Cerebral Emboli Detected During Bypass Surgery Are Associated With Clamp Removal

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Background and Purpose Transcranial Doppler ultrasonography detects embolic signals during coronary artery bypass surgery. The relationship between embolization and specific events of bypass surgery is unclear.

Methods With this technique, 20 patients undergoing bypass surgery were continuously monitored from inception to discontinuation of bypass.

Results Embolic signals were detected in all patients. Of all embolic signals, 34% were detected as aortic cross-clamps were removed, and another 24% as aortic partial occlusion clamps were removed. Only 5% were detected at inception of bypass. Rates for embolization were 15.15 embolic signals per minute at cross-clamp removal, 10.9 embolic signals per minute at partial occlusion clamp removal, and fewer than 3 embolic signals per minute at other times. Correlation was found between the number of emboli, severity of aortic atheromatosis, and neurocognitive deterioration.

Conclusions The majority of emboli detected during coronary artery bypass grafting are associated with the release of clamps. Clamp manipulation may lead to release of aortic atheromatous debris. These emboli may be relevant to neurocognitive outcome. (Stroke. 1994;25:2398-2402.)

Key Words • cerebral embolism and thrombosis • risk factors • surgery • ultrasonics

Coronary artery bypass surgery is associated with neurological deficits as a complication in significant numbers of patients. Although focal deficits are rare, cognitive impairment occurs in up to 30% of patients. The etiology of this dysfunction is presumed to be multifactorial and may include hypoperfusion, embolization, and anesthesia-related events. Refinements in extracorporeal circulation equipment, surgical technique, and anesthetic technique have helped reduce the incidence of severe neurological complications.

The advent of transcranial Doppler (TCD) ultrasonography has shifted the focus from hemodynamic factors such as hypoperfusion to emboli and their possible role in producing neurocognitive dysfunction. Using TCD techniques, embolic signals (ES) have been detected in middle cerebral arteries during bypass surgery in the majority of patients, suggesting an association with neurocognitive deterioration.

The introduction of arterial filters and membrane oxygenators has reduced the number of ES and possibly neurological complications. The source of ES, their constitution, and their timing in regard to specific events of bypass surgery require elucidation.

Subjects and Methods

Patient Selection

Twenty-seven patients undergoing coronary artery bypass were monitored with TCD. Patients were selected from a larger cohort taking part in prospective studies to determine the effects of cardiopulmonary bypass parameters on neurological and psychometric outcome. The protocol was approved by our institutional review board, and participating patients gave signed informed consent. From the larger study, patients with concomitant valvular disease and those with prior cardiac surgery were excluded.

Seven additional patients were excluded: three because a transtemporal window was not obtainable and four because the probe was dislodged before bypass termination. A total of 20 patients were adequately studied throughout the procedure. Seventeen patients underwent neuropsychological testing, and 12 patients underwent transesophageal echocardiography (TEE).

Anesthesia

Morphine, lorazepam, and midazolam were used for premedication, and thiopental, fentanyl, and pancuronium were used for induction. Anesthesia before and after bypass was maintained with additional boluses of fentanyl, midazolam, and isoflurane. Isoflurane was not used during bypass. Blood pressure was controlled with nitroprusside, nitroglycerine, or phenoxyphrine.

Cardiopulmonary Bypass

Membrane oxygenators were used in conjunction with nonpulsatile centrifugal pumps connected to the patient with polyvinyl chloride tubing. A 40-µm filter was incorporated into the arterial line. The cardiopulmonary bypass circuit was primed with 1.5 L of crystalloid solution. Bypass was initiated at flows of 2.4 L/min per meter squared at a body temperature of 37.5°C and reduced to 1.6 L/min per meter squared at 28°C. According to protocol, systemic blood pressure was regulated pharmacologically to maintain mean pressures between 50 and 100 mm Hg.

Surgical Technique

All patients underwent conventional multivessel coronary artery revascularization with the above-described techniques for cardiopulmonary bypass in conjunction with standard aortic cross-clamping and hypothermic hyperkalemic antegrade and retrograde intermittent cardioplegia. In each case,
distal anastomoses were constructed first under protection of aortic cross-clamping and cold cardioplegic arrest, supplemented by topical iced saline lavage or iced slush. All proximal anastomoses were constructed during a single application of partial occlusion vascular clamps. Anesthesia, perfusion, and surgical staffs were unaware of TCD findings during the operative procedure.

**Monitoring by Transcranial Doppler**

Patients were monitored continuously beginning after aortic cannulation, 5 to 10 minutes before beginning bypass, and 5 to 10 minutes after discontinuing bypass. A 2-MHz pulsed-wave Medasonics-CDS TCD probe was used. Transducers were placed on the patient’s temple, and their positions were adjusted until signals were obtained with the sample volumes set at 4.5- to 6.0-cm depths. Specially designed headgear was used to fix the probe to the patient’s head while allowing optimal positioning. Doppler auditory signals were transmitted by means of headphones.

Data were recorded continuously; ES (ie, high-amplitude, unidirectional, transient signals <0.1 second in duration associated with a characteristic chirping sound) were recorded, stored on disks, and subsequently reviewed and counted. Concurrently, the number of aggregate ES was recorded by automated counter. The numbers of ES occurring within 4 minutes of the following events were recorded: inception of bypass, aortic cross-clamping, removal of aortic cross-clamps, aortic partial occlusion clamping, removal of aortic partial occlusion clamps, and the discontinuation of bypass. All other ES occurring during stable bypass were categorized as interim signals, so that ES were categorized into 11 time intervals.

**Monitoring by Transesophageal Echocardiography**

Monoplane or biplane TEE was performed on 12 patients after induction of anesthesia. Aortic atheroma was graded as follows: 1, normal to mild intimal thickening; 2, severe intimal thickening without protruding atheroma; 3, atheroma protruding <5 mm into the lumen; 4, atheroma protruding ≥5 mm into the lumen; and 5, atheroma with a mobile component that moves forward and backward with systole and diastole.16

**Neurological Assessment**

A standard neurological examination was performed by a neurologist blinded to TCD data. Each patient was examined preoperatively, on the second and sixth postoperative days, and after 6 months. A stroke was defined as a fixed focal neurological deficit not present on preoperative testing and attributable to ischemia of the central nervous system.

**Neuropsychological Testing**

A standard psychometric battery of 10 tests was used to assess linguistic, memory, and psychomotor function. Patients were tested preoperatively, 1 week, and 6 months postoperatively. Clinically significant cognitive deterioration was defined as a score change ≥1 SD on three or more tests.

**Statistical Analysis**

The primary analysis focused on whether the rates of ES were uniform across the 11 bypass time intervals. The number of ES per minute was considered a random variable as its distribution may be related to 11 time intervals as well as to 20 individual patients. A generalized linear model (one-way ANOVA) was used to test the hypothesis that mean numbers of ES per minute were the same across all 11 intervals. An F test was used to address this hypothesis. The rates of ES were compared across 20 patients (one-way ANOVA) and across intervals, controlling for differing rates per patient (two-way ANOVA). To analyze the relation of rates of ES to age, simple linear regression was performed. All statistical calculations used SAS GLM procedures.

### Results

ES were recorded among all 20 patients during bypass surgery (Table), 19 of whom were men. Median age was 63.5 years (range, 47 to 82 years). Numbers of ES recorded from inception to discontinuation of bypass varied considerably (26 to 620) as did durations of bypass (52 to 164 minutes). Total numbers of ES and numbers of ES per minute during bypass surgery are shown in the Table for each patient. Rates of ES did not significantly differ across patients (P=.54, one-way ANOVA). A weak correlation between age and rates of embolization was present (correlation coefficient .28, 0.2<P<.3). The duration of procedure point intervals was defined as 4 minutes after the event. The rate of embolization (number of ES per minute) varied considerably across the 11 time points (P=.0001, one-way ANOVA; Fig 1).

The largest numbers of ES were noted at aortic cross-clamp and aortic partial occlusion clamp removal. Median (range) numbers of ES at removals of aortic cross-clamps and aortic partial occlusion clamps were 22 (0 to 540) and 10 (0 to 391), respectively. Median (range) numbers of ES at inception of bypass, aortic cross-clamping, aortic partial occlusion clamping, and discontinuation of bypass were 6 (0 to 37), 2 (0 to 44), 5 (0 to 46), and 1 (0 to 15), respectively. Of all ES, 34% occurred at aortic cross-clamp removal, and 24% occurred after aortic partial occlusion clamp removal; combined, clamp removal accounted for 58% of ES. Of all ES during bypass, 29% occurred at times other than the noted events.

### Table: Relation of Age to Rates of Embolization

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y</th>
<th>Total No. of ES</th>
<th>Duration of Bypass, min</th>
<th>No. of ES/min</th>
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<tr>
<td>1</td>
<td>47</td>
<td>59</td>
<td>86</td>
<td>0.69</td>
</tr>
<tr>
<td>2</td>
<td>48</td>
<td>26</td>
<td>61</td>
<td>0.43</td>
</tr>
<tr>
<td>3</td>
<td>49</td>
<td>87</td>
<td>164</td>
<td>0.53</td>
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<tr>
<td>4</td>
<td>50</td>
<td>263</td>
<td>85</td>
<td>3.09</td>
</tr>
<tr>
<td>5</td>
<td>53</td>
<td>163</td>
<td>77</td>
<td>2.12</td>
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<tr>
<td>6</td>
<td>55</td>
<td>207</td>
<td>148</td>
<td>1.40</td>
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<td>0.98</td>
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<td>8</td>
<td>62</td>
<td>56</td>
<td>96</td>
<td>0.58</td>
</tr>
<tr>
<td>9</td>
<td>62</td>
<td>95</td>
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<td>1.83</td>
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<td>10</td>
<td>63</td>
<td>178</td>
<td>115</td>
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</tr>
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<td>11</td>
<td>64</td>
<td>258</td>
<td>128</td>
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</tr>
<tr>
<td>12</td>
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<td>158</td>
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<td>132</td>
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<td>1.89</td>
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<tr>
<td>20</td>
<td>82</td>
<td>109</td>
<td>70</td>
<td>1.56</td>
</tr>
</tbody>
</table>

ES indicates embolic signals.
The greatest frequency of ES occurred at the six specific time points, rapidly tapering within 4 minutes. Mean rates of embolization were 15.15 per minute at aortic cross-clamp removal, 10.9 per minute at aortic partial occlusion clamp removal, and less than 3 per minute at all other times (Fig 2). One patient had a posterior cerebral artery infarct during surgery. This patient had 110 ES at aortic cross-clamp removal (ranking third highest) and 112 ES at aortic partial occlusion clamp removal (ranking second highest). The two patients with the largest numbers of ES at clamp removal (608 and 391) were the only two patients with grade 4 disease of the aortic arch (no patients had grade 5 disease). The correlation coefficient between the number of ES at clamp removal and the grade of atheroma of the aortic arch was .642 (P<.04). The patient with the largest number of ES at clamp removal had significant deterioration on cognitive testing 1 week after surgery. The mean number of ES at clamp removal was 166 in the six patients with deterioration and 73 in the 11 patients without (P<.05).

Discussion

Occurrences of ES during coronary artery bypass surgery using TCD ultrasonography have been documented previously. All 20 patients in this study were found to have ES, in accordance with Padayachee et al who detected ES in 20 of 21 patients. The association between ES and clamp removal has not been previously reported. In this study, 58% of all signals were detected immediately after aortic cross-clamp and aortic partial occlusion clamp removal. Correspondingly, rates of embolization were highest at these two time points: cross-clamp removal was associated with a sevenfold increase in the rate of embolization and partial occlusion clamp removal with a fivefold increase.

As previously reported, we detected ES at the inception of bypass, although in aggregate these only amounted to 5% of the total ES for the entire procedure. All 40 patients studied by Pugsley et al and all 14 patients studied by Padayachee et al were found to have emboli at the inception of bypass. These were eliminated in seven other patients in whom membrane oxygenators with arterial niters and bubble traps were used. The authors concluded that these emboli were air bubbles trapped in the bypass equipment. The relatively small numbers seen in our study are attributed to the use of such traps in all patients.

Aortic cannulation has also been associated with the occurrence of ES in the vast majority of patients stud-
Cerebral Emboli Associated With Clamp Removal

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Fig 2. Graph and table show number of embolic signals (ES) per minute during coronary artery bypass surgery.

The use of membrane traps made no difference in occurrence of emboli at this point in the procedure, suggesting that these emboli may be of a different origin. The use of a 40-μm arterial filter was found to substantially reduce the number of ES detected during stable bypass. Thus, the mean number of ES was reduced from 21 to 0 after using a membrane oxygenator. Both authors concluded that emboli detected during stable bypass were caused by air bubbles trapped in the bypass machinery, but neither addressed occurrences of ES immediately after aortic clamping or unclamping.

Associations of arterial clamping and clamp removal with ES were noted by Spencer et al during carotid endarterectomy. In fact, 35 of 91 patients (38%) were noted to have ES on release of carotid cross-clamps. Preliminary data from another recent study suggest that flurries of ES are detected in patients undergoing coronary artery bypass surgery at aortic cross-clamping and release, although the number of patients studied is unclear.

These findings and the correlation between the number of ES and severity of aortic atheroma suggest that ES detected at aortic clamping, and more importantly at clamp release, may represent dislodgment of fragments of atheromatous plaque from the aortic wall and not air bubbles or platelet clumps in the bypass equipment. In fact, preliminary data from Lieh et al also suggest that the largest numbers of ES occur in patients having the most severe aortic atheromatosis. A study involving TEE in patients undergoing coronary artery bypass surgery demonstrated strong correlations between protruding mobile aortic plaques and stroke. Three of 12 (25%) patients with severe aortic atheromatosis had stroke compared with two of 118 (2%) patients with mild aortic disease. We have indicated elsewhere the compelling association between descending aortic atheroma and stroke and the association of an increasing number of ES with advancing age (Table), which represents indirect evidence that these ES may be solid material dislodged from aortic atheroma rather than trapped air.

This study could not closely evaluate the relationship between ES and neurological deterioration in coronary bypass surgery, although the one patient in our study who had a stroke did in fact have large numbers of ES at clamp removal and neuropsychological deterioration. The number of ES in patients with neuropsychological decline was larger than in those without. Larger studies attempting to correlate ES with neuropsychological outcome are underway. Spencer et al clearly make the point that many of the ES detected before and after carotid endarterectomy are not associated with symptoms. The number, size, and constitution of emboli may
all be important. At present, although there is no certain way using TCD to differentiate between atheromatous material, air, and platelet clumps. ES amplitude and duration may provide some information about size and material.

Clear relationships between the severity of aortic disease, the number of ES at clamp removal, and neuropsychological outcome must be demonstrated before modifications of surgical techniques are indicated. A number of modifications could then be tested. The use of padded clamps as opposed to unpadded ones, strategic placement of clamps with TEE visualization for optimal disease-free aortic areas, and even placement of an aortic umbrella distal to the clamps (similar to that used to prevent pulmonary emboli from the inferior vena cava) are all possibilities to be tested in the future.

References
Cerebral emboli detected during bypass surgery are associated with clamp removal.
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