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Hong-Gook Lim, MD, PhD, Woong-Han Kim, MD, PhD, Chun-Soo Park, MD, Eui-Suk Chung, MD, Chang-Ha Lee, MD, PhD, Jeong Ryul Lee, MD, PhD, and Yong Jin Kim, MD, PhD

Department of Thoracic and Cardiovascular Surgery, Clinical Research Institute, Seoul National University Children's Hospital, College of Medicine, Seoul National University, Seoul; Department of Thoracic and Cardiovascular Surgery, Sejong General Hospital, Sejong Heart Institute, Bucheon; Department of Thoracic and Cardiovascular Surgery, Seoul National University Bundang Hospital, College of Medicine, Seoul National University, Bundang, Korea

Background. We assessed whether regional cerebral perfusion is neurologically safe during long-term follow up, and evaluated the effect of our current combined coronary perfusion strategy by comparing outcomes of nonworking beating hearts and arrested hearts under regional cerebral perfusion.

Methods. From March 2000 to October 2008, 159 neonates or infants with an aortic arch anomaly underwent one-stage biventricular repair with continuous cerebral perfusion. Patients (group A, n = 111) under continuous cerebral perfusion with a nonworking beating heart using the dual-perfusion technique through the innominate artery and aortic root were compared with patients (group B, n = 48) under continuous cerebral perfusion with an arrested heart.

Results. There were three hospital mortalities. A transient neurologic complication occurred in 3 patients, who recovered completely. During a mean (±standard deviation) of 37.9 ± 26.3 months (range, 0.5 to 95.4 months) of follow-up, 2 late deaths occurred without abnormal neurologic development. Group A had less myocardial ischemic time, which resulted in less total inotropic and vasopressin requirements, and also less delayed sternal closure, duration of ventilator care and chest tube drainage, amount of pleural effusion, and lengths of intensive care unit and hospital stay than group B, particularly in neonates and patients with complex anomalies.

Conclusions. One-stage total arch repair under regional cerebral perfusion provides an excellent means of minimizing neurologic complications during long-term follow up. Our perfusion strategy for arch anomaly under continuous cerebral perfusion with a nonworking beating heart using the dual-perfusion technique may also minimize myocardial complications and morbidities, and should be recommended, particularly in neonates and patients with complex anomalies.

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The primary repair of aortic arch obstructions and associated cardiac anomalies in neonates and infants presents a surgical challenge. Deep hypothermic circulatory arrest, which was used as a perfusion strategy for aortic arch repair, prolonged myocardial ischemia and might induce cerebral dysfunction. To eliminate these potential side effects, we [1–3] introduced a combined perfusion technique using dual arterial cannulas, one of which is placed in the innominate artery and the other in the aortic root. By snaring the innominate artery and cross-clamping the ascending aorta, we performed extended aortic arch anastomosis under continuous cerebral perfusion and a nonworking beating heart in neonates and infants.

The purpose of this study was to determine whether regional cerebral perfusion is neurologically safe in the long-term, and whether our current perfusion strategy, which involves combined coronary perfusion, effectively enhances myocardial recovery and reduces morbidities and hospitalization times as compared with regional cerebral perfusion with an arrested heart.

Material and Methods

Patient Profiles

From March 2000 to October 2008, 159 neonates or infants with an aortic arch anomaly underwent one-stage biventricular repair under continuous cerebral perfusion. Patients (group A, n = 111) with continuous cerebral perfusion and a nonworking beating heart by the dual-perfusion technique into the innominate artery and aortic root were compared with patients (group B, n = 48) with continuous cerebral perfusion only.

Preoperative diagnoses of arch anomalies were coarctation of the aorta (CoA) in 130 patients, and interruption of the aortic arch (IAA) in 29 patients. Combined anom-

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Address correspondence to Dr W-H Kim, Department of Thoracic and Cardiovascular Surgery, Seoul National University, College of Medicine, Seoul National University Children's Hospital, 28 Yongon-Dong, Jongno-Gu, Seoul, 110-744, Korea; e-mail: woonghan@snu.ac.kr.

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Table 1. Demographic Data and Diagnoses[a]

Variable	Classification I (n = 82)			Classification II (n = 77)		
	Group A (n = 53)	Group B (n = 29)	*p* Value	Group A (n = 58)	Group B (n = 19)	*p* Value
Demographics						
Sex (M/F)	27/26	14/15	0.82	36/22	7/12	0.06
Age (d)	39.9 ± 44.3	43.8 ± 38.1	0.69	43.7 ± 61.9	39.5 ± 62.5	0.80
Body weight (kg)	3.52 ± 1.54	3.66 ± 0.93	0.65	3.70 ± 1.17	3.76 ± 1.46	0.86
Height (cm)	52.5 ± 7.2	52.5 ± 4.4	0.99	53.2 ± 5.7	52.7 ± 7.2	0.80
BSA (m^2)	0.22 ± 0.06	0.22 ± 0.04	0.91	0.23 ± 0.05	0.22 ± 0.06	0.83
Diagnosis						
CoA	53	29		37	11	0.65
IAA	0	0		21	8	0.65
VSD	36	25	0.07	47	16	0.76
Aortic atresia with VSD	0	0		4	0	0.24
Truncus arteriosus	0	0		2	2	0.23
AVSD	0	0		4	0	0.24
AP window/AORPA	0	0		4	0	0.24
DORV	0	0		2	3	0.06
TAPVR/PAPVR/cor triatriatum	0	0		3	1	0.41
TGA/CCTGA	0	0		4	0	0.24
LVOTO	0	0		10	2	0.48
MS/MR	0	0		9	1	0.25
PS/DCRV	1	1	0.66	15	5	0.91
Vascular ring	0	0		1	0	0.57

[a] Classification I includes isolated coarctation of the aorta (CoA) with arch hypoplasia or CoA with ventricular septal defect (VSD); classification II includes interrupted aortic arch (IAA) with VSD or an arch anomaly with a complex anomaly; group A includes regional cerebral perfusion with coronary perfusion; group B includes regional cerebral perfusion without coronary perfusion.

AORPA = anomalous origin of the right pulmonary artery from ascending aorta; AP = aortopulmonary; AVSD = atrioventricular septal defect; BSA = body surface area; CCTGA = congenitally corrected transposition of the great arteries; DCRV = double-chambered right ventricle; DORV = double-outlet right ventricle; LVOTO = left ventricular outflow tract obstruction; MS = mitral stenosis; MR = mitral regurgitation; PAPVR = partial anomalous pulmonary venous return; PS = pulmonic stenosis; TAPVR = total anomalous pulmonary venous return; TGA = transposition of the great arteries.

alies were ventricular septal defect (VSD) in 124 patients, pulmonic stenosis in 22, left ventricular outflow tract obstruction in 12, mitral regurgitation in 7, aortic atresia with VSD in 4, truncus arteriosus in 4, Taussig-Bing anomaly in 4, anomalous origin of the right pulmonary artery from the ascending aorta in 4, atrioventricular septal defect in 4, transposition of the great arteries in 3, partial anomalous pulmonary venous return in 3, mitral stenosis in 3, aortopulmonary window in 2, double-chambered right ventricle in 2, total anomalous pulmonary venous return in 1, congenitally corrected transposition of the great arteries in 1, double-outlet right ventricle in 1, cor triatriatum in 1, and vascular ring in 1.

The study population was divided into patients with isolated CoA with arch hypoplasia, and CoA with VSD (group I), and IAA with VSD, and arch anomaly combined with complex congenital heart defects, such as aortic atresia with VSD, truncus arteriosus, Taussig-Bing anomaly, anomalous origin of the right pulmonary artery from the ascending aorta, atrioventricular septal defect, transposition of the great arteries, double-outlet right ventricle, total anomalous pulmonary venous return, left ventricular outflow tract obstruction, and others (group II; Table 1). Patients were excluded if they were being considered for univentricular repair. This study was approved by the Institutional Review Board of Seoul National University College of Medicine, Seoul National University Hospital (H-0812-017-265), and Sejong General Hospital, Sejong Heart Institute (2008-013), and individual parental consent for the study was waived.

Surgical Technique

After right radial arterial pressure monitoring, a standard midline sternotomy was made, and after full heparinization and pursestring sutures, a 6F (2.0 mm) arterial cannula (Cardiopulmonary AG; Maquet, Hirrlingen, Germany) or an 8F (2.7 mm) arterial cannula (RMI; Edwards Lifesciences LLC, Irvine, CA) was inserted directly through the innominate artery and a standard bicaval cannulation instituted. In cases of a ductal-dependent descending aortic circulation, an 8F flexible arterial cannula (DLP; Medtronic, Grand Rapids, MI) was introduced at the proximal patent ductus arteriosus (PDA) and advanced into the descending aorta. These two arterial cannulas were then Y-connected, and cardiopulmonary bypass was started. The PDA was snared immediately after beginning cardiopulmonary bypass. A left ventricular vent (10F, DLP; Medtronic Inc, Minneapolis, MN) was then introduced through the right upper pulmonary vein or left atrial appendage, if appropriate. A

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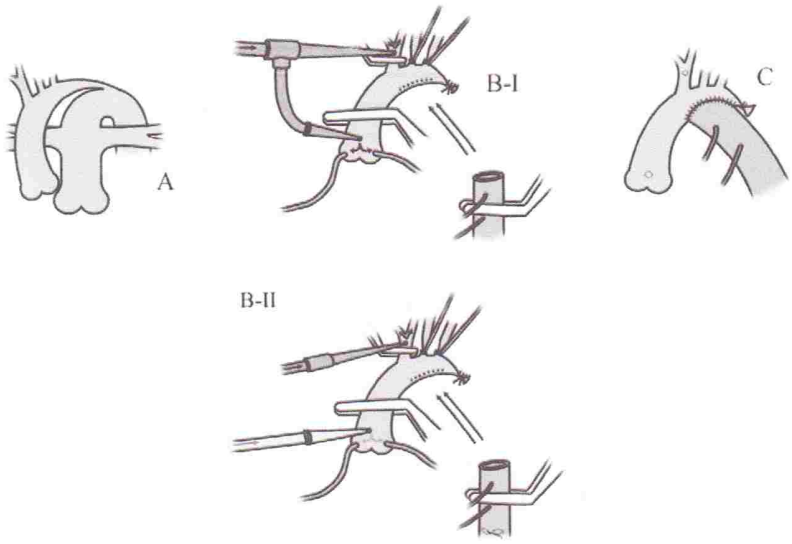

Fig 1. Extended aortic arch anastomosis is performed under continuous cerebral perfusion with or without coronary perfusion. Illustrations showing the operative technique. (A) Typical morphology of coarctation and arch hypoplasia. (B-I) Circuitry for isolated cerebral and myocardial perfusion. (B-I-1) Direct cannulation at the innominate artery. (B-I-2) Regional perfusion to both brain and myocardium. (B-II) Circuitry for isolated cerebral perfusion and myocardial arrest. (B-II-1) Direct cannulation at the innominate artery. (B-II-2) Regional perfusion to the brain only and infusion of cardioplegic solution to myocardium. (C) Extended end-to-side anastomosis using a native tissue-to-tissue technique.

pH-stat acid-base management strategy was used exclusively for cerebral protection. During cooling, distal pulmonary arteries up to the second branch level, arch vessels, and the descending aorta were extensively dissected and mobilized to relieve tension after anastomosis and to avoid airway compression. An aortic root cannula (4F, DLP; Medtronic Inc) was then inserted and T-connected with the side hole of the innominate artery cannula. When the rectal temperature reached 28°C, the proximal innominate, the left common carotid, and left subclavian arteries were snared down to initiate regional cerebral perfusion. As the ascending aorta was clamped just distal to the root cannula, simultaneous myocardial perfusion was maintained using a T-connected infusion line (group A), or myocardial arrest was induced by the infusion of cardioplegia (group B). Simultaneous myocardial perfusion or myocardial arrest during aortic arch reconstruction was selected according to surgeon's preference without an era effect. The descending aorta was also clamped as far as possible distally and gently elevated to produce a bloodless field and to reduce anastomotic tension. Mean blood pressure in the right radial artery was maintained at 50 to 60 mm Hg, and blood flow rate was regulated at 50 to 100 mL · kg^{-1} · min^{-1}. Mean hematocrit was maintained at around 30%. Extended aortic arch repair was performed using a native tissue-to-tissue technique [4]. All anastomoses were performed using 7-0 or 8-0 synthetic monofilament suture material. After the aortic arch repair was complete, arch vessel snares and the descending aortic clamp were removed after complete removal of air, and the flow rate was fully restored (150 to 200 mL · kg^{-1} · min^{-1}). Myocardial perfusion was then stopped and cardioplegia applied for intracardiac repair (Fig 1).

Neurologic Monitoring and Follow-Up

In general, a neurologist evaluated preoperative neurologic status. The neurologic and brain perfusion status of patients were evaluated preoperatively by electroencephalography (EEG) and brain sonography. Brain single photon emission computed tomography and magnetic resonance imaging were also evaluated in some patients for the purpose of research as well as in patients with a neurologic abnormality. During regional cerebral perfusion, blood pressures were monitored at the right radial artery. Brain perfusion status was continuously monitored by near-infrared spectroscopy (INVOS cerebral oximeter; Somanetics, Troy, MI) from the beginning of surgery, and near-infrared spectroscopy monitoring was maintained for 1 or 2 days after surgery. These data were sampled and stored every 30 seconds throughout the monitoring period for comparison and analysis. Transcranial Doppler ultrasonography was used to measure blood flow velocity directly in the middle cerebral arteries of some patients for the purpose of research [3]. Before discharge, EEG and brain sonography were performed again, and a neurologist evaluated neurologic status. Postoperative brain single photon emission computed tomography and magnetic resonance imaging evaluations were also performed in some patients for the purpose of research and in patients with a neurologic abnormality. After discharge, a neurologist conducted regular follow-up evaluations to monitor neurologic development, and these evaluations were continued until a neurologist deemed them no longer necessary. The follow-up status of patients was determined by retrospectively reviewing hospital records or by telephone interviews.

Table 2. Operative Data[a]

Variable	Classification I (n = 82)			Classification II (n = 77)		
	Group A (n = 53)	Group B (n = 29)	*p* Value	Group A (n = 58)	Group B (n = 19)	*p* Value
Bypass data (min)						
CPB time	140.6 ± 37.4	128.1 ± 36.0	0.15	182.3 ± 56.9	208.5 ± 86.2	0.13
ACC time	32.4 ± 22.6	67.0 ± 21.9	<0.01	63.2 ± 35.8	107.0 ± 44.3	<0.01
TCA time	0.34 ± 2.21	0.00 ± 0.00	0.41	0.07 ± 0.53	0.32 ± 1.00	0.17
Regional perfusion data						
DACC time (min)	26.6 ± 9.6	26.6 ± 8.7	0.98	28.1 ± 9.8	29.0 ± 11.6	0.75
Right radial artery pressure (mm Hg)	51.9 ± 6.6	52.1 ± 10.5	0.89	52.7 ± 6.5	53.2 ± 11.6	0.84
Regional flow (mL · min^{-1} · kg^{-1})	70.3 ± 15.5	60.1 ± 26.8	0.04	67.0 ± 13.6	57.1 ± 16.6	0.01

[a] Classification I includes isolated coarctation of the aorta with arch hypoplasia or coarctation of the aorta with ventricular septal defect; classification II includes interrupted aortic arch with ventricular septal defect or an arch anomaly with a complex anomaly; group A includes regional cerebral perfusion with coronary perfusion; group B includes regional cerebral perfusion without coronary perfusion.

ACC = aortic cross-clamp; CPB = cardiopulmonary bypass; DACC = descending aortic cross-clamp; TCA = total circulatory arrest.

Clinical Outcome Assessments

Intraoperative variables analyzed included duration of cardiopulmonary bypass, aortic cross-clamp time, total circulatory arrest time, regional perfusion time, and right radial arterial pressure and regional flow during selective regional perfusion. The outcome variables included total inotropic and vasopressin requirements, the need for delayed sternal closure, durations of intubation and chest tube drainage, total amount of pleural effusion, lengths of intensive care unit and hospital stays, neurologic morbidity, and mortality. Inotropic scores were calculated by summing the doses of dopamine (in micrograms per kilogram per minute), dobutamine (in micrograms per kilogram per minute), milrinone (in micrograms per kilogram per minute × 10), and epinephrine (in micrograms per kilogram per minute × 100), all multiplied by the number of hours that each drug was used [5–7].

Statistical Analysis

Statistical analyses were performed using SPSS version 17.0 (SPSS, Inc, Chicago, IL). All results are expressed as median and ranges or as mean ± standard deviations. The significance of differences between two groups was assessed using the unpaired Student's *t* test or Pearson's χ^2 test. Probability values of less than 0.05 were considered statistically significant.

Results

There were 84 boys and 75 girls. Median age at surgery was 20 days (range, 1 to 301 days); 61% of the patients were 1 month old or younger at the time of surgery, and 79% were 2 months old or younger. Median body weight and body surface area at surgery were 3.4 kg (range, 1.2 to 11.5 kg) and 0.22 m^2 (range, 0.12 to 0.50 m^2). Operative results are summarized in Table 2. The median cardiopulmonary bypass time was 147 minutes (range, 62 to 350 minutes), and the median aortic cross-clamp time for the 146 patients who underwent intracardiac repairs was 56 minutes (range, 6 to 197 minutes). Group A had shorter aortic cross-clamp times than group B (group I: 32.4 ± 22.6 minutes versus 67.0 ± 21.9 minutes; group II: 63.2 ± 35.8 minutes versus 107.0 ± 44.3 minutes; Table 2). The median regional perfusion time was 25 minutes (range, 15 to 69 minutes). Group A had more regional blood flow during selective coronary and cerebral regional perfusion than group B during selective cerebral regional perfusion (group I: 70.3 ± 15.5 mL · kg^{-1} · min^{-1} versus 60.1 ± 26.8 mL · kg^{-1} · min^{-1}; group II: 67.0 ± 13.6 mL · kg^{-1} · min^{-1} versus 57.1 ± 16.6 mL · kg^{-1} · min^{-1}; Table 2). Temporary circulatory arrest was applied in 3 patients for closure of a VSD in a neonate with an exceptionally low body weight (2.3 kg) and a bilateral superior venae cava, transfer of the arterial cannula from the innominate artery to the reconstructed main pulmonary artery during the Norwood procedure, and closure of an atrial septal defect. However, these arrest times were minimal (median, 4 minutes; range, 2 to 16 minutes).

Postoperative results are summarized in Table 3. Three hospital mortalities (1.89%) occurred. One patient in group IB was a 2-month-old infant weighing 2.1 kg with CoA, arch hypoplasia, and multiple VSDs. She was also premature, and needed preoperative ventilator care. She underwent one-stage biventricular repair that consisted of extended end-to-end coarctoplasty and closure of a perimembranous type VSD and a muscular outlet type VSD under regional cerebral perfusion with an arrested heart. Subsequently, she needed delayed sternal closure on the 3rd postoperative day, but expired owing to multiorgan failure on the 16th postoperative day. A second patient in group IIA was a 23-day-old female neonate weighing 2.0 kg who had type B IAA, subaortic stenosis, bicuspid aortic valve, VSD, PDA, and atrial septal defect. She had meconium aspiration, hepatic dysfunction, and sepsis preoperatively. She underwent IAA total repair, which consisted of extended end-to-end aortoplasty, VSD closure, atrial septal defect closure, and PDA ductal tissue wide excision under regional cerebral perfusion with a nonworking beating heart. She expired at 3 months postoperatively owing to gastrointestinal bleeding and hepatic dysfunction. The third patient in group IIB was a 17-day-old neonate weighing 3 kg with

Table 3. Postoperative Data[a]

Variable	Classification I (n = 82)			Classification II (n = 77)		
	Group A (n = 53)	Group B (n = 29)	*p* Value	Group A (n = 58)	Group B (n = 19)	*p* Value
Early outcome						
Hospital mortality	0	1	0.17	1	1	0.40
TND	1	1	0.66	1	0	0.57
Follow-up outcome[b]						
Late mortality	0	0		1	1	0.40
Neurologic problem	0	0		0	0	

[a] Classification I includes isolated coarctation of the aorta with arch hypoplasia or coarctation of the aorta with ventricular septal defect; classification II includes interrupted aortic arch with ventricular septal defect or an arch anomaly with a complex anomaly; group A includes regional cerebral perfusion with coronary perfusion; group B includes regional cerebral perfusion without coronary perfusion.

[b] Follow-up duration was 37.9 ± 26.3 months (range, 0.5–95.4 months).

TND = transient neurologic deficits.

CoA, arch hypoplasia, PDA, VSD, partial anomalous pulmonary venous return, restrictive atrial septal defect, and mild pulmonary vein narrowing. She also had tracheal stenosis preoperatively. She underwent one-stage biventricular repair consisting of extended end-to-end coarctoplasty, PDA division, VSD closure, and partial anomalous pulmonary venous return repair under regional cerebral perfusion with an arrested heart. Subsequently, she required sliding tracheoplasty for tracheal stenosis and right pulmonary artery translocation for left main bronchus compression by the right pulmonary artery on the 18th and 82nd postoperative day, respectively. At 4 months after the first operation, she expired owing to mediastinitis and multiorgan failure.

A transient neurologic complication was noted in 3 patients (1.9%), who recovered completely. One infant with anomalous origin of the right pulmonary artery from the ascending aorta in group IIA showed transient chorea during the postoperative period, but completely recovered after 11 months of follow-up. Fortunately, she had no abnormality by brain computed tomography or by EEG during the follow-up period. Furthermore, she has shown normal neurologic development during outpatient clinic follow-up visits for 6 years. A second infant with CoA and arch hypoplasia in group IA underwent arch repair with anterior translocation of the right pulmonary artery, which compressed the airway preoperatively. This patient showed one episode of seizurelike activity during the postoperative period, but had no abnormality by brain ultrasonography or EEG during follow-up. At 1 month after the incident, she no longer required anticonvulsant, and she exhibited a normal developmental status at 6 months after the operation. The third infant with CoA and VSD in group IB showed seizure during the postoperative period, but recovered shortly thereafter. She exhibited a normal developmental status during the 7 months after surgery. No difference was observed between the two groups in terms of early mortality or transient neurologic deficits.

The effects of coronary perfusion during regional perfusion are summarized in Table 4. Group A had less myocardial ischemic time (Table 2), which resulted in a lower inotropic score and vasopressin requirement, and also less delayed sternal closure, duration of ventilator care and chest tube drainage, total pleural effusion amount, and lengths of intensive care unit and hospital stays than group B, particularly for patients with a complex arch anomaly and neonates (Table 4).

Follow-up data were available on 153 patients (96.2%) during a mean period of 37.9 ± 26.3 months (range, 0.5 to 95.4 months). Two late deaths (1.3%) occurred but without neurologic abnormal development. One patient in group IIA was a 20-day-old neonate weighing 2.9 kg with aortic atresia, severe long segmental arch hypoplasia, and a large VSD. She was discharged uneventfully 38 days after one-stage biventricular repair that consisted of a modified Norwood procedure and Rastelli operation under regional cerebral perfusion with nonworking beating heart. However, at 7 months after the first operation, she went into cardiac arrest during catheterization for right ventricular outflow tract obstruction and was consequently supported using extracorporeal membrane oxygenation. She underwent right ventricular outflow tract reconstruction 7 days later, but expired owing to acute respiratory distress syndrome on the 6th postoperative day. The other patient in group IIB was a 2-month-old infant weighing 3.45 kg with type II truncus arteriosus, IAA, and multiple VSDs. She was discharged uneventfully 20 days after one-stage biventricular repair consisting of aortoplasty and the Rastelli operation under regional cerebral perfusion with an arrested heart. She expired after the second operation 6 years later. No difference was observed between the two groups in terms of late mortalities and neurologic complications. Also, no risk factors for death and neurologic complications were identified. No difference was observed between the two groups in terms of ventricular function in echocardiography or the need for cardiac medications during long-term follow-up.

Comment

Because of the decreasing mortality rate of congenital cardiac surgery, neurologic morbidity is now the primary

Table 4. Effect of Coronary Perfusion During Regional Perfusion[a]

Variable	Classification I			Classification II		
	Group A	Group B	*p* Value	Group A	Group B	*p* Value
All patients (n = 159)	n = 53	n = 29		n = 58	n = 19	
Inotropic score ($\mu g \cdot kg^{-1} \cdot min^{-1}$) × hours[b]	1,765.6 ± 1,048.7	2,120.3 ± 1,623.6	0.24	2,029.9 ± 1,677.1	3,736.5 ± 2,257.6	<0.01
Vasopressin use	2 (3.8%)	6 (20.7%)	0.01	1 (1.7%)	11 (57.9%)	<0.01
Vasopressin dose (units · $kg^{-1} \cdot min^{-1}$) × hours	0.00125 ± 0.00752	0.01543 ± 0.04747	0.04	0.00017 ± 0.00128	0.01753 ± 0.03358	<0.01
Delayed sternal closure	2 (3.8%)	4 (13.8%)	0.10	3 (5.2%)	9 (47.4%)	<0.01
Extubation (h)	127.2 ± 74.2	171.7 ± 195.3	0.14	160.3 ± 114.2	280.9 ± 211.5	<0.01
C- tube removal (days)	5.3 ± 5.2	5.8 ± 3.1	0.62	5.7 ± 3.2	9.1 ± 5.2	<0.01
Pleural effusion (mL/kg)	60.4 ± 100.1	91.1 ± 50.9	0.13	61.5 ± 51.6	136.9 ± 85.1	<0.01
ICU stay (days)	13.1 ± 8.7	18.5 ± 21.3	0.11	15.3 ± 13.1	30.5 ± 16.9	<0.01
Hospital stay (days)	19.4 ± 8.5	27.4 ± 22.6	0.02	23.8 ± 15.0	38.8 ± 16.1	<0.01
Neonate only (n = 97)	n = 31	n = 15		n = 36	n = 15	
Inotropic score ($\mu g \cdot kg^{-1} \cdot min^{-1}$) × hours[b]	1,825.8 ± 669.3	2,369.7 ± 969.6	0.03	2,256.6 ± 1,950.2	4,103.9 ± 2,417.2	<0.01
Vasopressin use	1 (3.2%)	6 (40.0%)	<0.01	1 (2.0%)	10 (66.7%)	<0.01
Vasopressin dose (units · $kg^{-1} \cdot min^{-1}$) × hours	0.00172 ± 0.00956	0.02880 ± 0.06271	0.02	0.00027 ± 0.00162	0.02454 ± 0.03690	<0.01
Delayed sternal closure	1 (3.2%)	2 (13.3%)	0.19	2 (3.9%)	7 (46.7%)	<0.01
Extubation (h)	121.6 ± 44.5	218.2 ± 256.7	0.05	161.6 ± 99.9	327.3 ± 215.6	<0.01
C- tube removal (days)	4.3 ± 2.0	5.6 ± 2.5	0.07	5.6 ± 3.0	9.1 ± 5.2	<0.01
Pleural effusion (mL/kg)	54.1 ± 57.1	287.5 ± 132.1	0.03	64.7 ± 46.3	149.0 ± 87.7	<0.01
ICU stay (days)	13.3 ± 5.7	22.2 ± 28.1	0.09	16.1 ± 13.5	31.0 ± 18.3	<0.01
Hospital stay (days)	19.7 ± 6.8	31.1 ± 29.3	0.04	25.1 ± 16.1	39.3 ± 17.1	<0.01

[a] Classification I includes isolated coarctation of the aorta with arch hypoplasia or coarctation of the aorta with ventricular septal defect; classification II includes interrupted aortic arch with ventricular septal defect or an arch anomaly with a complex anomaly; group A includes regional cerebral perfusion with coronary perfusion; group B includes regional cerebral perfusion without coronary perfusion.

[b] Inotropic scores were calculated by summing of doses of dopamine (in $\mu g \cdot kg^{-1} \cdot min^{-1}$), dobutamine (in $\mu g \cdot kg^{-1} \cdot min^{-1}$), milrinone (in $\mu g \cdot kg^{-1} \cdot min^{-1} \times 10$), and epinephrine (in $\mu g \cdot kg^{-1} \cdot min^{-1} \times 100$) and multiplying each by the number of hours that the drug was used.

ICU = intensive care unit.

concern after surgery. Regional brain perfusion was introduced to avoid the neurologic complications associated with circulatory arrest method [1, 8–11]. We use simultaneous cerebral perfusion combined with myocardial perfusion during the repair of aortic arch anomalies, which requires a somewhat higher flow rate of 50 to 100 mL · kg^{-1} · min^{-1} to maintain a perfusion pressure of 50 to 60 mm Hg, because pressure is related to cerebral blood flow rather than rate [12]. Previously, we [1–3] showed that unilateral brain regional perfusion in neonates and children is a useful technique that is free of significant neurologic deficits, and that our protocol of brain regional perfusion through the right innominate artery alone during aortic arch surgery supplies an adequate, even perfusion flow to both the left and right brain using near-infrared spectroscopy and transcranial Doppler ultrasonographic evaluations of the cerebral artery in neonates and children [3]. In addition, based on preoperative and postoperative EEG and brain single photon emission computed tomography, we [3] demonstrated that this method results in no significant neurologic deficits.

In the present series, both early and late mortality rates were acceptable. Early postoperative neurologic complications occurred in 3 patients (1.9%), and fortunately, all 3 recovered quickly and completely during follow-up. Preoperative hypoxic insults; individual characteristics such as associated anomalies in the central nervous system or a poorly developed circle of Willis or other collaterals; or thromboembolic events may be responsible for those neurologic problems. However, there was no evidence of cerebral hyperperfusion syndrome in our study populations because the risk of cerebral edema could be reduced using careful monitoring of right radial artery pressure, near-infrared spectroscopy and transcranial Doppler ultrasonographic flow measurement as an evaluation tool for direct confirmation for middle cerebral arterial blood flow, and modified ultrafiltration [13]. Furthermore, no abnormality was detected by brain computed tomography or EEG in any of the 3 patients. They had fully recovered during the follow-up period, as described above. Although postoperative EEG and brain single photon emission computed tomography occasionally produced slightly abnormal results in some of our patients, neurologic development was normal in all patients, and thus, we consider that these abnormal findings were of no clinical significance. In addition to the use of regional perfusion, we believe that several factors, such as the pH-stat strategy used for acid-base manage-

ment, high hematocrit, moderate hypothermia, improved surgical skills, and comprehensive perioperative intensive care contributed to our excellent long-term neurologic results. However, long-term special studies for neurodevelopmental abnormalities need to be evaluated further.

Hypothermic total circulatory arrest may induce myocardial injury as well as neurologic complications. In neonates and some infants, low cardiac output can persist after coarctation repair as a result of preoperative left ventricular dysfunction [14]. Sano and Mee [15] described an isolated myocardial perfusion technique for minimizing myocardial ischemia during total circulatory arrest, and Ishino and colleagues [16] used innominate artery perfusion in patients undergoing extended aortic arch reconstruction. In this latter study, distal arch anastomosis was performed with continuous cerebral and myocardial perfusion by clamping the arch just distal to the innominate artery. However, when this method is used, a short period of cardioplegic arrest is necessary to complete the proximal anastomosis. In a later study, Ishino and associates [17] also described a technique for extended aortic arch anastomosis with selective cerebral perfusion and a working beating heart, and demonstrated that when both ventricles are properly loaded, the heart keeps beating with the ascending aorta cross-clamped. The most important issue concerns the cardiopulmonary bypass technique used to maintain a working beating heart. They adjusted preload on the ventricles using electrocardiograms, but no cardiac dysfunction was observed in any of the 4 patients postoperatively. A further investigation is required to determine the nature of the relationships between ventricular preload and aortic root pressure or coronary blood flow to increase the safety of on-pump aortic surgery with a working beating heart.

Recently, we [1–3] reported a combined perfusion technique that uses two arterial cannulas; one is placed into the innominate artery and the other into the aortic root. By snaring the innominate artery and cross-clamping the ascending aorta, an extended end-to-side anastomosis was performed with continuous cerebral perfusion and a nonworking beating heart. Under separate myocardial perfusion during aortic arch reconstruction, hearts maintained an extremely slow, empty beating, and showed no signs of dilatation or functional derangement. Furthermore, this technique reduced the myocardial ischemic time (32.4 ± 22.6 minutes versus 67.0 ± 21.9 minutes in group I, 63.2 ± 35.8 minutes versus 107.0 ± 44.3 minutes in group II) and enabled us to repair arch anomaly completely without being restricted by time. In the present study, one hospital mortality occurred in group A and two in group B. Our regional perfusion strategy was found to decrease hospital resource utilization and to reduce hospital recovery times, particularly for patients with a complex arch anomaly and neonates. We do believe that our perfusion strategy not only improved their postoperative hemodynamics but also has certainly changed our practice by reducing the time required for each postoperative step, from earlier weaning from a ventilator, to intensive care unit discharge, removing chest tubes, and discharge from hospital to home. Our results also demonstrate that because the heart keeps beating during arch repair, the described technique not only enables us to minimize low cardiac output syndrome but is also free of early mortality associated with low cardiac output syndrome. Furthermore, at our institution, as the practical advantages of our perfusion strategy for arch repair, namely, less inotropic use, earlier ventilator weaning, shorter intensive care unit and hospital stays, and an overall sense of a more rapid recovery, became apparent, more surgeons, anesthesiologists, and cardiologists began promoting coronary perfusion during arch repair even for simple arch anomalies.

Separate myocardial perfusion during aortic arch reconstruction was performed routinely in cases requiring univentricular repair, as we previously described [1]. For univentricular palliation, including Norwood palliation, we believe that our protocol of simultaneous cerebral perfusion combined with myocardial perfusion during the repair of aortic arch anomalies is likely to result in better survival rates associated with better postoperative myocardial function than cerebral perfusion only. However, this comparison could not be made in the present study, because all patients who underwent univentricular palliation also underwent arch repair with regional cerebral and coronary perfusion. Our results for biventricular repair suggest that separate myocardial perfusion during aortic arch reconstruction should be used for less morbidity and mortality in univentricular palliation including Norwood palliation.

However, because the mean duration of follow up was not so long (37.9 ± 26.3 months; range, 0.5 to 95.4 months), the determination of whether our patients who were operated on at an early age have a lower risk of neurologic complication in adulthood will require further long-term special studies for neurodevelopmental abnormalities. It should be also noted that this study is limited by a lack of comparison with patients who were operated on under total circulatory arrest while in a state of deep hypothermia.

The regional cerebral perfusion technique for one-stage total arch repair has been successfully used in 159 neonates and infants, and has proven to be an excellent method that may minimize neurologic complications during long-term follow up. Moreover, our perfusion strategy for arch anomaly under continuous cerebral perfusion and a nonworking beating heart using the dual perfusion technique may also minimize myocardial complications and morbidities, and should be recommended particularly for patients with a complex arch anomaly and neonates.

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INVITED COMMENTARY

Lim and colleagues [1] are to be congratulated for developing and proving the safety and feasibility of novel pediatric cardiac surgical perfusion strategies. Previous publications from this group have documented that aortic arch reconstruction in neonates and infants using regional cerebral perfusion without circulatory arrest is feasible, safe, and may reduce potential neurologic complications compared with aortic arch reconstruction using circulatory arrest. In this study, they demonstrate that one-stage total arch reconstruction in neonates and infants using a dual perfusion technique with continuous cerebral and cardiac perfusion, and a nonworking beating heart, is feasible, safe, and may reduce neurologic and myocardial complications.

The authors are to be congratulated for their excellent results in these challenging patients and for their thoughtful analysis. Although they have demonstrated the safety and feasibility of these novel perfusion strategies, the choice of myocardial perfusion or myocardial arrest during arch reconstruction in their study was selected according to the surgeon's preference. Thus, confounding variables may account for some of the observations. Furthermore, evaluation of the efficacy and safety of continuous regional cerebral perfusion relative to that of hypothermic circulatory arrest requires longer follow-up with formal neurologic testing. Seizures, stroke, and motion disorders such as choreoathetosis represent a small fraction of neurologic complications. This study relied on imaging studies and serial examination by a neurologist, which is important and commendable. However, the assessment of neuroprotective strategies ultimately requires serial comparisons of objective measures of neurodevelopmental outcome in multiple domains.

Definitive evaluation of outcomes associated with alternative perfusion strategies requires (1) either a prospective randomized trial or a direct comparison of propensity matched groups, and (2) long-term follow-up. The Single Ventricle Reconstruction trial, supported by the National Heart, Lung, and Blood Institute and coordinated by the Pediatric Heart Network, is a model for how to conduct a prospective randomized trial in pediatric cardiac surgery. The Single Ventricle Reconstruction trial has demonstrated the challenges, including complexity and cost, of approaching the question of comparative effectiveness of treatment strategies for congenital heart disease by means of prospective randomized trials. Multi-institutional registries that track appropriate variables may also be used to facilitate comparisons of propensity matched groups. Transformation of the Society of Thoracic Surgeons Database into a platform for longitudinal follow-up may allow it to be used as a tool to answer questions about the long-term comparative effectiveness of treatment strategies.

Jeffrey Phillip Jacobs, MD

The Congenital Heart Institute of Florida
Cardiac Surgical Associates
625 Sixth Ave S, Ste 475
St. Petersburg, FL 33701
e-mail: jeffjacobs@msn.com

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