>337 ± 74</td>
<td>176 ± 47</td>
<td>0.08</td>
</tr>
<tr>
<td>Arterial Cannula Size</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 Fr, n (%)</td>
<td>51 (33.6%)</td>
<td>45 (34.1%)</td>
<td>0.60</td>
</tr>
<tr>
<td>10 Fr, n (%)</td>
<td>53 (34.9%)</td>
<td>52 (39.4%)</td>
<td></td>
</tr>
<tr>
<td>12 Fr, n (%)</td>
<td>48 (31.6%)</td>
<td>35 (26.5%)</td>
<td></td>
</tr>
</tbody>
</table>

CPB = cardiopulmonary bypass

GME = gaseous microemboli

MCA = middle cerebral artery

SEM = standard error of mean

VAVD = vacuum-assisted venous drainage
Table 3. Clinical Outcomes for Pulsatile vs. Non-pulsatile Neonatal/Pediatric Patients Utilizing 8, 10, and 12 Fr Arterial Cannulae (Median (25th, 75th percentiles))

<table>
<thead>
<tr>
<th>Clinical Outcomes</th>
<th>Non-pulsatile</th>
<th>Pulsatile</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients, n</td>
<td>152</td>
<td>132</td>
<td>~</td>
</tr>
<tr>
<td>Intubation Time (hours)</td>
<td>9.6 [6.3-30.9]</td>
<td>9.4 [6.4-28.4]</td>
<td>0.712</td>
</tr>
<tr>
<td>ICU LOS (days)</td>
<td>2.8 [1.3-5.5]</td>
<td>2.0 [1.2-4.0]</td>
<td>0.103</td>
</tr>
<tr>
<td>Hospital LOS (days)</td>
<td>5.3 [3.4-10.1]</td>
<td>4.5 [3.4-8.0]</td>
<td>0.195</td>
</tr>
<tr>
<td>Mortality within 180 days, n (%)</td>
<td>5 (3.3%)</td>
<td>2 (1.5%)</td>
<td>0.46</td>
</tr>
</tbody>
</table>

CPB = cardiopulmonary bypass

LOS = length of stay

SEM = Standard Error of Mean

STAT = Society of Thoracic Surgeons European Association for Cardio-Thoracic Surgery Congenital Heart Surgery
Figure Legends

**Figure 1.** Pulsatility Index at the Right Middle Cerebral Artery at Various Timepoints for each Perfusion Modality Group Stratified based on Arterial Cannula Sizes

* = p<0.05, comparison of pulsatility index at the given timepoint with its respective baseline value
† = p<0.05, comparison of pulsatility index between NP and P modality at a given timepoint

MCA = middle cerebral artery
PI = pulsatility index
XC = cross-clamp

**Figure 2.** Pulsatility Index in the Arterial Line at Various Timepoints for each Perfusion Modality Group Stratified based on Arterial Cannula Sizes

† = p<0.05, comparison of pulsatility index between NP and P modality at a given timepoint

PI = pulsatility index
XC = cross-clamp

**Figure 3.** Mean Flow Velocity in the Right Middle Cerebral Artery at Various Timepoints for each Perfusion Modality Group Stratified based on Arterial Cannula Sizes

* = p<0.05, comparison of pulsatility index at the given timepoint with its respective baseline value
† = p<0.05, comparison of pulsatility index between NP and P modality at a given timepoint

MCA = middle cerebral artery
MFV = mean flow velocity
XC = cross-clamp
Figure 4. Regional Oxygen Saturation in the Left Cortical Hemisphere at Various Timepoints for each Perfusion Modality Group Stratified based on Arterial Cannula Sizes

* = p<0.05, comparison of pulsatility index at the given timepoint with its respective baseline value

^ = p<0.05, comparison of MAP at a given timepoint with its respective baseline value for both pulsatile and non-pulsatile groups

NIRS = near-infrared spectroscopy

XC = cross-clamp

Figure 5. Graphical Abstract
**Pulsatility Index at the Right MCA**

* = p<0.05, comparison of PI at the given timepoint with its respective baseline value
† = p<0.05, comparison of PI between NP and P modality at a given timepoint
MCA = middle cerebral artery
Impact of Perfusion Modalities on Cerebral Hemodynamics and Clinical Outcomes in Pediatric Congenital Heart Surgery Patients

This retrospective review included 284 consecutive pediatric patients undergoing congenital cardiac surgery with CPB support utilizing only 8/10/12 Fr arterial cannulae.

<table>
<thead>
<tr>
<th>Clinical Outcomes</th>
<th>Non-pulsatile</th>
<th>Pulsatile</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients, n</td>
<td>152</td>
<td>132</td>
<td>-</td>
</tr>
<tr>
<td>Intubation Time (hours)</td>
<td>[9.6 [9.3-30.3], 9.4 [8.4-28.4]]</td>
<td>9.4 [8.4-30.9]</td>
<td>0.71</td>
</tr>
<tr>
<td>ICU LOS (days)</td>
<td>[2.8 [1.3-5.5], 2.0 [1.2-4.0]]</td>
<td>[2.8 [1.3-5.5], 2.0 [1.2-4.0]]</td>
<td>0.10</td>
</tr>
<tr>
<td>Hospital LOS (days)</td>
<td>[5.3 [3.4-10.1], 4.5 [3.4-6.0]]</td>
<td>[5.3 [3.4-10.1], 4.5 [3.4-6.0]]</td>
<td>0.20</td>
</tr>
<tr>
<td>Mortality within 180 days, n (%)</td>
<td>5 (3.3%)</td>
<td>2 (1.5%)</td>
<td>0.46</td>
</tr>
</tbody>
</table>

Although the pulsatility index was better maintained in the pulsatile group, mean cerebral blood flow velocity, regional cerebral oxygen saturation levels, GME counts, and clinical outcomes were statistically similar with the “non-pulsatile” group. These findings suggest that while pulsatile perfusion represents a safe modality for CPB support, its use may not translate into demonstrably superior short-term clinical outcomes.
Mean Flow Velocity at the Right Middle Cerebral Artery