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Cerebral Emboli during Cardiac Surgery in Children

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Background: **Microemboli occur commonly during cardiac surgery in adults, and, when present, increase the risk of neuropsychological deficits. Their incidence and significance during correction of congenital heart disease is unknown. The authors hypothesized that microemboli would occur before bypass with right-to-left cardiac shunts and would also occur in large numbers when the aortic crossclamp was released in children during repair of congenital heart defects.**

Methods: **In 25 children studied with carotid artery Doppler, embolic signals were counted and timed in relation to 13 intraoperative events. Patients were classified as either at high risk (obligate right-to-left shunt or uncorrected transposition of the great arteries) or at low risk (net left-to-right shunt or simple obstructive lesions) for paradoxical (venous to arterial) emboli.**

Results: **The median number of emboli detected was 122 (range, 2–2,664). Forty-two percent of all emboli were detected within 3 min of release of the aortic crossclamp. The high-risk group had significantly more emboli (median, 66; range, 0–116) during the time interval before cardiopulmonary bypass than did the low-risk group (median, 8; range, 0–73), with $P < 0.01$. There was no significant difference between the high- and low-risk groups in the total number of emboli detected. There was no apparent association between number of emboli and gross neurologic deficits.**

Conclusions: **Microemboli can be detected in the carotid arteries of children undergoing repair of congenital heart disease and are especially prevalent immediately after release of the aortic crossclamp. The role of emboli in causing neurologic injury in children undergoing repair of congenital heart disease remains to be determined. (Key words: Heart disease: congenital. Surgery: cardiac; cardiopulmonary bypass. Neurologic injury: cerebral emboli.)**

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MICROEMBOLI detectable by Doppler ultrasound are thought to underlie many new neuropsychological deficits in adults after cardiac surgery. Adults with neuropsychological deficits after coronary artery bypass surgery average twice as many microemboli as do those with no deficit, and cerebral complications occurred more commonly in patients with more emboli.[1–3] Although case reports have described the occurrence of emboli and of neurologic deficits in individual patients, no study has indicated whether or when microemboli occur consistently in children undergoing repair of congenital heart disease.[4] Because most repairs of congenital cardiac defects involve intracardiac surgery and the possibility of air entrainment, we hypothesized that significant numbers of microemboli would be detectable in these patients. We also hypothesized that children with obligate right-to-left intracardiac shunts would be at greater risk from emboli than other children undergoing cardiac surgery, because emboli could pass directly from systemic venous return to systemic arteries and organs. Therefore, we prospectively evaluated 25 infants and children undergoing open repair of congenital heart defects to determine the numbers of microemboli that could be detected in the carotid artery and the temporal relation of these emboli to various events during surgery.

Methods

After review and approval of our study protocol by our institutional review board and after obtaining informed consent from parents, 25 children (18 boys, 7

Table 1. Patient Demographics

Patient No.	Diagnosis	Procedure	Emboli Risk Class	TEE	Total Emboli
1	TGA	Arterial Switch	H	−	486
2	AVC	Repair	L	+	98
3	VSD/PDA	Repair	L	+	2
4	HLHS	Hemi-Fontan	H	−	120
5	AVC	Repair	L	+	50
6	TAPVC	Repair	H	−	393
7	TOF	Repair	H	+	163
8	ASD/VSD	Repair	L	+	2,039
9	HLHS	Hemi-Fontan	H	+	2,623
10	TAPVC	Repair PV stenosis	L	+	81
11	VSD	Repair	L	+	55
12	TA	Hemi-Fontan	H	−	44
13	VSD	Repair	L	+	24
14	1° ASD/VSD	Repair	L	+	726
15	TOF	Repair	H	+	142
16	TGA	S/P switch; repair PS	L	−	91
17	VSD	Repair	L	+	215
18	VSD	Repair	L	−	2,034
19	VSD	Repair	L	+	258
20	VSD/DCRV	Repair/resection muscle bundle	L	−	159
21	Unbalanced AVC Hypoplastic RV	Fontan	H	−	18
22	ASD	Repair	L	−	9
23	ASD	Repair	L	−	93
24	ASD	Repair	L	−	33
25	DCRV	Resection muscle bundle	L	+	122

TEE = intraoperative transesophageal echocardiography; TGA = transposition of the great arteries; AVC = atrioventricular canal; VSD = ventricular septal defect; PDA = patent ductus arteriosus; HLHS = hypoplastic left heart syndrome; TAPVC = total anomalous pulmonary venous connection; ASD = atrial septal defect; TA = tricuspid atresia; TOF = tetralogy of Fallot; DCRV = double chambered right ventricle; RV = right ventricle; PS = pulmonic stenosis.

girls) were enrolled in the study. The median age was 12 months, with a range of 3 months to 3.5 yr. Table 1 lists the cardiac diagnoses and surgical procedures performed. Patients were categorized by lesion as being at either low risk (net left-to-right intracardiac shunt or simple obstructive lesions; n = 17) or high risk (obligate right-to-left intracardiac shunt or uncorrected transposition of the great arteries; n = 8) for paradoxical arterial emboli of venous origin. Two children had preoperative neurologic deficits.

Anesthesia was induced with inhaled halothane, 2–3 mg/kg intravenous ketamine or intravenous fentanyl, and maintained with 50–100 μg/kg intravenous fentanyl. Neuromuscular blockade was accomplished with 0.1 mg/kg intravenous pancuronium. During cardiopulmonary bypass (CPB), a membrane oxygenator and 40-μm arterial line filter were used. The partial pressure of carbon dioxide in arterial blood and the *p*H were managed by the α-stat method. Median duration of CPB was 76 min, with a range of 30–176 min. Cardiopulmonary bypass flow rates were as follows: lowest flows ranged from 30–120 $ml \cdot kg^{-1} \cdot min^{-1}$, with a median of 75 $ml \cdot kg^{-1} \cdot min^{-1}$; highest flows ranged from 80–200 $ml \cdot kg^{-1} \cdot min^{-1}$, with a median of 150 $ml \cdot kg^{-1} \cdot min^{-1}$. Circulatory arrest was used in seven patients. The lowest nasopharyngeal temperatures ranged from 15.9–32.3°C, with a median of 22.5°C; rates of rewarming ranged from 0.21–0.60°C/min, with a median of 0.44°. Transmural needle aspiration of left-ventricular air was performed before the aortic crossclamp was released. In 14 cases, transesophageal echocardiography (TEE) was used to assess the completeness with which air had been evacuated from the left ventricle before aortic unclamping. There was no difference in the use of TEE between the high- and low-risk groups. Additional deairing procedures included aspiration *via* a left ventricular vent (in six patients) and *via* an aortic root cannula (in three patients).

After placement of peripheral venous, arterial, and central venous catheters, a modified Dopscan 1070 continuous wave ultrasound device (Carolina Medical Electronics, King, NC) fitted with a 5-mHz continuous-wave Doppler transducer was used to monitor the left common carotid artery beginning before skin incision and continuing throughout the operation. The Doppler signal was recorded on VHS tape and analyzed off-line by a trained observer, using both a visual track depicting alterations in the reflectivity index and an audio track.[1,5] Interpretation of individual tapes required as much as 8 h, depending on the number of emboli and artifacts. Microemboli were detected as unambiguous perturbations in the Doppler signal. On the audio track, emboli had a characteristic sound resembling a drop of water falling into a container of water, unlike artifactual signals, which have a variety of characteristic sounds, including the random loud whine of the electrical diathermy instrument and the thud denoting dislodgment of the microphone from the patient's neck. On the visual display, emboli had high amplitudes (greater than background by at least 30%) and narrow frequency spectra.[6] The diathermy signal had larger amplitude and higher frequency than did emboli. Dislodgment of the microphone yielded a broader-based, higher amplitude audiosignal than did emboli. Generally there was no difficulty in distinguishing artifacts from emboli; judgments based on experience were required for 10% or fewer of the signals. Our technique to detect emboli has been validated by *in vitro* and *in vivo* experiments using microspheres of known size and number.[7] We made no attempt to determine the composition of emboli (*i.e.*, gaseous or solid). If an embolic signal was detected in the 3-min period after 1 of 13 events, it was considered to be associated with that event. Emboli were classified as occurring before CPB if they were detected before the snares were tightened around the venous cannulae.

Charts were reviewed by a single observer to determine the presence of neurologic deficits before operation, in the early postoperative period, and during follow-up visits after discharge from the hospital.

Risk group differences for both the number of total emboli and pre-CPB emboli were compared using the nonparametric Wilcoxon rank-sum test. Spearman rank correlations were performed to identify any associations between bypass time and total number of emboli or number of emboli occurring before CPB. Results were considered significant when $P < 0.05$.

Results

Every patient had at least two emboli (figure 1). The median total number of emboli detected was 122 (range, 2–2,664). More emboli were detected after release of the aortic crossclamp than at any other time, with 42% of all emboli occurring during this period (figures 1 and 2). The intraoperative period associated with the next largest number of emboli was in the 3 min after incision, with 22% of all emboli occurring during then. At 10 of 13 times, the median number of emboli was zero or one.

Emboli occurring before CPB were considered separately in patients classified as being at either low or high risk for paradoxical (arterial emboli of venous origin) emboli. We considered pre-CPB emboli separately because paradoxical emboli could occur only before exclusion of the heart (and systemic venous return) from the systemic arterial circulation at the onset of CPB. Table 2 presents the data. The high-risk group had significantly more pre-CPB emboli (median, 66; range, 0–116) than did the low-risk group (median, 8; range, 0–73), with $P < 0.01$ by the Wilcoxon rank-sum test. The two groups had comparable total numbers of emboli ($P = 0.34$). There was no correlation between total number of emboli and duration of CPB ($r = 0.26$; $P = 0.21$ by the Spearman rank correlation test).

Two patients had newly detected neurologic deficits after operation. One child had a seizure and a unilaterally dilated pupil; the total number of emboli detected in this patient was 55. Another child had right leg weakness in the early postoperative period, which resolved at the time of follow-up 10 months after surgery; he had 44 total emboli detected during operation.

There were two perioperative deaths. One child with hypoplastic left heart syndrome had 2,623 total emboli; death was attributed to poor cardiac output. The other perioperative death occurred in a child with tetralogy of Fallot (142 total emboli), in whom junctional ectopic tachycardia developed.

Three patients had more than 2,000 total emboli: one patient undergoing atrial septal defect repair, one patient having combined atrial septal defect and ventricular septal defect closure, and one patient undergoing staged palliation of hypoplastic left-heart syndrome using the hemi-Fontan operation. In these three patients, large showers of emboli were detected in the period after release of the aortic crossclamp; one such shower of emboli lasted nearly 10 min. As noted before, the

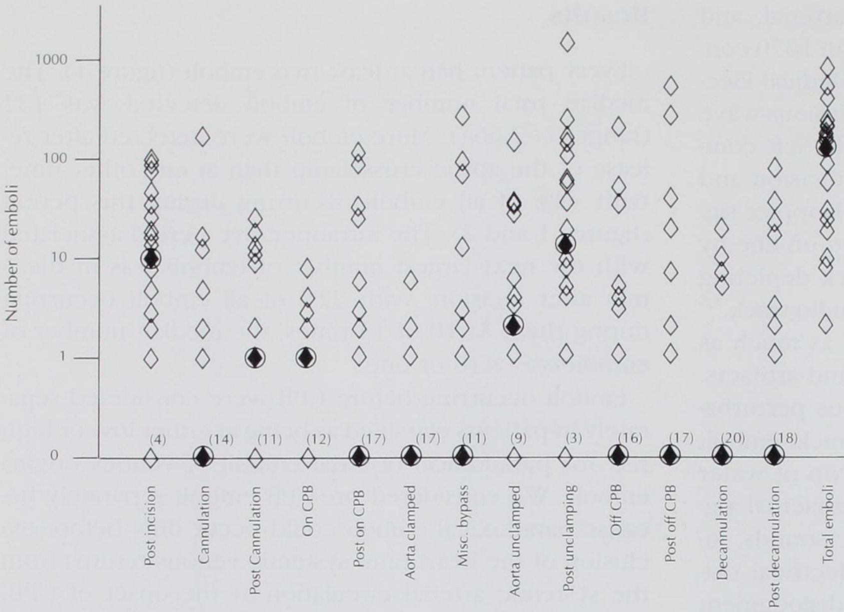

Fig. 1. Total number of emboli recorded in each patient within 3 min of 13 defined surgical events. Each symbol denotes one patient. A logarithmic scale is used due to the wide variation in the number of emboli observed. The superscripts associated with the symbols along the zero emboli lines indicate the number of children who had no emboli within 3 min of that surgical event. The median number of emboli recorded at each time is indicated by an encircled, filled diamond. At 10 of 13 times, the median number of emboli was none or one. Postincision = within 3 min of skin incision; cannula = within 3 min of aortic and venous cannulation; postcannula = >3 min after cannulation; on CPB = within 3 min of initiation of bypass; post on CPB = >3 min after initiation of bypass; aorta clamped = within 3 min of aortic clamping; misc. bypass = all other undefined times during bypass; aorta unclamped = within 3 min of release of aortic clamp; postunclamping = > 3 min after aortic unclamping; off CPB = within 3 min of discontinuation of bypass; post off CPB = >3 min after discontinuation of bypass; decannulation = within 3 min of removal of aortic cannula; postdecannulation = >3 min after removal of aortic cannula; total emboli = total number of emboli counted during the operation.

child with hypoplastic left-heart syndrome died perioperatively; the other two children with the highest emboli counts had no detectable neurologic deficits on postoperative examination.

Discussion

Children with congenital heart disease have long been known to be at high risk for neurologic injury,[8] which can be variously manifested as seizures,[9] cognitive and developmental deficits,[10] choreoathetosis,[11] and focal neurologic deficits.[12] In these children, neurologic injury might result from any of many causes, including chronic hypoxemia, ischemia during deep hypothermic circulatory arrest, inhomogeneous cooling of the brain, paradoxical emboli, and emboli occurring during CPB. Many congenital heart defects include large communications and obligate shunts between the systemic veins and the systemic arteries, predisposing these children to passage of venous emboli to the brain. An association has been identified between the number of cerebral microemboli and the development of perioperative neurologic and neuropsychological deficits in adults,[1,3] but the role of microemboli in causing such injuries in children is unknown.

Our results confirm that many children undergoing repair of congenital heart disease have detectable microemboli in the carotid artery during surgery. In our patients, more emboli were detected after release of the aortic crossclamp than in association with any other surgical maneuver. We suspect intracardiac microbubbles as the most likely source for these emboli. A similar peak in embolic signals has been found in some studies after aortic unclamping and during early ejection in adults undergoing valve replacement surgery or coronary artery bypass grafting.[13] This, in the former, can suggest that intracardiac surgery predisposes patients to the introduction of intracardiac air; in the latter case, that patients with aortic atherosclerosis may experience atheroembolism after aortic clamping. Clearly both atheroemboli and air microbubbles can be detected in the carotid artery. We observed a second major peak in numbers of emboli in the 3-min period after skin incision. Possible explanations for this include air microbubbles introduced *via* intravenous lines as additional anesthetics and muscle relaxants are administered, and particulate matter released from the bone marrow during sternotomy.

Intra-arterial air has been of concern in cardiac surgery since Carrel's observations in 1914.[14] In 1973, Gallagher

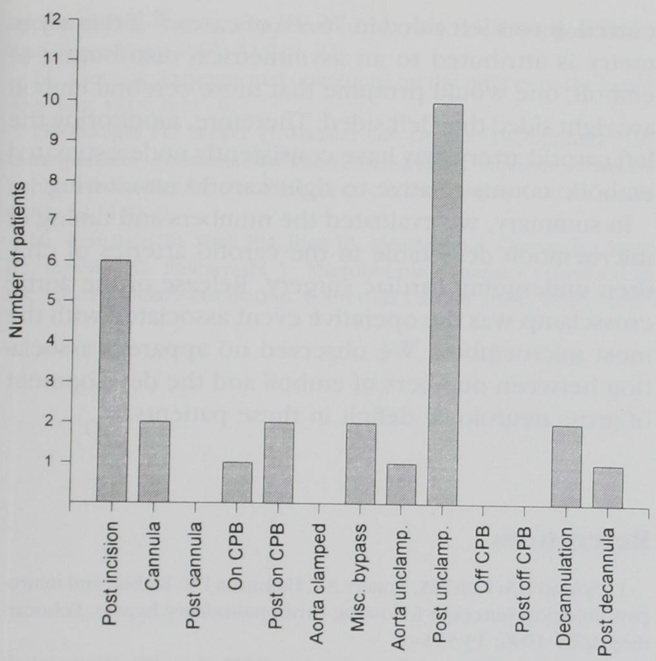

Fig. 2. The time interval associated with the most emboli in each of 25 patients. The greatest number of emboli were apparent either after skin incision or >3 min after the aortic clamp was released. Two patients are counted twice on this graph because they had a maximal number of emboli at two times. In one of these two patients, the maximal count was one embolus; in the other patient, the maximal count was 13 emboli. See the legend for figure 1 for definitions of the time intervals.

and Pearson described a 6-yr-old child who underwent carotid artery Doppler evaluation during closure of an atrial septal defect. After left ventricular ejection resumed, many emboli were detected. After operation the child had focal neurologic deficits, seizures, and decerebrate posturing, after which she died on the sixth postoperative day.[4] Other reports have given a less discouraging picture of the neurologic effect of air microemboli.[3,15] Nonetheless, experimental studies have shown various deleterious effects of gaseous microemboli on the cerebral vasculature. Capillary obstruction and stasis,[4,16,17] secondary vasoconstriction with related endothelial damage,[18] complement activation, leukocyte aggregation, and platelet adherence and aggregation[19] have all been demonstrated. The role of gaseous microemboli in causing clinically important neurologic injury in humans, particularly in children, remains to be further clarified. Our data set is too small to permit us to draw definitive conclusions about the relative neurologic risk associated with specific numbers of microemboli.

We have assumed that most microemboli detected in our study were gaseous rather than particulate. In our patients, atherosclerotic plaques, which may represent major sources of cerebral emboli in adults, are assumed to be absent. We cannot, however, rule out particulate emboli originating in the surgical field or in the CPB circuit, such as platelet aggregates or other debris, because our technology did not permit such a distinction. More than one half of our patients were monitored with TEE during surgery. That technology appears to be very sensitive for detecting intracardiac air. The similar numbers of carotid emboli in patients with and without TEE suggests that clinicians have not yet been successful at using TEE to reduce the number of emboli that escape the heart into the arterial tree.

In our study, children with obligate right-to-left intracardiac shunts or uncorrected transposition of the great arteries were at substantially greater risk for cerebral emboli during the prebypass period than were the other children in our study. We considered emboli occurring during this period separately because once the ligatures are tightened around the venous cannulae and CPB is initiated, intracardiac (paradoxical) emboli can no longer occur. The difference between the groups is also noteworthy because our low-risk group is, nevertheless, at higher risk for paradoxical emboli than healthy persons, given the presence of communication between the right and left hearts in most of these children, and the dynamic nature of intracardiac shunting. The total number of emboli was similar in the two groups, probably a consequence of the overwhelming number of emboli occurring in both groups after release of the aortic crossclamp. Thus it appears that the presence of obligate systemic venous to arterial shunting adds little incremental risk of cerebral emboli during cardiac surgery.

In previous studies in patients undergoing coronary artery surgery, we found a median total number of 100

Table 2. Total and Pre-CPB Emboli in High- and Low-risk Groups

Risk Category	Total Emboli	Pre-CPB Emboli
High (n = 17)	152.5 (18–2,623)	66 (0–136)
Low (n = 8)	98 (2–2,039)	8 (0–73)
P value (Wilcoxon rank sum test)	0.3364	0.0086

Values are median (range).

emboli, with a maximum of 2,099 and a minimum of 1 embolus. In patients having coronary surgery, there were no time intervals (associated with surgical manipulation) in which the median number of emboli exceeded 5. Thus although the character of the emboli in patients undergoing coronary artery surgery would be expected to differ from that of pediatric patients (*i.e.*, atheromatous emboli would not be expected in children but would be possible in adults), the median and range of total embolic load appears very similar in the two patient populations.

Frank neurologic deficits were detected after operation in 2 of 23 surviving patients (8.7%). There was no apparent association in this study between the total numbers of emboli and neurologic deficit, as both of the patients with deficits had total emboli counts less than the median. Conversely, high emboli counts (>2,000) in two children with atrial septal defects were not associated with any gross neurologic deficit. We cannot, however, rule out the possibility that subtle neurologic deficits detectable by formal developmental and neurobehavioral testing might be related to the number of emboli, as previous studies have shown a low sensitivity for gross neurologic examination in detecting perioperative neurologic events such as seizures.[9]

In our experience, Doppler scanning of the common carotid artery may yield different results from studies in which the middle cerebral artery is interrogated, although no published studies have simultaneously evaluated both sampling sites. One might also postulate that carotid artery sampling would detect emboli that do not pass on to the cerebral circulation, passing instead *via* the external carotid artery to other tissues. Conversely, middle cerebral artery sampling could underestimate the total number of cerebral emboli, because many emboli (particularly gaseous emboli) may pass preferentially to the anterior cerebral artery in the supine patient. Our methodology would, therefore, be expected to detect more emboli than comparable studies in which emboli were identified using transcranial Doppler monitoring of the middle cerebral artery.[5] Further study is required to establish the relation between emboli detected at either site and neurologic injury.

We monitored the left carotid artery in all patients; it is possible that there is asymmetry between the right and left carotid arteries in terms of distribution of emboli. An earlier study of neurologic deficits after cardiac surgery found that when hemiparesis or hemiplegia occurred, it was left sided in 76.9% of cases.[20] If this asymmetry is attributed to an asymmetrical distribution of emboli, one would presume that more cerebral emboli are right sided than left sided. Therefore, monitoring the left carotid artery may have consistently underestimated embolic counts relative to right carotid monitoring.

In summary, we evaluated the numbers and timing of microemboli detectable in the carotid arteries of children undergoing cardiac surgery. Release of the aortic crossclamp was the operative event associated with the most microemboli. We observed no apparent association between numbers of emboli and the development of gross neurologic deficit in these patients.

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