The effects of pulsatile versus nonpulsatile 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 patients undergoing congenital heart surgery

Krishna Patel, BS,[a,b] Yongwook Dan, MD,[a,b] Allen R. Kunselman, MA,[a,c] Joseph B. Clark, MD,[a,b] John L. Myers, MD,[a,b] and Akif Ündar, PhD[a,b,d]

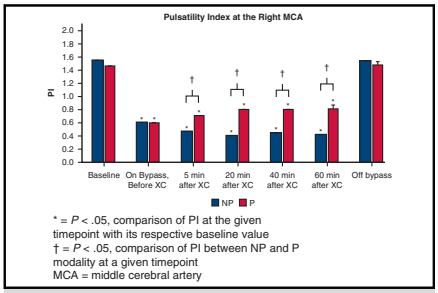
ABSTRACT

Objective: The objective of this retrospective review was to evaluate whether or not 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 support utilizing nonpulsatile (n = 152) or pulsatile (n = 132) flow. Intraoperative cerebral gaseous microemboli 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 cardiopulmonary bypass characteristics between groups were similar. Although the pulsatility index during aortic crossclamping was consistently higher in the pulsatile group ($P < .05$), a significant degree of pulsatility was also observed in the nonpulsatile group. No significant differences in mean cerebral blood flow velocity, regional cerebral oxygen saturation, or gaseous microemboli 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 nonpulsatile group. These findings suggest that while pulsatile perfusion represents a safe modality for cardiopulmonary bypass support, its use may not translate into detectably superior clinical outcomes. (JTCVS Open 2023;16:786-800)



Pulsatility index at the right MCA.

CENTRAL MESSAGE

Pulsatile flow during pediatric cardiopulmonary bypass does not demonstrate superior clinical outcomes over nonpulsatile flow for patients with similar characteristics.

PERSPECTIVE

Although pulsatile flow during cardiopulmonary bypass may offer more physiologic perfusion, definitive evidence is lacking that this advantage translates to improved postoperative outcomes compared with nonpulsatile flow. This study evaluates the influence of perfusion modalities on cerebral hemodynamics and clinical outcomes in pediatric patients undergoing congenital cardiac surgery.

From the Departments of [a]Pediatrics, [b]Surgery, [c]Public Health Sciences, and [d]Biomedical Engineering, Penn State Hershey Pediatric Cardiovascular Research Center, Penn State College of Medicine, Penn State Health Children's Hospital, Hershey, Pa.

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Ms Patel and Dr Dan contributed equally to this article.

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Address for reprints: Akif Ündar, PhD, Department of Pediatrics, Penn State College of Medicine, H085, 500 University Dr, PO Box 850, Hershey, PA 17033-0850 (E-mail: aundar@pennstatehealth.psu.edu).

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Abbreviations and Acronyms

CPB = cardiopulmonary bypass
GME = gaseous microemboli
ICU = intensive care unit
LOS = length of stay
MCA = middle cerebral artery
MFV = mean flow velocity
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

Significant progress has been made over the decades toward decreasing the morbidity and mortality experienced by patients undergoing congenital heart surgery.[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 1 such tool which can provide noninvasive 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 nonpulsatile flow during CPB in improving postoperative outcomes in patients undergoing congenital heart surgery. More importantly, the safety of pulsatile perfusion using 8, 10, and 12 Fr 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 8, 10, and 12 Fr arterial cannulas. We utilized TCD intraoperatively to calculate the PI and quantify the pulsatility of flow in the MCA, continuously monitor cerebral hemodynamics by measuring cerebral blood flow velocity at the MCA, record the GME counts delivered to the MCA in real time, 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 influence of pulsatile perfusion on cerebral blood flow velocities, GME counts, cerebral PI at the MCA, and clinical outcomes in pediatric patients undergoing congenital heart surgery when compared with nonpulsatile perfusion, while demonstrating its safety in 8, 10, and 12 Fr 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 on July 13, 2023, at Penn State College of Medicine (No. PRAMS030476EP). Three hundred eighty-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 nonpulsatile group as surgeons' preferences at the time of surgery, surgeons have blinded which patients have had a complete multimodality neuromonitoring research datasheet for further analysis. We included an average of 75 patients (30 in the pulsatile and 45 in the nonpulsatile groups) per year with a completed intraoperative multimodality neuromonitoring research datasheet. Only 3 patients out of 385 were excluded due to incomplete or missing data sheets.

In the initial analysis of 382 patients, patients' demographic data were significantly different between the groups, so it was impossible to make a meaningful comparison. Because our study focused on perfusion modalities, inclusion criteria in terms of arterial cannula sizes of 8 Fr (n = 51 [33.6%] in the nonpulsatile group, and n = 45 [34.1%] in the pulsatile group), 10 Fr (n = 53 [34.9%] in nonpulsatile group, and n = 52 [39.4%] in the pulsatile group), and 12 Fr (n = 48 [31.6%] in the nonpulsatile group and n = 35 [26.5%] in the pulsatile group) allowed us to create homogeneous groups for direct and meaningful comparison. The exclusion criteria included 98 pediatric patients (79 patients from the nonpulsatile group) (younger than age 18 years) with the following cannula sizes (6 Fr = 16 patients, 14 Fr = 24 patients, 16 Fr = 28 patients, 18 Fr = 22 patients, 20 Fr = 7 patients, and 22 Fr = 1 patient). The final cohort of consecutive patients who met all selection criteria (n = 284) was divided into 2 groups based on the perfusion modality used during CPB (nonpulsatile vs pulsatile).

Supplemental Methods

Each perfusion modality group was further subdivided based on mortality risk, which was calculated using the Society of Thoracic Surgeons European Association for Cardio-Thoracic Surgery Congenital Heart Surgery (STAT) 2020 Mortality Score and Categories.[14] Patients in STAT mortality categories 1 through 3 were allotted to the low/middle-risk group, and patients in STAT mortality categories 4 and 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/minute; 7 to 15 kg = 100 beats/min; and <6.9 kg = 120 beats/minute. Specific details regarding anesthesia and perfusion protocols were published previously[15] and are included Appendix 1.

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). 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 (V_{max}) and the minimum diastolic (V_{min}) blood flow velocity over the mean blood flow velocity (V_{mean}).[16]

$$PI = \frac{V_{max} - V_{min}}{V_{mean}}$$

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

The MFV was calculated by adding the end diastolic velocity (EDV) to one-third of the difference between peak systolic velocity (PSV) and EDV.

$$MFV = EDV + 1/3\ (PSV - EDV)$$

Near-Infrared Spectroscopy

Near-infrared spectroscopy (NIRS) using an INVOS 5100B monitor (Somanetics) was performed to assess regional cerebral oxygen saturation (rSo_2). This device utilizes 2 near-infrared wavelengths of 730 and 805 nm to quantify the proportion of oxyhemoglobin to deoxyhemoglobin. Pediatric SomaSensors (Somanetics) were placed caudad 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 rSo_2 was measured by the NIRS machine at 5-second intervals. Intraoperative PI, mean flow velocity, and rSo_2 measurements were collected at each of the following time points: baseline preincision; initiation of CPB before aortic crossclamp; 5, 20, 40, and 60 minutes after aortic crossclamp; 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 crossclamp time, pump flow index, arterial line pressure, vacuum-assisted venous drainage level, ultrafiltration, modified ultrafiltration, 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 rSo_2 at various time points during CPB were also compared between nonpulsatile and pulsatile groups.

Statistical Analysis

Unpaired *t* tests were used to compare continuous demographic/characteristic and clinical outcome variables (eg, age, weight, CPB time, aortic crossclamp time, pump flow index, and intubation time) between perfusion modalities. In the event the distributions did not meet parametric assumptions (eg, normality), Wilcoxon rank-sum tests were used to compare these continuous variables (ie, intubation time, ICU LOS, and hospital LOS) between perfusion modalities. The χ^2 test, or Fisher exact tests if the expected cell counts were small, were used to compare categorical demographic/characteristic and clinical outcome variables (eg, gender and mortality within 180 days) between perfusion modalities. Pearson 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 (eg, 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 2-sided and all analyses were performed using SAS software version 9.4 (SAS Institute Inc).

RESULTS

Demographics and CPB Characteristics

Patient demographics for overall nonpulsatile 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 nonpulsatile and pulsatile cohorts is reported in Table 2. No significant differences were noted in CPB time, aortic crossclamp time, pump flow index, vacuum-assisted venous drainage levels, ultrafiltration volume, modified ultrafiltration volume, urine output during CPB, and distribution of arterial cannula size usage. Arterial line pressures were statistically higher in the non-pulsatile group (nonpulsatile 126.9 ± 3.0 mm Hg vs pulsatile 115.8 ± 1.9 mm Hg; $P = .003$). Nonpulsatile patients had a statistically similar number of GME counts delivered to the right MCA during CPB when compared with pulsatile patients (nonpulsatile 337 ± 74 vs pulsatile 176 ± 47; $P = .079$).

PI in the MCA and in the Arterial Line

Figures 1 and 2 display PI measurements recorded at the right MCA and in the arterial line at various time points for

TABLE 1. Demographics for pulsatile versus nonpulsatile neonatal/pediatric patients utilizing 8, 10, and 12 Fr arterial cannulae

Demographic/characteristic	Nonpulsatile	Pulsatile	*P* value
No. of patients	152	132	–
Male sex	90 (59.2)	68 (51.5)	.23
Age (mo)	17.5 ± 1.8	13.5 ± 1.5	.09
Neonates	20 (13.2)	21 (15.9)	
Pediatric	132 (86.8)	111 (84.1)	
Weight (kg)	8.4 ± 0.4	7.7 ± 0.5	.27
Height (cm)	70.9 ± 1.6	67.5 ± 1.6	.14
STAT mortality category	0.40 ± 0.05	0.31 ± 0.03	.14
1	88 (57.9)	74 (56.1)	
2	36 (23.7)	39 (29.5)	
3	11 (7.2)	8 (6.1)	
4	8 (5.3)	10 (7.6)	
5	9 (5.9)	1 (0.8)	

Values are presented as n (%) or mean ± SEM. *STAT*, Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery Congenital Heart Surgery.

TABLE 2. Characteristics of cardiopulmonary bypass (CPB) for pulsatile versus nonpulsatile neonatal/pediatric patients utilizing 8, 10, and 12 Fr arterial cannulae

Characteristic	Nonpulsatile	Pulsatile	*P* value
CBP time (min)	116.1 ± 5.0	111.2 ± 4.0	.45
Aortic crossclamp time (min)	68.3 ± 3.2	73.8 ± 2.9	.21
Pump flow index (L/m^2/min)	2.4 ± 0.0	2.4 ± 0.0	.40
Arterial line pressure (mm Hg)	126.9 ± 3.0	115.8 ± 1.9	**.003**
VAVD (mm Hg)	−16.8 ± 0.7	−16.5 ± 0.8	.81
Ultrafiltration (mL/kg)	22.0 ± 2.2	26.2 ± 2.9	.25
Modified ultrafiltration (mL/kg)	107.5 ± 6.0	107.1 ± 4.6	.96
Urine output during CPB (mL/kg/h)	5.0 ± 0.4	4.2 ± 0.4	.21
GME counts-right MCA	337 ± 74	176 ± 47	.08
Arterial cannula size (Fr)			.60
8	51 (33.6)	45 (34.1)	
10	53 (34.9)	52 (39.4)	
12	48 (31.6)	35 (26.5)	

Values are presented as mean ± SEM or n (%). Boldface indicates statistical significance. *CPB*, Cardiopulmonary bypass; *VAVD*, vacuum-assisted venous drainage; *GME*, gaseous microemboli; *MCA*, middle cerebral artery.

each perfusion modality group stratified by arterial cannula sizes. PI in the arterial line was consistently higher in the pulsatile group compared with the nonpulsatile group during aortic crossclamping for all arterial cannula sizes. PI at the right MCA was significantly higher in the pulsatility group during aortic crossclamping 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

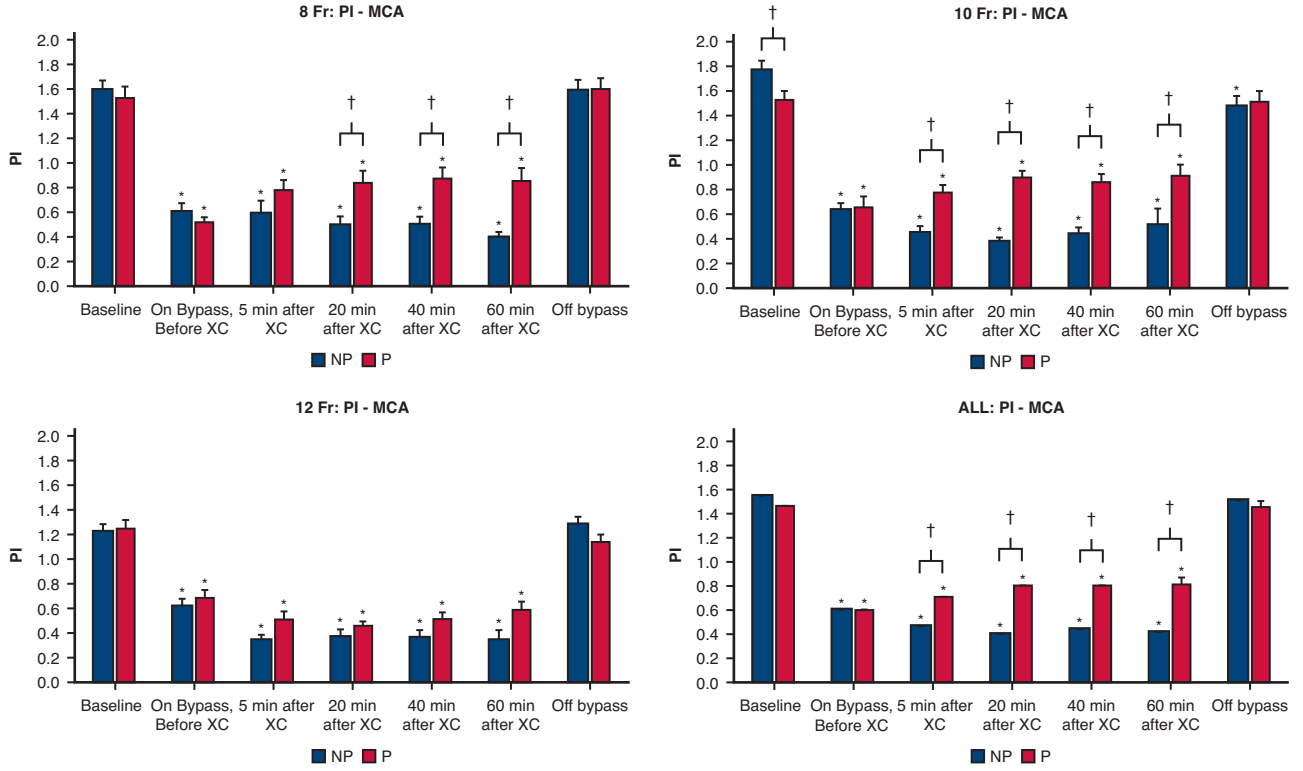

FIGURE 1. Pulsatility index at the right middle cerebral artery at various time points for each perfusion modality group stratified based on arterial cannula sizes *$P < .05$; comparison of pulsatility index (*PI*) at the given time point with its respective baseline value. †$P < .05$; comparison of pulsatility index between nonpulsatile (*NP*) and pulsatile (*P*) modality at a given time point. *MCA*, Middle cerebral artery; *XC*, crossclamp.

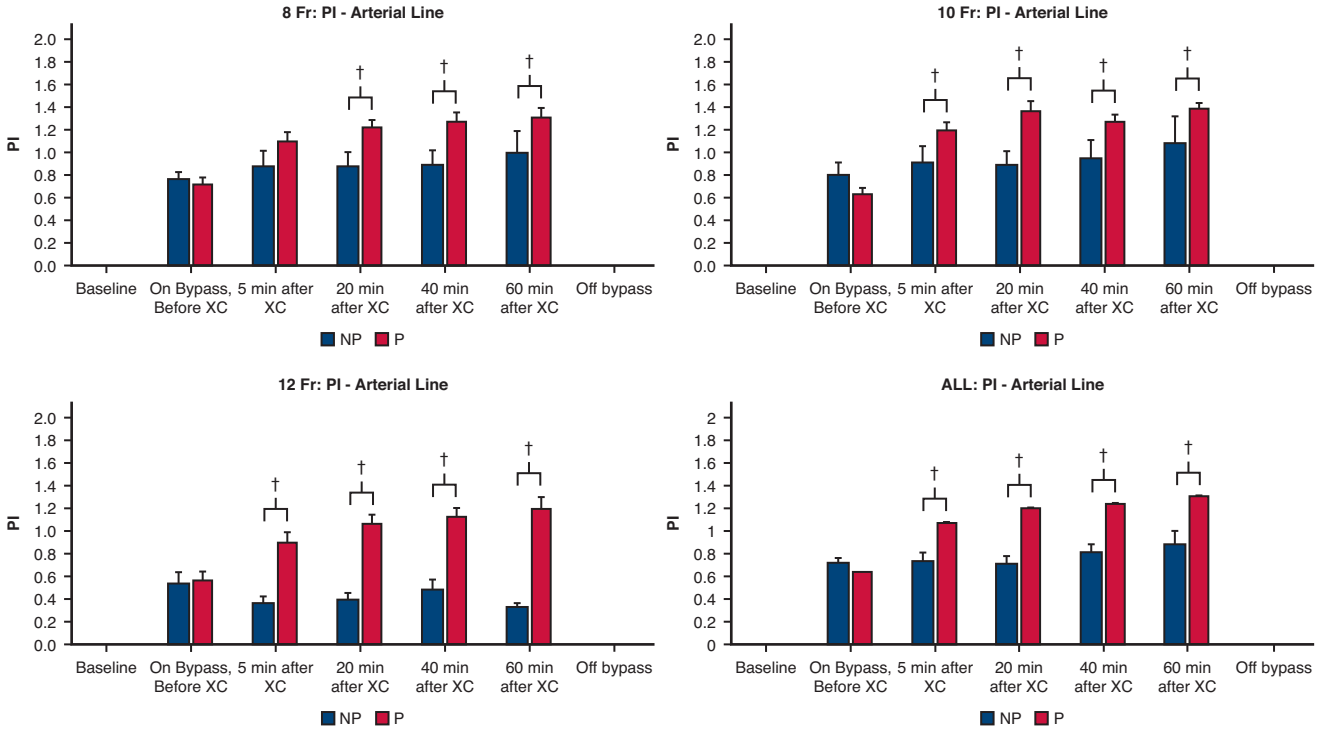

FIGURE 2. Pulsatility index in the arterial line at various time points for each perfusion modality group stratified based on arterial cannula sizes. †$P < .05$, comparison of pulsatility index (*PI*) between nonpulsatile (*NP*) and pulsatile (*P*) modality at a given time point. *XC*, Crossclamp.

for both pulsatile and nonpulsatile groups for all arterial cannula sizes. As expected, this decline was more pronounced in the nonpulsatile group. Additionally, PI in the right MCA returned to baseline values after CPB was terminated in both pulsatile and nonpulsatile groups for all arterial cannula sizes.

MFV

Figure 3 depicts the MFV recorded at the right MCA at various time points for each perfusion modality group stratified by arterial cannula sizes. MFV decreased in both perfusion modality groups during aortic crossclamping compared with 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 crossclamping. No significant differences in MFV between nonpulsatile and pulsatile groups during and after CPB for all arterial cannula sizes were noted.

rSo_2

Figure 4 displays the rSo_2 in the left cortical hemisphere and the mean arterial pressure at various time points for both nonpulsatile 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 rSo_2 could be identified between the nonpulsatile and pulsatile perfusion groups.

Correlation Coefficients Among Cerebral Parameters and Temperature

PI in the MCA does not have any relation with rSo_2 levels but has weak relations ($0.25 < r < 0.50$; $P < .05$) with MFV-MCA at several experimental stages (Table E1). The PI-MCA has weak to moderate relations ($0.5 < r < 0.75$; $P < .05$) with the PI in the arterial line, but no relations with the mean arterial pressures (Table E2).

The temperature has moderate reverse relations with the rSo_2 levels, particularly with the 8 Fr 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 classclamping. All detailed correlations at each experimental stage are presented in Tables E3 and E4.

Clinical Outcomes for Nonpulsatile Versus Pulsatile Patients

Clinical outcomes for each perfusion modality group are reported in Table 3. Patients in the nonpulsatile and pulsatile groups had similar intubation times (nonpulsatile median, 9.6 hours [range, 6.3-30.9 hours] vs pulsatile median,

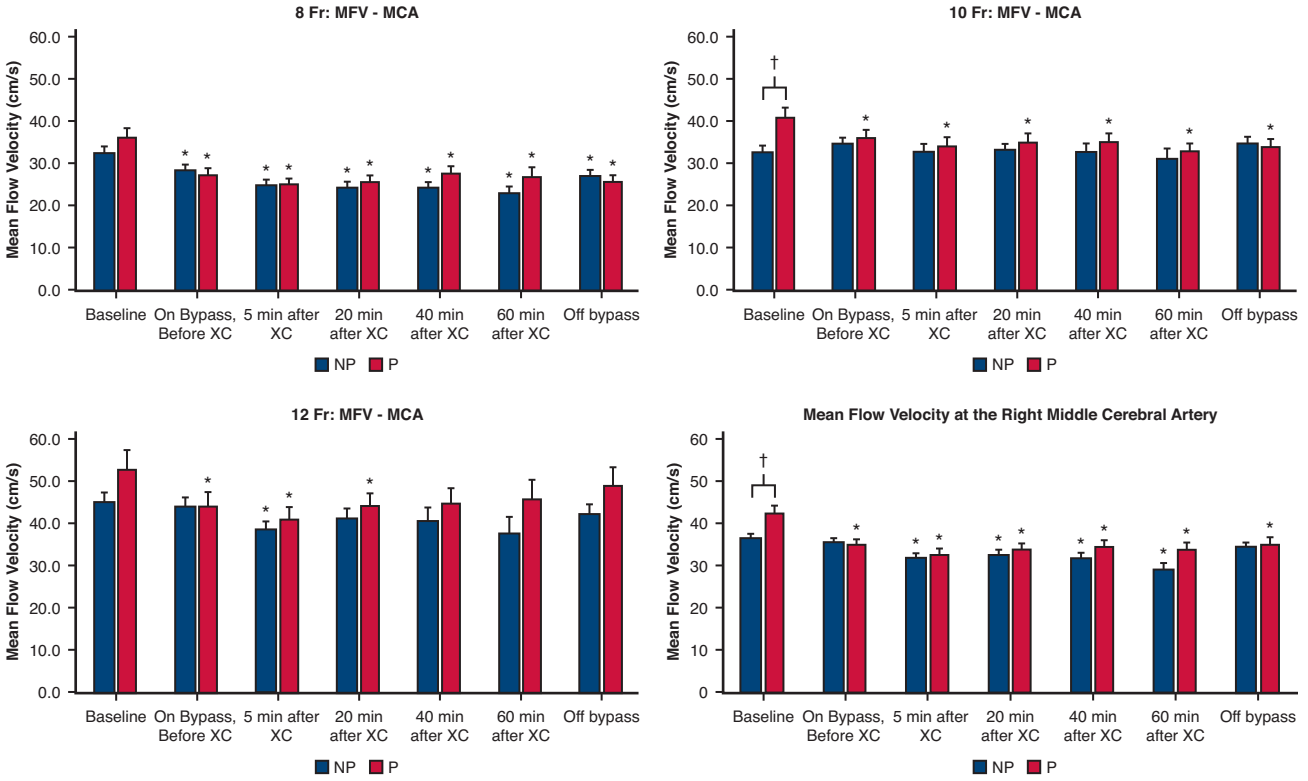

FIGURE 3. Mean flow velocity in the right middle cerebral artery at various time points for each perfusion modality group stratified based on arterial cannula sizes. *$P < .05$; comparison of pulsatility index at the given timepoint with its respective baseline value. †$P < .05$; comparison of pulsatility index between nonpulsatile (*NP*) and pulsatile (*P*) modality at a given time point. *MFV*, Mean flow velocity; *MCA*, middle cerebral artery; *XC*, crossclamp.

9.4 hours [range, 6.4-28.4 hours]; $P = .712$), ICU LOS (nonpulsatile median, 2.8 days [range, 1.3-5.5 days] and pulsatile median, 2.0 days [range, 1.2-4.0 days]; $P = .103$) and hospital LOS (nonpulsatile median, 5.3 days [range, 3.4-8.0 days] vs pulsatile median, 4.5 days [range, 3.4-8.0 days]; $P = .195$). 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 Table E5. The number of patients utilizing deep hypothermic circulatory arrest, antegrade cerebral perfusion, and types of operations are displayed in Table E6.

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 Table E7. In the high-risk mortality group (STAT 4 or 5), patients with nonpulsatile perfusion demonstrated higher baseline mortality scores, aortic crossclamp 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 nonpulsatile and pulsatile groups, whereas aortic crossclamp times were shorter in the nonpulsatile group. Additionally, no statistical differences were noted in the GME counts between nonpulsatile and pulsatile perfusion in any mortality risk groups.

Supplemental Clinical Outcomes for Risk-Stratified Nonpulsatile Versus Pulsatile Patients

Clinical outcomes for risk-stratified non-pulsatile and pulsatile patients are depicted in Table E8. 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 (nonpulsatile median, 53.3 hours [range, 28.4-151.9 hours] vs pulsatile median, 28.6 hours [range, 7.0-68.4 hours]; $P = .119$), and ICU LOS (nonpulsatile median, 8.6 days [range, 2.9-23.5 days] vs pulsatile median, 3.1 days [range, 1.9-4.9 days]; $P \leq .060$), and more extended hospital LOS (nonpulsatile median, 16.6 days [range, 11.7-44.0 days] vs pulsatile median, 7.3 days [range, 4.3-11.6 days]; $P = .014$) in high-risk patients using nonpulsatile perfusion compared with high-risk patients using pulsatile perfusion. Additionally, no differences in mortality were observed

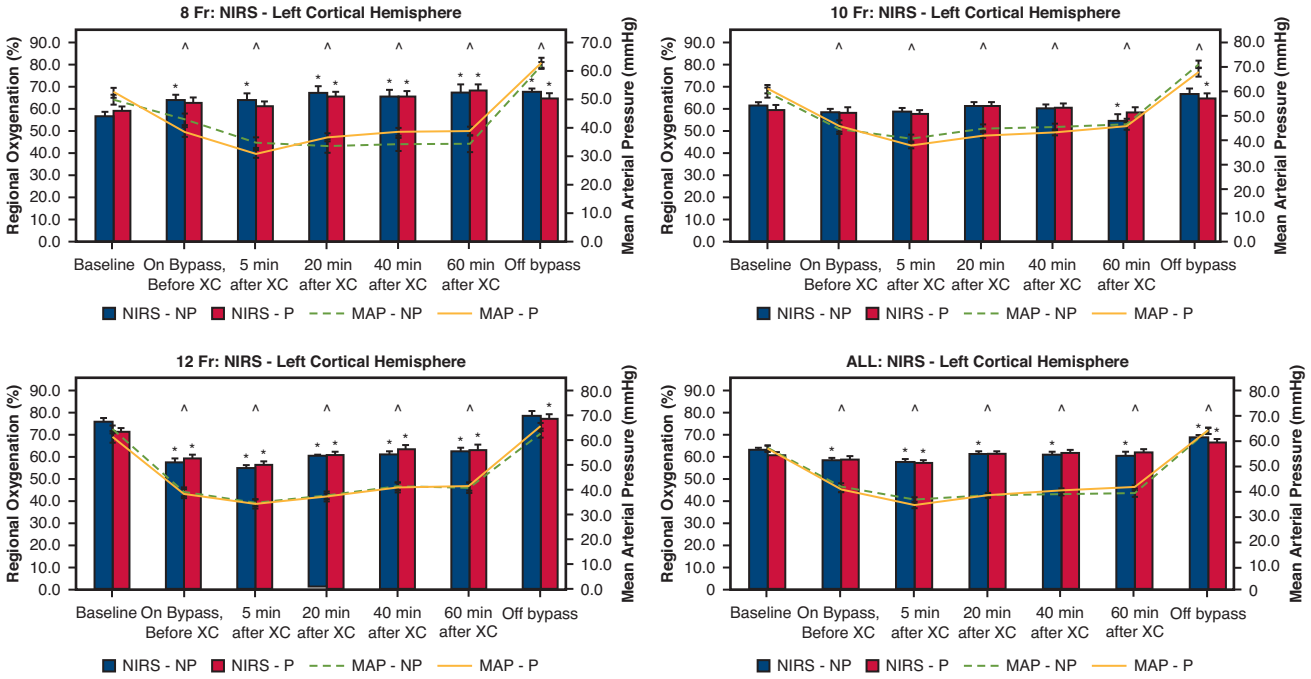

FIGURE 4. Regional oxygen saturation in the left cortical hemisphere at various time points for each perfusion modality group stratified based on arterial cannula sizes. *$P < .05$; comparison of pulsatility index at the given time point with its respective baseline value. ^$P < .05$; comparison of mean arterial pressure (*MAP*) at a given time point with its respective baseline value for both pulsatile and nonpulsatile groups. *NIRS*, Near-infrared spectroscopy; *XC*, cross-clamp; *NP*, nonpulsatile; *P*, pulsatile.

between pulsatile and nonpulsatile 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 nonpulsatile group, a significant degree of pulsatility was also generated under conventional nonpulsatile 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 2 groups.

TABLE 3. Clinical outcomes for pulsatile versus nonpulsatile neonatal/pediatric patients utilizing 8, 10, and 12 Fr arterial cannula

Clinical outcome	Nonpulsatile	Pulsatile	*P* value
No. of patients	152	132	–
Intubation time (h)	9.6 (6.3-30.9)	9.4 (6.4-28.4)	.712
ICU LOS (d)	2.8 (1.3-5.5)	2.0 (1.2-4.0)	.103
Hospital LOS (d)	5.3 (3.4-10.1)	4.5 (3.4-8.0)	.195
Mortality within 180 d	5 (3.3)	2 (1.5)	.46

Values are presented as n, median (25th-75th percentiles), or n (%). *ICU*, Intensive care unit; *LOS*, length of stay.

PI

The PI was calculated as the difference between the maximum systolic blood flow velocity and the minimum diastolic blood flow velocity divided by the mean blood flow velocity. Under 100% nonpulsatile flow conditions, the difference between systolic and diastolic blood flow velocities would be 0, and the PI would be 0. In our study, PI during nonpulsatile CPB was between 0.4 and 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 nonpulsatile flow are unable to generate 100% nonpulsatile flow with 8, 10, and 12 Fr arterial cannula for patients undergoing congenital heart surgery. Therefore, we acknowledge that our study compared 2 different pulsatile modalities rather than purely nonpulsatile versus pulsatile perfusion. Nevertheless, the TCD is an excellent tool to not only monitor cerebral hemodynamics and GME counts, but also quantify perfusion modalities in the MCA and in the arterial line of the CPB circuitry for patients undergoing congenital heart surgery. Although the observation of pulsatility under nonpulsatile settings is a limitation of the

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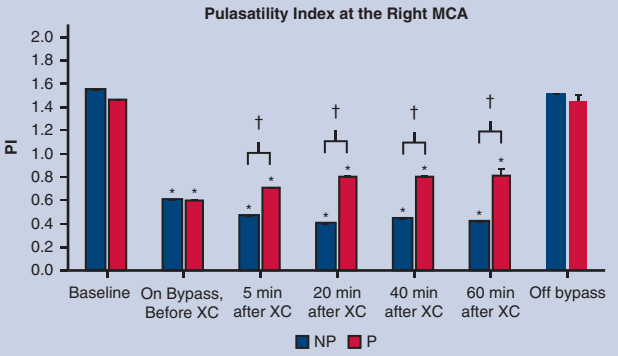
Impact of Perfusion Modalities on Cerebral Hemodynamics and Clinical Outcomes in Pediatric Congenital Heart Surgery Patients

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

Clinical Outcomes	Non-pulsatile	Pulsatile	*P*-value
Number of patients, *n*	152	132	–
Intubation Time (hours) (Median [25th - 75th percentile])	9.6 [6.3-30.9]	9.4 [6.4-28.4]	.71
ICU LOS (days) (Median [25th - 75th percentile])	2.8 [1.3-5.5]	2.0 [1.2-4.0]	.10
Hospital LOS (days) (Median [25th - 75th percentile])	5.3 [3.4-10.1]	4.5 [3.4-8.0]	.20
Mortality within 180 days, *n* (%)	5 (3.3%)	2 (1.5%)	.46



* = $P < .05$, comparison of PI at the given timepoint with its respective baseline value
† = $P < .05$, comparison of PI between NP and P modality at a given timepoint
MCA = middle cerebral artery

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.

FIGURE 5. Graphical abstract. *CPB*, Cardiopulmonary bypass; *ICU*, intensive care unit; *LOS*, length of stay; *MCA*, middle cerebral artery; *PI*, pulsatility index; *XC*, crossclamp; *NP* nonpulsatile; *P*, pulsatile; *GME*, gaseous microemboli.

current study, this finding may represent a serendipitous, unintended consequence of the long-term efforts toward CPB circuit optimization and evolution that now provide highly efficient and effective levels of circulatory support.

GME Counts and Arterial Line Pressures

Patients in the pulsatile group have a statistically similar number of GME counts delivered to the right MCA during CPB compared with nonpulsatile patients (176 ± 47 vs 337 ± 74; $P = .079$). 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 patients undergoing congenital heart surgery.

In addition, we used an empiric approach to determine the pulsatility settings for this study. We used identical heart–lung machines for pulsatile and nonpulsatile 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 nonpulsatile (n = 135) groups had an identical mortality score of 0.22 ± 0.01 (Table E1). However, the high-risk (STAT 4 or 5) patients in the nonpulsatile (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; $P < .05$). Thus, the significantly higher mortality scores may be the reason for higher intubation time, ICU, and hospital length of stay in the nonpulsatile group observed in this study (Table E2).

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) rather than the 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 influence on primary clinical outcomes regarding intubation durations, ICU LOS, and hospital LOS selected for this study.

CONCLUSIONS

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

The results of this study indicate that whereas pulsatile perfusion is a safe modality for CPB support, its use may not translate into demonstrably superior short-term clinical outcomes (Figure 5). Further studies with multicenter data comparing nonpulsatile and pulsatile flow are necessary to provide a more conclusive answer.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: congenital heart surgery, cardiopulmonary bypass, pulsatility index, cerebral hemodynamics, gaseous microemboli, pulsatile flow, clinical outcomes

APPENDIX 1. SUPPLEMENTAL METHODS AND RESULTS

Methods

Each of perfusion modality groups was further subdivided based on mortality risk, calculated using the Society of Thoracic Surgeons European Association for Cardio-Thoracic Surgery Congenital Heart Surgery (STAT) 2020 Mortality Score and Categories.[E1] Patients in STAT mortality categories 1 through 3 were allotted to the low/middle-risk group, and patients in STAT mortality categories 4 and 5 were allotted to the high-risk group.

Anesthesia and perfusion. Isoflurane, pancuronium, and fentanyl were utilized for general anesthesia. A median sternotomy incision was performed for all cases. The cardiopulmonary bypass (CPB) circuit consisted of a Maquet HL-20 heart-lung machine—capable of maintaining either pulsatile or non-pulsatile perfusion—(Maquet Cardiopulmonary, Getinge Group), a Capiox hollow fiber membrane oxygenator, a Capiox pediatric 32 mm arterial filter (Terumo Cardiovascular Systems), cardioplegia set (66483-01), a Minntech hemoconcentrator (HemoCor HPH400TS; Medivators Inc), PVC tubing (LivaNova Smart Perfusion Pack), a Stockert heart-cooler system (Sorin Group USA), and arterial cannulas selected from either the DLP series (Medtronic), the Sarns Tender Flow series, or the Fem-Flex II series (Edwards Lifesciences). All circuit components were optimized based on our previous in vitro studies[E2-E4] and pilot clinical trial.[E5] Priming of the CPB circuit was accomplished with 400 mL Plasmalyte-A and 50 mL 25% human albumin. Included in this prime was 15 mEq sodium bicarbonate and 1000 U heparin. Between 120 mL and 180 mL priming solution was removed, while 250 mL packed red blood cells were added. This removed prime was then used for additional volume during the case, as needed. The goal hematocrit during CPB was $\geq$26%. We used pH-stat blood gas management during cooling and alpha-stat during rewarming phases of the CPB. A 0.5 g/kg dose of mannitol was administered to the circuit after the implementation of CPB. Finally, the prime was then flushed from the cardioplegia circuitry. All patients received modified ultrafiltration before discontinuation from CPB.

Results based on STAT risk stratification analysis. *Supplemental demographics and CPB characteristics for risk-stratified nonpulsatile versus pulsatile patients.* Demographics, CPB characteristics, and gaseous microemboli (GME) counts for risk-stratified nonpulsatile and pulsatile patients are displayed in Table E7. In the high-risk mortality group (STAT 4 or 5), patients with nonpulsatile perfusion demonstrated higher baseline mortality scores, aortic crossclamp 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 nonpulsatile and pulsatile groups, whereas aortic crossclamp times were shorter in the nonpulsatile group. Additionally, no statistical differences were noted in the GME counts between nonpulsatile and pulsatile perfusion in any mortality risk groups.

Supplemental clinical outcomes for risk-stratified nonpulsatile versus pulsatile patients. Clinical outcomes for risk-stratified nonpulsatile and pulsatile patients are depicted in Table E8. 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 (nonpulsatile median, 53.3 hours [range, 28.4-151.9 hours] vs pulsatile 28.6 [range, 7.0-68.4 hours]; $P = .119$), and intensive care length of stay (nonpulsatile mean 8.6 days [range, 2.9, 23.5 days] vs pulsatile mean 3.1 days [range, 1.9-4.9 days]; $P \leq .060$), and more extended hospital length of stay (nonpulsatile median, 16.6 days [range, 11.7-44.0 days] vs pulsatile median, 7.3 days [range, 4.3-11.6 days]; $P = .014$) in high-risk patients using nonpulsatile perfusion compared with high-risk patients using pulsatile perfusion. Additionally, no differences in mortality were observed between pulsatile and nonpulsatile perfusion in both risk groups.

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TABLE E1. Intraoperative correlations among pulsatility index (PI) in the middle cerebral artery (MCA), mean flow velocity (MFV), and regional cerebral oxygen saturation (rSo_2) using 8, 10, and 12 Fr arterial cannulae*

	MFV-MCA				rSo_2-left cortical hemisphere			
PI-MCA	8 Fr	10 Fr	12 Fr	All	8 Fr	10 Fr	12 Fr	All
Baseline	**−0.37050**	**−0.37234**	**−0.38108**	**−0.41702**	**−0.42747**	**−0.29643**	**−0.27084**	**−0.43201**
	0.0003	**0.0002**	**0.0006**	**<.0001**	**<.0001**	**0.0035**	**0.0196**	**.0001**
On bypass before XC	**−0.23754**	−0.14280	0.07379	0.01524	−0.13574	0.12680	0.19323	0.06024
	0.0242	0.1745	0.5236	0.8071	0.2155	0.2391	0.0967	0.3448
5 min after XC	**−0.37531**	**−0.45216**	**−0.34059**	**−0.40375**	0.23616	−0.06736	0.08213	0.14222
	0.0003	**<.0001**	**0.0026**	**<.0001**	0.0316	0.5258	0.4897	0.0254
20 min after XC	−0.03743	**−0.33353**	0.10140	−0.02193	0.04157	−0.00186	−0.10007	0.00606
	0.7277	**0.0012**	0.3933	0.7280	0.7073	0.9862	0.4098	0.9251
40 min after XC	**−0.26111**	**−0.32065**	**−0.46226**	**−0.36573**	−0.01678	0.07540	−0.02092	0.00285
	0.0171	**0.0057**	**0.0003**	**<.0001**	0.8840	0.5320	0.8806	0.9678
60 min after XC	−0.18775	**−0.34904**	**−0.35460**	**−0.27596**	0.06971	−0.11859	−0.20050	−0.04766
	0.1342	**0.0121**	**0.0268**	**0.0005**	0.5966	0.4221	0.2341	0.5692
Off bypass	**−0.36440**	0.00922	**−0.33584**	−0.02255	−0.06013	−0.09170	−0.14936	−0.08737
	0.0004	0.9301	**0.0028**	0.7164	0.5823	0.3927	0.2072	0.1702

XC, Crossclamp. *In each experimental stage, the first number is Pearson's correlation coefficient, *r*, and the second is the *P* value. r < 0.25 = no relationship; 0.25 < r < 0.5 = weak relationship; 0.5 < r < 0.75 = moderate relationship; and *r* > 0.75 = strong relationship]. If there is a relationship with *P* value < .05, then numbers are presented in boldface type.

TABLE E2. Intraoperative correlations among pulsatility index (PI) in the middle cerebral artery (MCA), pulsatility index in the arterial line, and mean arterial pressures (MAP) using 8, 10, and 12 Fr arterial cannula*

	PI-arterial Line				MAP			
PI-MCA	8 Fr	10 Fr	12 Fr	All	8 Fr	10 Fr	12 Fr	All
Baseline					**−0.41926**	**−0.36703**	**−0.34805**	**−0.40496**
					<.0001	**0.0002**	**0.0018**	**<.0001**
On bypass before XC	0.19951	0.18556	0.07565	0.12931	0.02558	0.05476	0.03330	0.03549
	0.1481	0.1709	0.6517	0.1173	0.8109	0.6082	0.7737	0.5711
5 min after XC	0.25782	**0.52819**	**0.57756**	**0.43935**	**−0.34126**	0.04182	−0.03967	−0.15194
	0.0707	**<.0001**	**<.0001**	**<.0001**	**0.0012**	0.6890	0.7337	0.0148
20 min after XC	**0.48811**	**0.68804**	**0.33482**	**0.56141**	**−0.32106**	−0.23320	−0.01614	−0.19479
	0.0002	**<.0001**	**0.0302**	**<.0001**	**0.0022**	0.0253	0.8922	0.0018
40 min after XC	**0.28576**	**0.57893**	**0.63675**	**0.46876**	**−0.30448**	−0.23734	−0.09872	**−0.25910**
	0.0421	**<.0001**	**0.0002**	**<.0001**	**0.0051**	0.0432	0.4650	**0.0001**
60 min after XC	0.29685	**0.35879**	**0.66037**	**0.40740**	−0.12378	−0.21328	−0.14944	−0.11216
	0.0665	**0.0475**	**0.0008**	**<.0001**	0.3259	0.1329	0.3639	0.1647
Off bypass					−0.24711	−0.13918	−0.20878	−0.07668
					0.0176	0.1858	0.0703	0.2178

XC, Crossclamp. *In each experimental stage, the first number is Pearson's correlation coefficient, *r*, and the second is the *P* value. *r* < 0.25 = no relationship; 0.25 < *r* < 0.5 = weak relationship; 0.5 < *r* < 0.75 = moderate relationship; and *r* > 0.75 = strong relationship. If there is a relationship with *P* value < .05, then numbers are presented in boldface type.

TABLE E3. Intraoperative correlations among temperature, regional cerebral oxygen saturation (rSo_2), mean flow velocity (MFV), and pulsatility index (PI) in the middle cerebral artery (MCA) using 8, 10, and 12 Fr arterial cannula*

Temperature	rSo_2-left cortical hemisphere				MFV-MCA				PI-MCA			
	8 Fr	10 Fr	12 Fr	All	8 Fr	10 Fr	12 Fr	All	8 Fr	10 Fr	12 Fr	All
Baseline	0.07097 0.5263	0.03041 0.7748	0.13946 0.2327	0.20454 0.0012	0.05929 0.5899	0.18833 0.0691	−0.06524 0.5755	0.14928 0.0171	0.22298 0.0402	−0.07850 0.4520	0.06285 0.5896	0.01038 0.8690
On bypass before XC	**−0.59101** **<.0001**	−0.08332 0.4350	−0.14307 0.2084	**−0.39563** **<.0001**	**0.27763** **0.0081**	0.11804 0.2651	−0.12339 0.2818	**0.27646** **<.0001**	0.00154 0.9885	0.17638 0.0963	0.05657 0.6251	0.09264 0.1394
5 min after XC	**−0.70490** **<.0001**	0.01963 0.8535	−0.18381 0.1120	**−0.48557** **<.0001**	**0.43650** **<.0001**	**0.29772** **0.0036**	0.22952 0.0446	**0.40685** **<.0001**	**−0.36267** **0.0006**	**−0.25632** **0.0126**	−0.06872 0.5553	**−0.32516** **<.0001**
20 min after XC	**−0.69553** **<.0001**	0.02880 0.7876	−0.07754 0.5174	**−0.46043** **<.0001**	**0.36905** **0.0004**	**0.25507** **0.0141**	**0.31797** **0.0058**	**0.43203** **<.0001**	−0.10814 0.3159	−0.09655 0.3599	0.02294 0.8473	−0.08624 0.1715
40 min after XC	**−0.69048** **<.0001**	−0.08203 0.4902	−0.22364 0.0975	**−0.48054** **<.0001**	**0.40949** **0.0001**	0.17777 0.1297	**0.31870** **0.0148**	**0.41205** **<.0001**	−0.06237 0.5778	−0.07250 0.5422	−0.21498 0.1083	−0.15034 0.0286
60 min after XC	**−0.68235** **<.0001**	−0.17666 0.2197	**−0.36250** **0.0253**	**−0.54902** **<.0001**	**0.30234** **0.0144**	0.00469 0.9737	**0.33997** **0.0342**	**0.34959** **<.0001**	0.01879 0.8819	−0.04810 0.7375	−0.11870 0.4717	−0.03061 0.7054
Off bypass	−0.04285 0.6935	−0.08652 0.4175	**0.36857** **0.0012**	0.04741 0.4546	0.04949 0.6395	0.08153 0.4372	0.21821 0.0566	0.15937 0.0098	0.11540 0.2733	−0.05218 0.6194	−0.21262 0.0634	−0.01268 0.8382

XC, Crossclamp. *In each experimental stage, the first number is Pearson's correlation coefficient, *r*, and the second is the *P* value. $r < 0.25$ = no relationship; $0.25 < r < 0.5$ = weak relationship; $0.5 < r < 0.75$ = moderate relationship; and $r > 0.75$ = strong relationship]. If there is a relationship with *P* value < .05, then numbers are presented in boldface type.

TABLE E4. Intraoperative correlations among temperature, pulsatility index (PI) in the arterial line, and mean arterial pressures (MAP) using 8, 10, and 12 Fr arterial cannula*

Temperature	PI-arterial Line				MAP			
	8 Fr	10 Fr	12 Fr	All	8 Fr	10 Fr	12 Fr	All
Baseline					−0.08274 0.4461	0.20646 0.0459	−0.01468 0.8972	0.20162 0.0011
On bypass before XC	**−0.43638** **0.0009**	0.06189 0.6474	−0.18288 0.2524	**−0.25862** **0.0012**	0.01453 0.8907	0.05689 0.5880	−0.19883 0.0733	0.00061 0.9921
5 min after XC	−0.17447 0.2256	−0.10306 0.4373	−0.08270 0.6026	−0.17992 0.0271	**0.32103** **0.0022**	0.13062 0.2095	0.17914 0.1142	**0.29111** **<.0001**
20 min after XC	−0.26493 0.0552	−0.06775 0.6134	−0.12028 0.4423	−0.21013 0.0089	**0.58515** **<.0001**	0.15295 0.1433	0.19289 0.0950	**0.45724** **<.0001**
40 min after XC	−0.18098 0.2037	−0.18141 0.2276	−0.33695 0.0638	−0.21688 0.0139	**0.57191** **<.0001**	0.03935 0.7375	−0.10834 0.4140	**0.45641** **<.0001**
60 min after XC	−0.09815 0.5468	0.00568 0.9750	−0.18467 0.3989	−0.11767 0.2535	**0.56277** **<.0001**	0.05611 0.6899	−0.15385 0.3369	**0.45599** **<.0001**
Off bypass					−0.03284 0.7547	−0.07691 0.4637	−0.02080 0.8575	0.01365 0.8256

XC, Crossclamp. *In each experimental stage, the first number is Pearson's correlation coefficient, *r*, and the second is the *P* value. $r < 0.25$ = no relationship; $0.25 < r < 0.5$ = weak relationship; $0.5 < r < 0.75$ = moderate relationship; and $r > 0.75$ strong relationship. If there is a relationship with *P* value < .05, then numbers are presented in boldface type.

TABLE E5. Number and causes of mortalities within 180 days of operation based on Society of Thoracic Surgeons European Association for Cardio-Thoracic Surgery Congenital Heart Surgery (STAT) mortality categories

STAT mortality category	No. of mortalities within 180 d	Mode of perfusion	Cause of mortality
1	0	–	–
2	3	Nonpulsatile	Postoperative course complicated by esophageal perforation from nasogastric tube that led to a pneumothorax, effusion, and subsequent empyema. Patient acutely decompensated while undergoing decortication of the right lung
		Pulsatile	Patient died at home. No other details available
		Pulsatile	Unknown cause of death
3	1	Nonpulsatile	Persistent postoperative atrial septal defect and pulmonary insufficiency postoperatively leading to ventricular fibrillation and cardiac arrest s/p return of spontaneous circulation. Ultimately, while patient was on maximal support, family decided to withdraw care
4	1	Nonpulsatile	Patient readmitted nearly 6 mo following surgery for a seizure. Patient developed pneumonia, acute respiratory distress syndrome, and subsequent death
5	2	Nonpulsatile	Patient died at home approximately 6 wk after surgery. Unclear cause of death. Possibly, aspiration vs arrhythmia
		Nonpulsatile	Witnessed arrest at home by mom before initiating feeding. Patient was taken by emergency medical services to nearest hospital and was pronounced dead soon after arrival

TABLE E6. Types of operations included in the study and number of patients utilizing deep hypothermic circulatory arrest (DHCA) and antegrade cerebral perfusion (ACP)

Operation	No. of patients	No. of patients using DHCA	No. of patients using ACP
Atrial septal defect repair	19	0	0
Ventricular septal defect repair	74	0	0
Tetralogy of Fallot eepair	26	0	0
Pulmonary valve repair and replacement	3	0	0
Mitral valve repair and replacement	3	0	0
Aortic valve repair and replacement	1	0	0
Fontan procedure	23	0	0
Glenn procedure	28	0	0
Norwood procedure	8	1*	7†
Aortic arch augmentation	4	0	4‡
Arterial switch operation	13	0	0
Rastelli operation	2	0	0
Atrioventricular canal repair	25	0	0
Other	55	0	0

*Nonpulsatile. †All nonpulsatile. ‡1 pulsatile, 3 nonpulsatile.

TABLE E7. Demographics, cardiopulmonary bypass (CPB) characteristics, and gaseous microemboli (GME) counts for pulsatile versus nonpulsatile neonatal/pediatric patients utilizing 8, 10, and 12 Fr arterial cannulae stratified based on Society of Thoracic Surgeons European Association for Cardio-Thoracic Surgery Congenital Heart Surgery (STAT) mortality risk

STAT mortality category	Low/middle risk (Mortality categories 1-3)			High risk (Mortality categories 4-5)		
	Nonpulsatile	Pulsatile	*P* value	Nonpulsatile	Pulsatile	*P* value
No. of patients	135	121	–	17	11	-
Demographics						
Male sex	80 (59.3)	59 (48.8)	.09	10 (58.8)	9 (81.8)	.21
Age (mo)	19.2 ± 1.9	13.3 ± 1.6	**.02***	4.1 ± 1.9	14.8 ± 6.9	.17
Weight (kg)	8.8 ± 0.4	7.6 ± 0.5	.06	4.7 ± 0.9	8.6 ± 2.9	.05
Height (cm)	72.4 ± 1.7	67.8 ± 1.6	.06	56.9 ± 3.9	63.9 ± 6.7	.35
CPB characteristics						
Mortality score	0.22 ± 0.01	0.22 ± 0.01	.84	1.8 ± 0.2	1.2 ± 0.2	**<.001***
Aortic crossclamp time (min)	65.3 ± 3.4	75.3 ± 3.1	**.03***	92.5 ± 7.4	57.3 ± 8.9	**.01***
CPB time (min)	108.8 ± 5.1	111.3 ± 4.3	.71	174.2 ± 11.8	110.0 ± 11.3	**.002***
Flow index (L/m^2/min)	2.4 ± 0.0	2.4 ± 0.0	.48	2.4 ± 0.1	2.4 ± 0.1	.67
Arterial line pressure (mm Hg)	129.2 ± 3.2	116.0 ± 2.0	**<.001***	108.7 ± 8.4	113.2 ± 6.8	.71
VAVD (mm Hg)	−16.6 ± 0.8	−16.5 ± 0.8	.94	−18.6 ± 1.9	−17.0 ± 3.0	.64
Ultrafiltration (mL/kg)	23.4 ± 2.4	27.7 ± 3.1	.26	10.8 ± 3.7	9.5 ± 2.8	.91
Modified ultrafiltration (mL/kg)	95.9 ± 4.1	105.9 ± 4.7	.19	199.0 ± 36.5	120.7 ± 19.1	**<.001***
Urine output during CPB (mL/kg/hr)	5.1 ± 0.4	3.4 ± 0.6	.31	4.5 ± 0.4	1.9 ± 0.5	.32
GME counts						
GME counts – right MCA	287 ± 69	162 ± 45	.19	734 ± 376	335 ± 278	.18

Values are presented as n (%) or mean ± SEM. *VAVD*, Vacuum-assisted venous drainage; *MCA*, middle coronary artery. *$P < .05$, comparison between nonpulsatile versus pulsatile within each risk group. If there is a relationship with P value < .05, then numbers are presented in boldface type.

TABLE E8. Clinical outcomes for pulsatile versus nonpulsatile neonatal/pediatric patients utilizing 8, 10, and 12 Fr arterial cannulae stratified based on Society of Thoracic Surgeons European Association for Cardio-Thoracic Surgery Congenital Heart Surgery (STAT) mortality risk

	Low/middle risk (Mortality categories 1-3)			High risk (Mortality categories 4-5)		
STAT mortality category	**Nonpulsatile**	**Pulsatile**	***P* value**	**Nonpulsatile**	**Pulsatile**	***P* value**
No. of patients	135	121	–	17	11	–
Intubation time (h)	8.8 (5.9-28.3)	9.3 (6.3-27.8)	.805	53.3 (28.4-151.9)	28.6 (7.0-68.4)	.119
ICU LOS (d)	2.2 (1.2-4.9)	2.0 (1.2-3.9)	.326	8.6 (2.9-23.5)	3.1 (1.9-4.9)	.60
Hospital LOS (d)	4.7 (3.4-8.5)	4.4 (3.4-7.9)	.618	16.6 (11.7-44.0)	7.3 (4.3-11.6)	**.014***
Mortality within 180 d	2 (1.5)	2 (1.7)	1.0	3 (17.6)	0 (0.0)	.26

Values are presented as median (25th-75th percentiles) or n (%). Boldface indicates statistical significance. *ICU*, Intensive care unit; *LOS*, length of stay. *$P < .05$, comparison between nonpulsatile versus pulsatile within each risk group.