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Does Cardioplegic Protection of the Pediatric Patient Heart Vary According to the Cardiac Defect?

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Abstract

The technique of myocardial protection utilized during pediatric cardiac surgery may be influenced by the congenital lesion, and be related to the pathophysiological changes associated with myocardial dysfunction and altered systemic and pulmonary circulations. The present study is a retrospective examination of the cardioplegic and cardiopulmonary bypass parameters utilized during pediatric cardiac surgery.

1016 pediatric patients were subdivided according to cardiac lesion, with the following parameters recorded: Age at operation, weight, body surface area, cardioplegia (CP) volume administered, cardioplegia dose schedule, cardiopulmonary bypass and cross clamp times, and low perfusate temperature. Cardioplegia volume administration was indexed according to weight and body surface area and patients were categorized as being either acyanotic or cyanotic The following results (Mean ±SEM) were obtained between groups not significantly different in respect to weight and body surface area:

Defect	CP/Unit Weight (ml/Kg)	P Value
ASD vs Pulmonary Stenosis	26.7±0.8 vs 38.0±2.6	.001
ASD vs Pulmonary Atresia	26.7±0.8 vs 34.1±3.4	.001
A/VSD vs Truncus Arteriosus	30.5±2.1 vs 48.1±4.5	.009
VSD vs Tetralogy of Fallot	36.3±4.2 vs 35.2±1.1	.79
LV Outflow vs RV Outflow Lesions	32.3±2.8 vs 35.5±0.9	.27

Patients with pulmonary obstructive lesions had significantly more cardioplegic volume administered than certain acyanotic lesions. This may reflect a greater susceptibility to ischemic and reperfusion related phenomena in cyanotic compared to acyanotic patients. Cardioplegic protection of the pediatric heart may be influenced by multiple factors related to the cardiac lesion, necessitating preferential preservation strategies.

Introduction

Myocardial protection during cardiac surgery continues to be closely scrutinized as innovative advances in preservation techniques improve the ability of the heart to recover from induced ischemia. The quantity of research and literature devoted to this subject may reflect a clinical attitude that is continuously reevaluating previously accepted theorems and techniques. Indeed, retrograde cardioplegia (1), substrate enhanced cardioplegia (2,3) and warm induction normothermic cardioplegia (4) all have been evaluated for their efficacy in limiting or preventing irreversible ischemic injury.

Perhaps no group of cardiac patients represents a less homogeneous mixture than pediatric patients treated for congenital heart lesions. The current literature is well represented by advocates who state that the immature myocardium is more tolerant to both hypoxia and ischemia then mature myocardium (2,5,6,7) - although an increasing body of knowledge reports the opposite (8,9). One reason for this discrepancy stems from the extreme difficulty, if not impossibility, of establishing a consistent model to evaluate cardioprotective strategies in pediatric patients. The pathophysiology of congenital defects is a result of a multitude of abnormalities which include outflow and inflow tract obstructions, interchamber communications, abnormal attachments, and absence of anatomical features. Additionally, the systemic and pulmonary systems may adapt to both excessive and diminutive blood flow, by altering the distribution of flow from one system to the other. Lesions which create a reduction in pulmonary blood flow, resulting in increased quantities of reduced hemoglobin, frequently are accompanied by enhanced collateral distribution from systemic to pulmonary arteries (10-13). This redirection of flow not only alters systemic perfusion characteristics, but effects cardioplegic administration and retention.

The present study is an attempt to evaluate whether the administration of cardioplegia during pediatric cardiac surgery is dependent upon the type of congenital lesion, and the resultant physiologic and anatomical adaptations of the pulmonary and systemic vascular systems.

Materials and Methods

1016 cardiopulmonary bypass (CPB) records were retrospectively reviewed which represent all pediatric cardiac patients treated with CPB at University of Michigan

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Hospitals, between January 1986 and January 1990. A previous report identified the distribution of patients as well as anthropomorphic data (14). In that study patients were classified as having either acyanotic or cyanotic lesions as described by Arciniegas (15). The present study further subclassified the congenital cardiac defects according to specific lesions. When patients had multiple lesions, classification was achieved according to the defect which contributed most significantly to the pathophysiology encountered. No attempt was made to classify patients into more than a single major category, and therefore, each observation represents a single data point (patient).

Cardiopulmonary Bypass

The conduct CPB has previously been described (14). Briefly, silicone coil membrane oxygenators[a] were used in all patients with selection of the membrane size made according to the recommendations of the manufacturer. The bypass circuits consisted of a filtered cardiotomy reservoir[b], arterial line filter[c], and in line monitors for arterial and venous blood gas parameters and saturation[d,e]. The prime consisted of a balanced electrolyte solution supplemented with sodium bicarbonate, heparin, albumin, and mannitol. The decision to add homologous red blood cells to the prime was made by calculating the anticipated postdilutional hematocrit and relating this value to the severity of the lesion. Generally, preoperative asymptomatic patients and patients with anticipated short CPB periods, were hemodiluted to greater levels than symptomatic patients. Hemic prime solutions were used in the majority of neonatal patients, and fresh frozen plasma was also added to the prime. Maintenance of the hematocrit during CPB was generally inversely related to the temperature of the perfusate - with a low hematocrit at deep hypothermia around 18-20%, and dependent upon the severity and pathology of the lesion.

Arterial cannulation was achieved in either the ascending aorta, femoral artery, or ductus arteriosus (hypoplastic left heart syndrome). Venous cannulation was achieved by either a single atrial cannula, bicaval cannulation, or a femoral vein cannula. The majority of patients had left ventricular vents placed through the right superior pulmonary vein, although some patients had intracavitary drainage by direct aspiration with a pump sucker. An aortic root vent was routinely utilized following the release of the aortic cross clamp and removed just prior to the separating the patient from CPB. A dual roller pump[f] was used as the main arterial head in all procedures. Acid-base status was maintained according to alpha stat management.

a Sci Med 0400-4500 Oxygenators, Sci-Med, Inc., Minneapolis ,MN
b Polystan Cardiotomy, Vitaclor, Inc., Westmont, IL
c Pall Pediatric Filter 40 micron, Pall Biomedical, Glen Cove, NY
d CDI 300, 3M/Cardiovascular Devices, Inc., Irvine, CA
e Bentley Oxy-Sat, Baxter Labs., Irvine, CA
f Sarns 7000, 3M/Sarns, Inc., Ann Arbor, MI

Myocardial Protection

The protocol for myocardial protection has also been previously described (14). Cardioplegia (CP) was prepared prior to each case from a 1 liter bag of balanced electrolyte solution that was supplemented with potassium (20 mEq), sodium bicarbonate (25 mEq) and dextrose (5 grams). CP was delivered to the majority of patients through a coil bath recirculating delivery system. After the initiation of CPB oxygenated blood was added to the CP solution with the final delivery hematocrit ranging from 3 to 5%. In patients less than 4 Kg, cardioplegia was administered by a syringe at the table. Myocardial temperature was monitored in most patients by placement of a thermistor probe in the ventricular septal region. Topical slush was liberally applied to the heart throughout the procedure. The initial dose of CP was 30 ml Kg^{-1} body weight, and additional dosing was achieved when the septal temperature rose above 15°C or electrocardiographic activity was observed on the bed side monitor. The surgeon was notified throughout the cross clamp period of the elapsed time since previous CP dosing.

The following information was obtained from each patient: Congenital cardiac defect, gender, age, weight, body surface area (BSA), CPB time, cross clamp (CC) time, low perfusate temperature, CP volume, and the number of doses of CP. Additional indices of CP distribution were calculated for each patient and included CP Kg^{-1} body weight, CP m^{-2} BSA, CP min^{-1} CC time, and CP min^{-1} of CPB

Table 1. Pediatric patient classification of congenital heart defects.

Congenital Heart Defect	Classification (Cyanotic Acyanotic)	Patient Number	Gender	
		Number	Male	Female
Ventricular Septal Defect	Acyanotic	93	47	46
Atrial Septal Defect	Acyanotic	81	31	50
Left Vent. Outflow Tract	Acyanotic	78	50	28
Atrioventricular Canal	Acyanotic	71	35	36
Conduction Disturbance	Acyanotic	45	31	14
Mitral Valve Lesions	Acyanotic	25	11	14
Heart Transplants	Acyanotic	18	14	4
Atrial / Septal Vent. Defect	Acyanotic	18	6	12
Part. Anom. Pulm. Ven. Ret.	Acyanotic	16	5	11
Tetralogy of Fallot	Cyanotic	112	65	47
Transposition	Cyanotic	109	80	29
Pulmonary Stenosis	Cyanotic	69	40	29
Hypo. Left Heart Synd.	Cyanotic	57	40	17
Pulmonary Atresia	Cyanotic	30	14	16
Double Outlet Right Vent.	Cyanotic	27	18	9
Truncus Arteriosus	Cyanotic	20	8	12
TOTALS		869	495	374

Table 2. Patient and operative parameters for acyanotic lesions.

Lesion	(#)	Age (months)	Weight (Kg)	BSA (m^2)	CPB Time (mins)	CC Time (mins)	Low Perf Temp (°C)
VSD	(93)	26.3±4.7	10.0±1.2	0.43±.03	60.7±2.1	30.3±1.3	25.5±0.5
ASD	(81)	79.2±9.3	22.0±1.8	0.81±.04	44.4±1.7	18.0±1.0	31.5±0.3
LVOT	(78)	96.3±11.0	28.8±2.9	0.92±.07	77.0±5.6	49.2±3.2	28.0±0.8
AVCN	(71)	30.2±6.6	10.2±1.2	0.45±.03	102.8±11.2	57.8±2.3	23.6±0.6
COND	(45)	175.1±11.0	57.6±3.6	1.57±.06	121.1±6.3	43.4±2.6	30.9±0.6
MVL	(25)	77.4±18.4	18.5±3.5	0.70±0.1	111.4±10.1	63.8±6.9	23.2±0.6
HRT TP	(18)	96.9±17.0	27.0±4.8	0.93±.12	129.2±12.4	90.8±15.3	23.3±0.9
A/VSD	(18)	13.4±4.4	7.6±1.4	0.37±.05	61.3±6.0	30.7±2.6	23.8±1.4
PAPVR	(16)	41.9±20.3	14.0±4.8	0.53±.11	67.6±4.7	38.2±3.3	23.9±1.6

Legend. ASD=Atrial Septal Defect: AVCN=Atrioventricular Canal: A/VSD= Atrial and Septal Defect: CPB=Cardiopulmonary Bypass: CC=Cross Clamp: COND=Conduction Disturbance: HRT TP= Heart transplant: LVOT=Left Ventricular Outflow Tract Lesions: MVL=Mitral Valve Lesion: Perf=Perfusate: PAPVR=Total Anomalous Pulmonary Venous Return: VSD=Ventricular Septal Defect:. All data Mean ± SEM.

Table 3. Patient and operative parameters for cyanotic lesions.

Lesion	(#)	Age (months)	Weight (Kg)	BSA (m^2)	CPB Time (mins)	CC Time (mins)	Low Perf Temp (°C)
TOF	(112)	39.0±4.1	12.1±0.8	0.53±.02	83.2±2.2	43.5±1.4	21.6+0.3
TGA a	(71)	1.2±0.6	3.7±0.2	0.23±.01	133.2±5.4	61.0±2.2	19.4+0.4
PS	(69)	79.9±12.2	20.4±2.2	0.74±.05	85.2±6.8	47.9±4.0	27.7+0.8
HLHS	(57)	0.83±0.3	3.6±0.1	0.22±.01	133.8±4.0	66.3±2.7	15.8±0.4
TGA b	(38)	60.2±10.6	18.5±2.5	0.71±.07	112.8±6.4	67.0±4.8	22.9±0.8
PA	(30)	84.8±16.8	21.4±3.0	0.78±.07	102.8±6.7	53.0±5.2	22.9±0.9
DORV	(27)	46.2±6.9	15.1±1.9	0.63±.05	115.1±10.7	59.0±5.3	22.9±0.8
TA	(20)	11.8±6.0	5.6±1.3	0.3±.05	105.5±8.1	68.6±4.4	21.3±1.4

Legend. CPB=Cardiopulmonary Bypass: CC=Cross Clamp: DORV=Double Outlet Right Ventricle: HLHS=Hypoplastic Left Heart Syndrome: PA=Pulmonary Atresia: PS=Pulmonary Stenosis: Perf=Perfusate: TOF=Tetralogy of Fallot: TGA a=Transposition of the Great Arteries repaired by Arterial Switch Operation: TGA b= Transposition of the Great Arteries repaired by atrial switch or other methods: TA=Truncus Arteriosus. All data Mean ±SEM.

time. To determine if CP distribution varied during CC times between similar sized groups an additional indice was established which took both these factors into consideration.

Statistics

All data was collected and loaded onto a microprocessor in a spreadsheet format. Both one way and two way ANOVA were performed to determine differences between groups. When significant 'f' ratios were achieved additional multiple comparison tests were performed which included Fisher's plot of least significant differences and

Table 4. Cardioplegic distribution for acyanotic lesions.

Lesion	(#)	CPS Vol (cc)	CPS Dose (#)	CPS Kg^{-1} (cc Kg-1)	CPS M^{2-1} (cc M^{2-1})	CPS CC^{-1} (cc min^{-1})
VSD	(93)	315.6±34	1.1±.03	36.3±4.2	692.1±63.3	3.9±0.6
ASD	(81)	516.5±29	1.1±.03	26.7±0.8	646.9±17.1	32.6±1.8
LVOT	(78)	832.6±67	1.5±.08	32.3±2.8	841.1±61.5	19.8±1.8
AVCN	(71)	359.6±33	1.5±.07	39.7±1.7	783.6±33.5	7.3±0.9
COND	(45)	1060.3±63.6	1.3±.08	21.1±2.0	709.8±51.2	26.1±1.6
MV L	(25)	663.4±124.8	1.7±0.2	39.0±3.0	865.1±74.8	10.0±1.3
HRT TP	(18)	521.8±88.8	1.6±0.2	21.8±2.7	548.9±62.3	7.9±1.7
A/VSD	(18)	262.2±64.3	1.1±.08	30.5±2.1	598.1±64.1	3.9±0.6
PAPVR	(16)	406.3±109.4	1.3±0.2	35.8±6.1	688±92.6	10.7±2.4

Legend. ASD=Atrial Septal Defect: AVCN=Atrioventricular Canal: A/VSD= Atrial and Septal Defect: CC=Cross Clamp: COND=Conduction Disturbance: CPB=Cardiopulmonary Bypass: CPS=Cardioplegia Solution: HRT TP= Heart transplant: LVOT=Left Ventricular Outflow Tract Obstruction: MVL=Mitral Valve Lesion: Perf=Perfusate: PAPVR=Total Anomalous Pulmonary Venous Return: VSD=Ventricular Septal Defect:. All data Mean ± SEM.

Table 5. Cardioplegic distribution for cyanotic lesions.

Lesion	(#)	CPS Vol (cc)	CPS Dose (#)	CPS Kg^{-1} (cc Kg-1)	CPS M^{2-1} (cc M^{2-1})	CPS CC^{-1} (cc min^{-1})
TOF	(112)	417.0±27.1	1.4±0.1	34.9±0.9	743.5±22.2	9.7±0.5
TGA a	(71)	103.2±6.4	1.3±0.1	30.6±1.8	487.1±21.5	1.8±0.1
PS	(69)	697.9±82.1	1.4±0.1	38.0±2.6	899.7±65.1	16.9±1.7
HLHS	(57)	109.3±12.5	1.1±0.1	27.9±2.1	464.9±37.6	1.8±0.2
TGA b	(38)	715.7±102.6	1.7±0.1	40.1±2.4	930.6±71.2	16.0±4.7
PA	(30)	696.7±97.8	1.6±0.1	34.1±1.7	829.7±48.4	13.2±2.0
DORV	(27)	558.1±65.8	1.6±0.2	40.2±3.9	906.5±90.8	10.5±1.2
TA	(20)	254.5±82.5	1.7±0.1	48.1±4.5	778.8±75.4	4.1±1.2

Legend. CPB=Cardiopulmonary Bypass: CC=Cross Clamp: CPS=Cardioplegia Solution: DORV=Double Outlet Right Ventricle: HLHS=Hypoplastic Left Heart Syndrome: PA=Pulmonary Atresia: PS=Pulmonary Stenosis: Perf=Perfusate: TOF=Tetralogy of Fallot: TGA a=Transposition of the Great Arteries repaired by Arterial Switch Operation: TGA b= Transposition of the Great Arteries repaired by atrial switch or other methods: TA=Truncus Arteriosus. All data Mean ±SEM.

Scheffe's F-Test. Significance was accepted at or below the .05 level and, unless otherwise stated, all data is reported as mean ± standard error of the mean (SEM).

Results

Of the 1016 patient records reviewed 869 were able to be classified into a single specific defect as listed in table 1. The remaining 147 patients had either insufficient diagnostic information or had a complex congenital lesion that could not be differentiated into a specific defect. Tables 2 through 5 list the operative results of the 869 patients in this study.

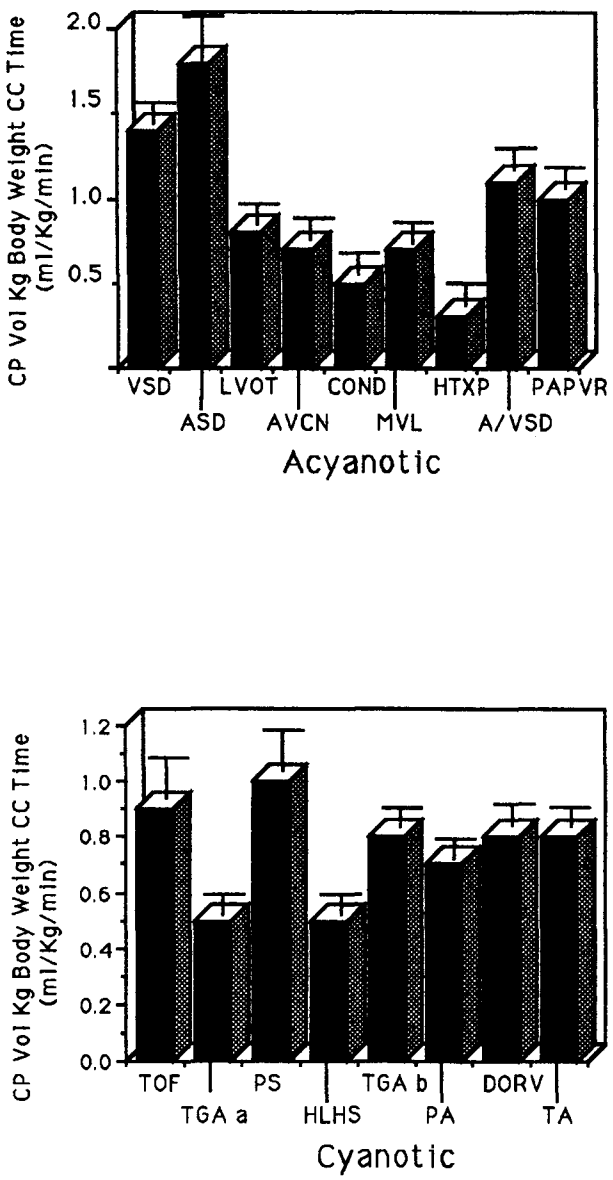

Figure 1.
Cardioplegia volume per Kg of body weight per minute of cross clamp time. ASD=Atrial Septal Defect; AVCN=Atrioventricular Canal; A/VSD=Atrial and Septal Defect; CC=Cross Clamp; COND=Conduction Disturbance; CP=Cardioplegia; DORV=Double Outlet Right Ventricle; HLHS=Hypoplastic Left Heart Syndrome; HRT TP=Heart Transplant; LVOT=Left Ventricular Outflow Tract Obstruction; MV LS=Mitral Valve Lesion; PAPVR=Total Anomalous Pulmonary Venous Return; PA=Pulmonary Atresia; PS=Pulmonary Stenosis; Perf=Perfusate; TOF=Tetralogy of Fallot; TGA a=Transposition of the Great Arteries repaired by Atrial Switch Operation; TGA b=Transposition of the Great Arteries repaired by atrial switch or other methods; TRUN=Truncus Arteriosus; VSD=Ventricular Septal Defect. All data Mean ± SEM.

Table 6. Comparison of cardioplegic distribution between similar sized and aged patient groups from cyanotic and acyanotic classifications.

Acyanotic Lesion		Cyanotic Lesion
Atrial Septal Defect	vs	Pulmonary Stenosis
Atrial Septal Defect	vs	Pulmonary Atresia
Atrial and Septal Defects	vs	Truncus Arteriosus
Atrioventricular Canal Defect	vs	Tetralogy of Fallot
Atrioventricular Canal Defect	vs	Double Outlet Right Ventricle
Ventricular Septal Defect	vs	Tetralogy of Fallot
Mtiral Valve Lesions	vs	Pulmonary Atresia
Mitral Valve Lesions	vs	Pulmonary Stensosis

In the acyanotic lesions ventricular septal defects (VSD) were the most common defect encountered, followed by atrial septal defects (ASD), left ventricular outflow tract lesions (LVOT), and atrioventricular canal defects (AVCN). LVOT defects included aortic stenosis, aortic atresia, aortic insufficiency, and aortic aneurysms and disections. Other acyanotic lesions included conduction disturbances (COND), mitral valve lesions (MVL), heart transplants (HRT TP), atrial and septal defects (A/VSD), and partial anomalous pulmonary venous return (PAPVR). Table 2 lists the anthropomorphic data along with CPB parameters. As expected the lowest perfusate temperatures corresponded with the longest CPB and CC times. Table 4 represents a compilation of the CP volume distribution across acyanotic lesions. There was a wide distribution of CP across all groups with a range of CP Kg^{-1} from 21.1±2.0 in COND patients to 39.0±3.0 in patients with isolated MVL.

Tables 3 and 5 list the cyanotic groups accumulated data. Tetralogy of Fallot (TOF) patients made up the largest group of patients, followed by transposition of the great arteries treated with arterial switch (TGA AS), pulmonary stenosis (PS) and hypoplastic left heart syndrome (HLHS). A second transposition class included patients treated with some other corrective procedure including atrial switch procedures and redo operations. Other cyanotic lesions included pulmonary atresia (PA), double outlet right ventricle (DORV), and truncus arteriosus (TA).

We attempted to normalize the volume distribution of CP throughout all groups by comparing CP min^{-1} of CC time for both Kg body weight (Figure 1) and m^2 of BSA (Figure 2). In the acyanotic groups ASD, VSD, AVSD and PAPVR had the greatest quantity of CP given over the CC period. In the cyanotic groups there was a more even distribution of CP during the cross clamping. The greatest volume of CP per Kg of body weight was in patients with either PS and TOF lesions.

Figure 2 depicts CP volume m^{-2} of BSA min^{-1} CC in both acyanotic and cyanotic lesions. ASD patients had the greatest amount of CP which is most likely a result of the shorter CC period in these patients. In the cyanotic patients TGA AS and HLHS groups both had the least CP m^{-2} min^{-1} CC. Although the treatment of both these lesions includes long CC or circulatory arrest periods, the use of profound hypothermia (table 3) with absent or low CPB flow rates most

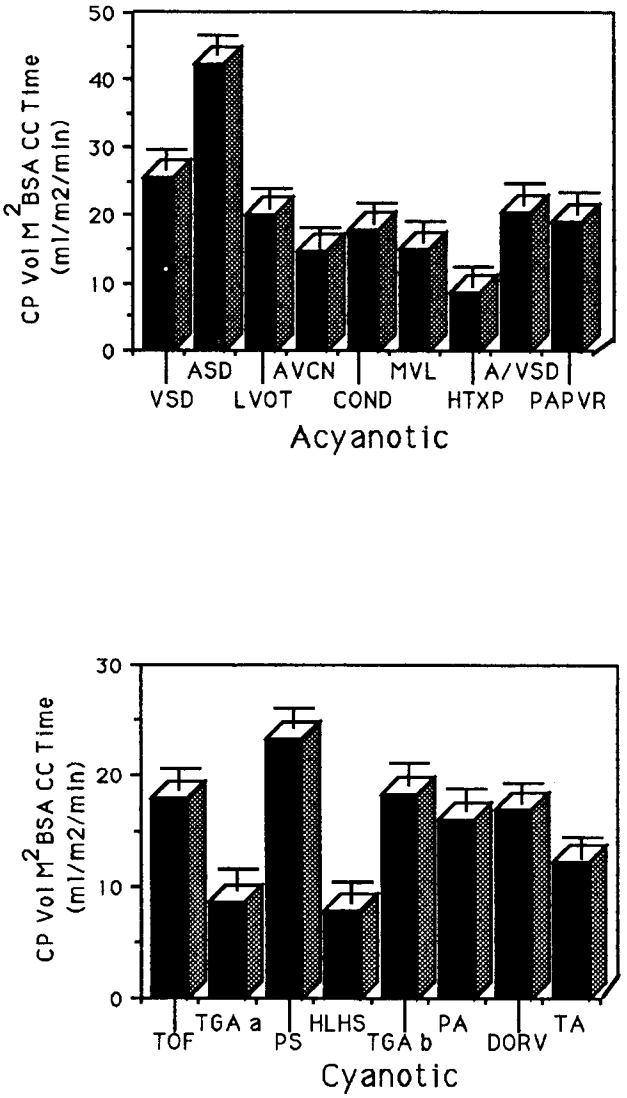

Figure 2.

Cardioplegia volume per M^2 body surface area per minute of cross clamp time. ASD=Atrial Septal Defect; AVCN=Atrioventricular Canal; A/VSD=Atrial and Septal Defect; CC=Cross Clamp; COND=Conduction Disturbance; CP=Cardioplegia; DORV=Double Outlet Right Ventricle; HLHS=Hypoplastic Left Heart Syndrome; HRT TP=Heart Transplant; LVOT=Left Ventricular Outflow Tract Obstruction; MV LS=Mitral Valve Lesion; PAPVR=Total Anomalous Pulmonary Venous Return; PA=Pulmonary Atresia; PS=Pulmonary Stenosis; Perf=Perfusate; TOF=Tetralogy of Fallot; TGA a=Transposition of the Great Arteries repaired by Atrial Switch Operation; TGA b=Transposition of the Great Arteries repaired by atrial switch or other methods; TRUN=Truncus Arteriosus; VSD=Ventricular Septal Defect. All data Mean ± SEM.

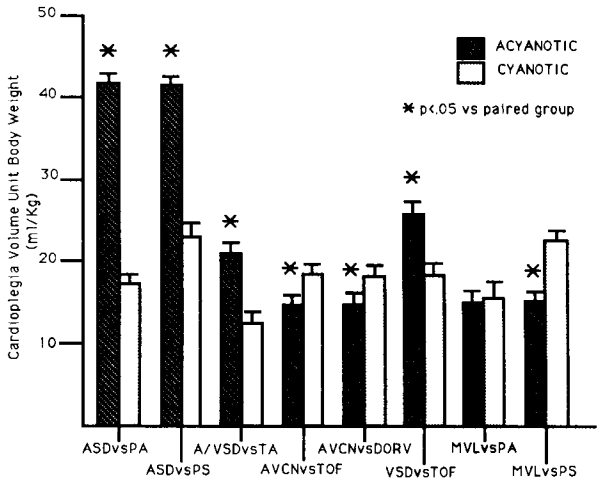

Figure 3.

Cardioplegia volume per unit of body weight in paired lesions from acyanotic and cyanotic groups. ASD vs PA=Atrial Septal Defect vs. Pulmonary Atresia; ASD vs. PS=Atrial Septal Defect vs. Pulmonary Stenosis; AVCN vs. DORV=Atrioventricular Canal Defect vs. Double Outlet Right Ventricle; AVCN vs TOF=Atrioventricula Canal Defect vs. Tetralogy of Fallot; A/VSD vs. TA=Atrial and Ventricular Septal Defect vs. Truncus Arteriosus; MVL vs. PA=Mitral Valve Lesion vs. Pulmonary Atresia; MVL vs. PS=Mitral Valve Lesion vs. Pulmonary Stenosis. All data are Mean ± SEM.

likely resulted in low washout rates of the myocardial CP which limited CP volume administration. The comparison of CP distribution corrected for BSA and Kg body weight across all groups may be of limited value due to the large discrepancy in both age and size of patients. Therefore, we attempted to further normalize the data by selecting similar sized patients from both the cyanotic and acyanotic groups and pairing them for analysis. Comparisons were made only when there was no significant difference in age, weight or BSA between the paired groups. The inter-group pairs are shown in table 6 and data from these groups are depicted in Figures 3 through 5.

A statistical comparison was made between the paired groups and it was found that patients with ASDs had significantly greater CP Kg^{-1} administered than patients with either PA or PS (Figure 3). This was also true in the acyanotic patients with A/VSD and VSD when compared to TA and TOF patients, respectively. In certain paired groups (AVCN vs TOF, AVCN vs DORV, and MVL vs PS) the cyanotic group had significantly greater CP than its acyanotic counterpart. CP administration per m^2 of BSA has also been described in the literature so we analyzed this distribution in Figure 4. Patients with PA, PS, and TA had significantly greater quantities of CP then either ASD or A/VSD patients. Although this relationship was also seen in the groups AVCN vs DORV and MVL vs PS, statistical significance was not acheived.

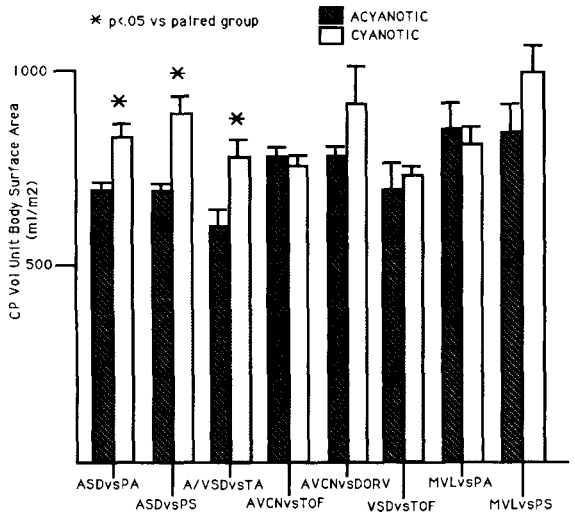

Figure 4.
Cardioplegia volume per unit of body surface in paired lesions from acyanotic and cyanotic groups. ASD vs PA=Atrial Septal Defect vs. Pulmonary Atresia; ASD vs. PS=Atrial Septal Defect vs. Pulmonary Stenosis; AVCN vs. DORV=Atrioventricular Canal Defect vs. Double Outlet Right Ventricle; AVCN vs TOF=Atrioventricula Canal Defect vs. Tetralogy of Fallot; A/VSD vs. TA=Atrial and Ventricular Septal Defect vs. Truncus Arteriosus; MVL vs. PA=Mitral Valve Lesion vs. Pulmonary Atresia; MVL vs. PS=Mitral Valve Lesion vs. Pulmonary Stenosis. All data are Mean ± SEM.

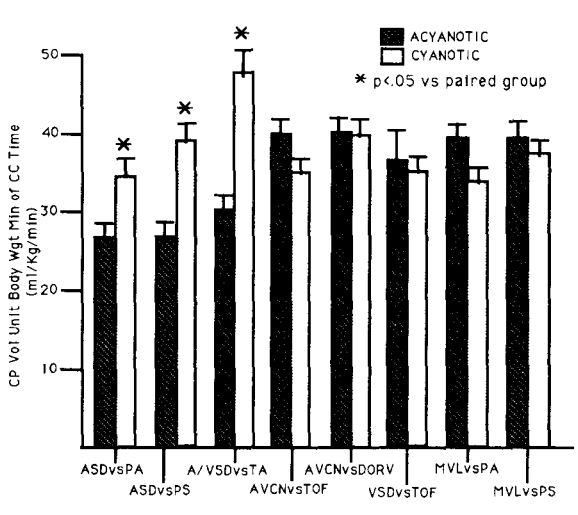

Figure 5.
Cardioplegia volume per unit of body weight per minute of cross clamp time in paired lesions from acyanotic and cyanotic groups. ASD vs PA=Atrial Septal Defect vs. Pulmonary Atresia; ASD vs. PS=Atrial Septal Defect vs. Pulmonary Stenosis; AVCN vs. DORV=Atrioventricular Canal Defect vs. Double Outlet Right Ventricle; AVCN vs TOF=Atrioventricula Canal Defect vs. Tetralogy of Fallot; A/VSD vs. TA=Atrial and Ventricular Septal Defect vs. Truncus Arteriosus; MVL vs. PA=Mitral Valve Lesion vs. Pulmonary Atresia; MVL vs. PS=Mitral Valve Lesion vs. Pulmonary Stenosis. All data are Mean ± SEM.

The relationship between CP volume, size of the patient, and the length of CC time is extremely important in ascertaining total volume distribution indices. When CP is delivered according to patient size, as in pediatric cardiac protection where patient size is non-homogeneous, analysis of CP volume may best be accomplished on a per minute of CC time basis. When this CP volume was normalized for patient weight over the CC period (Figures 5), the cyanotic lesions PA, PS, and TA had significantly greater quantities administered then the acyanotic lesions ASD and A/VSD. Statistical significance was not reached in the other analyzed pairs of acyanotic and cyanotic patients.

Discussion

Pharmacologic hypothermic cardioplegic arrest is currently the accepted treatment for myocardial protection during elective myocardial ischemia (1,16-19), although some recent literature supports initial warm cardioplegia to prevent contracture (4). Emphasis of all cardioplegic strategies is to limit or prevent the changes in myocardial cellular function and structure associated with hypoxic, ischemic, and reperfusion related phenomena. Perhaps nowhere else in the field of cardiac surgery does substantial controversy, and lack of agreement, persist in a technique utilized daily in hundreds of surgical centers. Although the methods utilized to achieve the goal of myocardial preservation vary, near uniform consensus is present on the importance of cardioplegia as a treatment in assuring postischemic mechanical function.

As with any drug, its efficacy is influenced by the pharmacokinetics of delivery techniques to the target tissue: Cardioplegia is no different. Multiple dosing of cardioplegia is a routine practice in both coronary artery bypass and valvular surgery (20). Controversy exists as to the beneficial nature of consecutive doses of cardioplegia in preventing myocardial injury in immature myocardium (8,21). Reasons for the inability of multiple doses to protect the immature heart include: Inadequate formulation of the cardioplegic solution (8), reperfusion related injury possibly from reoxygenation phenomena (21,22), and generation of contracture (23).

An additional controversy exists as to whether the pediatric heart possesses a greater - or lesser - susceptibility to ischemic stress than mature myocardium (2,5-9). One of the confounding issues marring interpretation of cardioplegic scientific studies involves the use of healthy immature myocardium as a model which may or may not reflect the treatment response of abnormal tissue. Indeed, in pediatric cardiac surgery the pathophysiology of the lesion not only results in cardiac alterations, but often creates pulmonary and systemic changes as reflex responses to the lesion. In some cardiac anomalies the absence or presence of associated defects will alter the clinical course

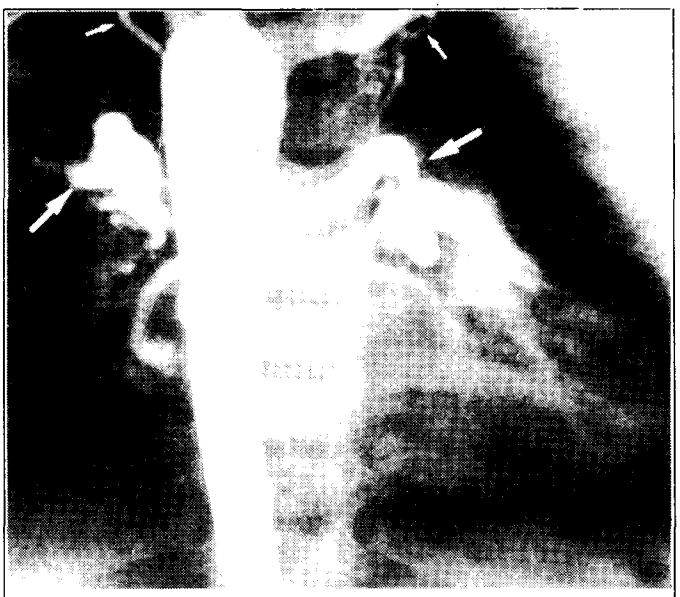

Figure 6.
Anterior posterior aortic angiogram of Tetralogy of Fallot patient with large aortopulmonary collaterals. Large arrows indicate direct aortic branches while the small arrows indicate indirect aortic branches.

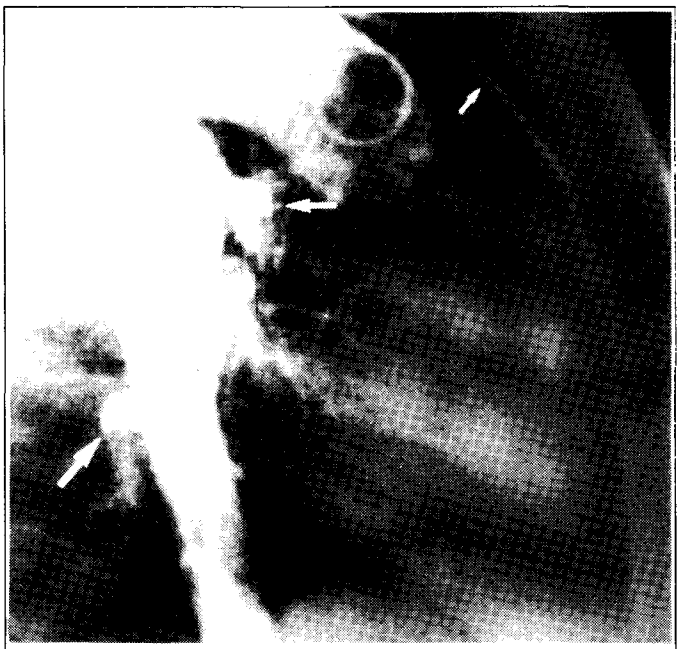

Figure 7.
Lateral angiogram aortic angiogram of Tetralogy of Fallot patient with large aortopulmonary collaterals. Large arrows indicate direct aortic branches while the small arrows indicate indirect aortic branches.

of the disease, ie: closure of the ductus arteriosus in hypoplastic left heart syndrome or the presence of a non-restrictive inter-chamber communication in transposition. In general, the classification of congenital cardiac defects is often related to the quantity of pulmonary blood flow, which directly affects the degree of arterial saturation. Our study was an attempt to examine the effects of cardioplegic protection in both cyanotic and acyanotic hearts.

Certain cyanotic lesions may be more susceptible to ischemic and reperfusion injury during cardiac surgery (16,24,25). It is thought that hearts stressed by low oxygen tensions may be at or near their maximum functioning capacity, and have little room for myocardial reserve (13). When exposed to the stress of cardiac surgery and ischemia they are unable to metabolically maintain the membrane functions necessary for cellular homeostasis, and return of systolic function (25). Some authors have shown that substrate enhancement of cardioplegic solutions with amino acid supplements improves postischemic recovery (2,3). It is also well known that hypertrophied myocardium requires greater myocardial protection then non-hypertrophied tissue (26,27). Even when cardioplegia, low myocardial temperature, and short ischemic times are all achieved, pediatric hearts continue to be susceptible to inadequate myocardial protection and ischemic injury (23,28).

Another frequent finding in patients with pulmonary outflow tract obstruction (10-12) and transposition of the great arteries (29) is the presence of aortopulmonary collaterals. Baile has stated that non-coronary collateral flow originates from medistinal, bronchial, and pericardial sources (13), and that this flow contributes to early myocardial rewarming. Rabinovitch and associates studied a post-mortem series of 17 patients with cyanotic lesions and identified 3 types of systemic collateral arteries: Bronchial arteries, direct aortic branches, and indirect aortic branches (10). They also identified points of anastomosis in the pulmonary circuit which included intrapulmonary (bronchial arteries), hilar (direct aortic branches) and extrapulmonary (indirect aortic connections). A clinical radiographic study by Uddin confirmed the presence of significant precapillary bronchopulmonary collateral vessels at the level of the pulmonary arteries, with significant systemic to pulmonary blood flow (11). Indeed the presence of collateral aortic to pulmonary blood flow is essential for survival in patients with Tetralogy of Fallot with pulmonary atresia and pulmonary stenosis (12), and this flow may well be greater than that originating from the right ventricle. Deal has reported in patients with Tetralogy of Fallot that the amount of bronchopulmonary precapillary flow could be as great as 11% of the patients flow during bypass (30). Figures 6 and 7 are angiograms of significant collateralization of a patient with Tetralogy of Fallot with pulmonary atresia which show both direct and non-direct aortic branch communications with the pulmonary system.

Aortopulmonary blood flow will drain into both the right and left atria, although the majority of blood returns to the left side (8). The use of a left ventricular vent helps remove this collateral blood flow (13), but does not diminish its return, and hence, will result in myocardial temperature equilibrium with the bypass perfusate temperature.

Figure 8.
Digital subtraction angiogram of patent right Blalock-Taussig shunt with failed ligation at time total repair for Tetralogy of Fallot. Arrow points to shunt.

Figure 9.
Embolized Blalock-Taussig shunt with arrow pointing to coil embolus.

The relationship between the degree of cardioplegic washout and collateral flow in the pediatric heart is unknown, although it has been addressed in the adult literature (8,28). In our study the increased cardioplegia necessary to maintain lower myocardial temperatures and prevent cardiac electrical activity was more pronounced in the cyanotic hearts; specifically those with right ventricular outflow lesions. A well known response to outflow tract obstruction is ventricular hypertrophy which is seen in the majority of Tetralogy of Fallot, pulmonary stenosis, and pulmonary atresia patients. In retrospect it would have been interesting to measure the quantity of topical slush applied to hypertrophied and non-hypertrophied hearts to maintain cardiac septal temperatures, since hypertrophied hearts tend to be more susceptible to temperature fluctuations (26,27).

There have been several studies which suggested that enhanced myocardial protection may be necessary in treating patients with Tetralogy of Fallot (13,16,24). The presence of aortic to pulmonary shunt flow not only influences myocardial rewarming rates and cardioplegic solution administration doses, but also influences the conduct of cardiopulmonary bypass. Perfusion flow will always take the path of least resistance and in patients with aortopulmonary communications, 'flooding' of the lungs with systemic perfusate is often observed. The sequelae of decreased systemic venous oxygen saturation, hypotension, inadequate myocardial draining, and excessive vent return are all consequences of aortic to pulmonary shunting. Patients with right ventricular outflow tract obstructions are also at an enhanced risk of suffering cerebral hypoperfusion and corrective cardiopulmonary bypass strategies should be implemented. Preoperative embolization of large aortic to pulmonary collateral branches with coils and thrombin saturated foam plugs, as shown in Figures 8 and 9, is a technique employed in the cardiac catheterization laboratory. Although specific perfusion strategies have not been identified in the literature, the following alterations in perfusion protocol to maintain cerebral perfusion are worthy of examination: Maintenance of higher bypass hemoglobin concentrations, increased perfusion pressures, high bypass cardiac index, and acid base homeostasis with pH stat techniques.

Our study emphasizes the importance of recognizing specific differences in cardioplegic treatment of cyanotic versus acyanotic patients. Randomization of cardioplegic treatment would have been impossible in this series of patients, and was not the clinical goal of this study. Post operative functional studies were not routinely performed on all patients, and would have been of limited usefulness in attempting to quantify differences between cyanotic and acyanotic congenital cardiac defects due to the vast diversity of lesions. The intent of this study was not to compare various cardioplegia strategies, but to examine the response of each individual patient to cardioplegic protocol. Although this study was completed retrospectively, cer-

tain benefits can be derived from the homogeneity of cardioplegic treatment. First, one surgeon completed over 96% of the corrective surgeries and did not dramatically alter his cardioplegic strategy over the 4 years of this study. This included myocardial temperature monitoring, venting of most hearts, a set, initial cardioplegia dose based on patient weight, with consecutive dosing based more upon cardiac needs, as assessed by myocardial temperature and presence of electrocardiographic activity, rather than on strict time related factors. Furthermore, the conduct of perfusion of these pediatric patients was accomplished according to established protocol, with minimal deviation. All patients were included in this study with omission criteria limited to multiple cardiac defects without specific pathological identification, or complex congenital lesions not fitting a specific category.

Summary

Through the examination of cardioplegic strategies in a large series of pediatric patients we have been able to identify specific lesions which require greater cardiac protection before, during, and after aortic cross clamping. The presence of substantial collaterals in certain cyanotic lesions may predispose these patients at increased risk for inadequate myocardial protection. Perfusion protocols may need to be altered to assure proper maintenance of cerebral perfusion and protection during the bypass period.

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Questions and Comments

Steve Thompson, Baltimore, Md.

Q. I wonder if you can ascertain or theorize from any of your information whether myocardia protection techniques are necessitated or different in groups that are treated with deep hypothermia circulatory arrest, if you can speak to that?

A. An initial study, for which I didn't present that data here, showed that our preservation strategies were indeed altered with the deeper hypothermia. Our circulatory arrest patients received actually less cardioplegia than our patients who were presenting with less significant pathological lesions. So we actually show a statistically significant greater cardioplegia volume the warmer we stay on bypass. It's just the theorization that the colder you go, the better posterior mediastinal protection you're going to acheive, and of course, if you go circulatory arrest the only temperature gradients in the heart will be from operative light sources or the actual surgical manipulation of the heart itself.

Ron Baras, New Brunswick, N.J.

Q. I would like to ask you a question about the temperature probe. When you put the temperature probe in, was it moved around at all or did you leave it in one specific point in the heart?

A. Good point. It really depended upon our lesion. The cardiac surgeon in this study ascertained exactly where the most compromised portion of the myocardium would be, which was usually in the right ventricular outflow tract lesions. The amount of right ventricular mass would lend itself toward more profound needs for myocardial preservation. We would be more apt to record temperature from a more anterior aspect, toward the right ventricle myocardium, than in the more traditional ventricular septal region. He would leave the probe in and not move it around.

Q. At what temperature was your cardioplegia delivered?

A. We used a coil bath delivery technique for our temperature and we maintained it at 4° C. We never used any warm reperfusion or warm induction or continuous warm cardioplegia. It was always given at 4° C.

Q. Is there any evidence in these immature hearts that these cold temperatures would possibly damage the myocardium? Has there been any work done? What is your feeling on that? In other words, whould we give it at 8 degrees, 10 degrees? Is 4 degrees too cold for these immature hearts?

A. Although controversial, it is generally reported in the literature that septal temperature less than 15°C fails to show enhanced myocardial protection. There's not a linear relationship with the amount of myocardial preservation as you go colder. With myocardial protective strategies, there is a lot of redundance in cardiac protective mechanisms with additives to cardioplegia solutiosn, that have similar

effects whether deep hypothermia or normothermia is used. As far as myocardial contracture during the ischemic period, a reported powerful endogenous vasodilator, adenosine, is released, which counteracts the contracture that you would see during the normal cardioplegia distribution of 0-4 degrees. But this is only after the concentration of adenosine has increased, which is during the hydrolysis of ATP. Perhaps warm induction cardioplegia techniques would be most efficacious prior to an ischemic event.

Jeff Riley, Charleston, S.C.

Q. Besides needing more cardioplegia in these systemic to pulmonary shunts, the presumption is that blood ends up inside the heart and warms the heart, what other signs and symptoms and problems come with the collateral blood flow?

A. In our recent experience we operated on a patient with tetralogy-pulmonary atresia who developed basal ganglia dysfunction in the post-operative period after a normal operative correction. During the bypass run we routinely see in patients with large systemic to pulmonary collaterals a massive drop in systemic pressure. Because of the hypotension seen during the bypass run, there is a decrease in systemic venous oxygen saturation, an increase in left ventricular blood flow, flooding of the field due to inadequate drainage. The same things you would see in a patient with an undiagnosed patent ductus arteriosus. That's exactly what happened here. The most important consequences center on a reduction of cerebral blood flow, Although we did not examine the prevalence of decreased cerebral blood, specific indications may be indicated to changing our conduct of perfusion from a normal routine that exists within the pediatric population, to perhaps more specific control of these patients with outflow tract lesions. Perhaps in these patients pH stat control of blood gas management is needed to increase cerebral perfusion because of the decreased cerebral perfusion. It is surely worthy of consideration.