Single crossclamp improves 6-month cognitive outcome in high-risk coronary bypass patients: The effect of reduced aortic manipulation

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Objective: We hypothesized that a strategy that reduced aortic manipulation would reduce the incidence of cognitive deficits in patients undergoing coronary artery bypass grafting compared with the “traditional” approach and that neurobehavioral outcomes with the reduced aortic manipulation strategy would approach those obtained with off-pump coronary artery bypass surgery.

Methods: Consenting high-risk patients (those with older age, diabetes, or hypertension) scheduled for coronary artery bypass grafting and cardiopulmonary bypass were randomly assigned to 1 of 2 aortic management protocols: (1) a traditional approach in which distal anastomoses were accomplished while the aorta was crossclamped but in which proximal anastomoses were sewn while a partial occlusion clamp was applied to the aorta (multiple aortic clamping group) or (2) a reduced aortic manipulation approach in which the aorta was clamped a single time with a reduced-pressure clamp (single aortic clamping group) and the partial occlusion clamp was not used. A contemporaneous group of patients undergoing off-pump coronary artery bypass surgery without cardiopulmonary bypass was also enrolled. Subjects in all 3 groups underwent neurologic and neuropsychological testing before and after surgery. After randomization, patients assigned to either approach could be changed to another strategy if the attending surgeon determined that patient safety demanded this change. The study design anticipated that surgical techniques would evolve over the course of patient enrollment and anticipated that some patients would have intraoperative echocardiographic findings that would demand that the traditional approach (eg, severe aortic atherosclerosis) or the reduced manipulation protocol (eg, severe ischemia or poor left ventricular function) be abandoned. Thus, an unequal distribution of patients was expected. By surgeon decision, 20 of 84 multiple aortic clamping patients crossed over to single aortic clamping, and 3 of 85 single aortic clamping patients switched to multiple aortic clamping. Eligible patients had a battery of neuropsychological tests before surgery and at 6 months after surgery. A 20% decrement in 2 or more tests was defined as a neuropsychological deficit.

Results:

	MAC	OPCAB	SAC
Hospital mortality	3/67 (4%)	1/68 (1%)	0/102 (0%)
Hospital stroke	3/67 (4%)	1/68 (1%)	3/102 (3%)
Tested patients NPD 3-5 d	25/42 (60%)	33/47 (70%)	44/74 (60%)
Tested patients NPD 3-6 wk	25/49 (51%)	20/51 (40%)	27/85 (32%)
Tested patients NPD 6 mo	24/42 (57%)	13/41 (32%*)	22/74 (30%*)

MAC, Multiple aortic clamping; OPCAB, off-pump coronary artery bypass; SAC, single aortic clamping; NPD, neuropsychological deficit. * $P < .05$ vs MAC.

Conclusions: A surgical strategy designed to minimize aortic manipulation can significantly reduce the incidence of cognitive deficits in coronary artery bypass grafting patients compared with traditional techniques. In this series, the results of

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the reduced aortic manipulation strategy were not significantly different from those in patients having off-pump coronary artery bypass surgery, thus emphasizing surgical technique as the primary cause of brain damage in coronary artery bypass grafting patients.

Cognitive dysfunction after coronary artery bypass grafting (CABG) has been the subject of numerous publications, including our retrospective series published in 1997, which suggested that a protocol to reduce aortic manipulation would improve cognitive outcome.¹ Since that time, the patient population has significantly changed in that patients are older and have more comorbid risk factors. Additionally, off-pump coronary artery bypass surgery (OPCAB) has been proposed as a solution for brain injury during coronary bypass surgery relating to the hypothesis that cardiopulmonary bypass is the primary factor that causes brain injury during CABG surgery.² Recently, 2 series have been published that link aortic manipulation with an increasing incidence of either stroke or cognitive dysfunction in patients having OPCAB surgery.^{3,4} It was the purpose of this study to prospectively analyze sequential measures of cognitive function after CABG surgery by using 3 separate techniques: a randomized study group using multiple aortic clamping (MAC) and single aortic clamping (SAC) with reduced aortic manipulation was compared with a concurrent series of patients undergoing OPCAB procedures in our institution.

Patients and Methods

From January 1999 to July 2004, patients undergoing isolated CABG using cardiopulmonary bypass were evaluated at our medical center. With approval from our institutional review board, patients were screened, and patients with neurodegenerative disease, major depressive disorder within the last 5 years, class IV congestive heart failure, cirrhosis or renal failure with creatinine greater than 1.8 mg/dL, or any other serious life-threatening disease were excluded. Patients who for physical or mental status reasons could not perform neuropsychological testing were excluded as well. The remainder of the patients underwent a comprehensive neurologic history and physical examination, including a vision examination. A history of stroke, known asymptomatic bruits, previous endarterectomy, or other neurologic deficits were recorded and analyzed separately as a risk factor. Patients underwent an 11-part neuropsychological examination, which was administered by a psychologist. The elements of the test and its results in large numbers of patients in this institution and others have previously been published.⁵

On the day of operation, patients were premedicated with midazolam (1-2 mg intravenously). A standard anesthetic technique of a moderate-dose narcotic was supplemented as necessary with volatile agents sufficient to maintain stable hemodynamics. Neuromuscular blockade was established with pancuronium 0.1

mg/kg intravenously, and all patients were intubated orotracheally and ventilated with 100% oxygen.

Before sterile preparation, each patient was instrumented over the left carotid artery with a specially designed 5-MHz focused active sonar transducer connected to an EDAC (Embolus Detection and Classification System; Raleigh, NC) device, which imaged the carotid artery in such a way that solid and gaseous emboli could be discriminated. EDAC data were continuously monitored by a technician assigned to archive all episodes of embolic activity during surgery. Archived data were later reviewed to remove artifacts from the final data set. After median sternotomy and before cannulation, each patient underwent epiaortic ultrasound scanning and mapping of the ascending aorta. Transesophageal ultrasound scanning was performed on the descending thoracic aorta as well. By using these data, an assessment of the ascending aorta was made and graded into separate categories: grade 0, normal; grade 1, extensive intimal thickening with no plaques greater than 2 mm and no plaques protruding into the aortic lumen; grade 2, plaque greater than 2 mm thick with no protrusion into the aortic lumen; grade 3, sessile plaque protruding less than 5 mL into the lumen; grade 4, plaque protruding greater than 5 mL into the aorta with no mobile elements; and grade 5, plaque protruding greater than 5 mL into the lumen with mobile elements, calcification, or both. Because we believed that patients with grade 5 aortas were at risk in a randomized study relating to multiple aortic crossclamping, patients with such aortas were then excluded from the randomized portion of the study.

The remainder of the patients underwent a randomization procedure in which patients were picked from a random-number table and divided into 1 of 2 groups. The first group underwent our traditional CABG with distal anastomoses constructed during a single period of aortic crossclamping and with proximal anastomoses constructed during a single period of partial occlusion of the ascending aorta during rewarming (MAC group). A second group of patients (SAC group) was randomized into a procedure in which proximal and distal anastomoses were constructed during a single period of aortic crossclamping and in which the aorta was cross-clamped by using a clamp (Bahnsen Aortic Clamp; Pilling Co, Ft Washington, Pa) that, when tested in our laboratories, exerted significantly less force on the aorta than the standard Fogarty (Applied Medical, Rancho Santa Margarita, Calif) aortic crossclamp, which was used in patients with MAC. After randomization, the surgeon had the option to place patients in the other group if the patient was at risk because of the randomization group. Examples of this logic would be if a patient were randomized to SAC and the surgeon were concerned about the length of the crossclamp time or if a patient randomized to multiple clamp had plaques by epiaortic ultrasonography that might interfere with placement of a partial occlusion clamp or placement of holes for proximal anastomoses.

Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
EDAC	= Embolus Detection and Classification System
MAC	= multiple aortic clamping
OPCAB	= off-pump coronary artery bypass surgery
SAC	= single aortic clamping

The investigators in this study anticipated that surgical techniques would evolve over the course of patient enrollment and anticipated that some patients would have intraoperative findings that would preclude their inclusion in 1 group or the other. Thus, an unequal distribution of patients was expected. In addition, a separate group of patients undergoing OPCAB surgery concurrent with the randomized groups also gave preoperative consent and underwent neurologic and neuropsychologic testing, in accordance with the previously mentioned exclusion criteria. Patients were picked for OPCAB surgery on the basis of cardiologist, surgeon, or patient preference.

Patients who underwent operation with cardiopulmonary bypass were treated with a noncoated oxygenator and tubing (model SX-25; Terumo, Elkton, Md) at standard flow rates ($2.2 \text{ L min}^{-1} \cdot \text{m}^{-2}$). Core temperature was allowed to drift to 30°C to 32°C , and aortic and left ventricular venting was at the surgeon's discretion. Myocardial protection was provided with antegrade and retrograde blood cardioplegia. Aortic partial occlusion was provided with 1 of a variety of clamps (Kay-Lambert, Cooley, or Shumaker; Codman Co, Piscataway, NJ). OPCAB patients were maintained at normothermia, and exposure to the coronary arteries was performed with a variety of commercially available stabilizers and retraction devices. Distal coronary arteries undergoing bypass were snared proximally, and visualization was ensured by using jets of a mixture of carbon dioxide and saline. Intracoronary shunts were used in patients suspected of having distal ischemia during the performance of the anastomosis. In OPCAB patients, aortic graft anastomosis was performed with mechanical connectors (St Jude Medical, St Paul, Minn) or aortic shields (Guidant Corp, Fremont, Calif). No partial occlusion clamps were used in the OPCAB group. Patients underwent repeat postoperative neuropsychological testing and a complete neurologic examination at 3 to 7 days after the operation or just before discharge and at 3 to 6 weeks and 6 months after surgery.

Definition of Terms

Patient data were collected and analyzed according to the Society of Thoracic Surgeons National Cardiac Database guidelines and definitions.⁶ Operative mortality was defined as death occurring within 30 days of the operation. Stroke was defined as a global or focal neurologic deficit that was evident after emergence from anesthesia (acute stroke) or later in the postoperative period (late stroke). Neurologic events were verified by neurologists and further assessed by computed tomographic or magnetic resonance imaging scanning.

TABLE 1. Preoperative demographics

Variable	Multiple clamp (n = 67)	OPCAB (n = 68)	Single clamp (n = 102)
Age (y)			
Mean $\pm$ SD	67.4 $\pm$ 8.1	60.8 $\pm$ 11.1*	63.0 $\pm$ 7.9
Median	66	61	62
Female (No.)	17 (25.4%)	25 (36.8%)	17 (16.7%)
Tobacco (No.)	41 (61%)	37 (54%)	60 (59%)
Prior PCI (No.)	9 (13%)	12 (18%)	22 (22%)
Prior CVD (No.)	4 (6%)	3 (4%)	9 (9%)
Atrial Fib (No.)	4 (6%)	2 (3%)	5 (5%)
CA Dis (No.)	39 (58%)	46 (68%)	70 (69%)
PV Dis (No.)	4 (6%)	4 (6%)	14 (14%)
Diabetes I (No.)	4 (6%)	4 (6%)	3 (3%)
Diabetes II (No.)	18 (27%)	14 (21%)	37 (36%)
Hypertension (No.)	44 (66%)	49 (72%)	77 (76%)
Hyperlipidemia (No.)	44 (66%)	43 (63%)	65 (64%)
Dialysis (No.)	0 (0%)	2 (3%)	3 (3%)
Redo (No.)	2 (3%)	2 (3%)	7 (7%)
Ejection fraction %			
Mean $\pm$ SD	51.4 $\pm$ 12.5	54.5 $\pm$ 11.6	50.7 $\pm$ 11.8
Median	51	55	54

* $P < 0.01$, Multiple vs. OPCAB, Multiple vs. Single. *PCI*, percutaneous coronary intervention; *CVD*, cerebrovascular disease; *CA*, coronary artery; *PV*, peripheral vascular.

Data Analysis

SigmaStat 2.03 for Windows (SSPS Inc, Chicago, Ill) was used for all statistical analysis. Nominal variables were compared by using χ^2 analysis. Continuous parametric data were compared by using the Student *t* test. Continuous nonparametric distributed variables were compared by using the Kruskal-Wallis analysis of variance on ranks. Post hoc comparisons were performed with the Dunn method for all pairwise multiple comparisons.

Results

After intraoperative exclusions and postoperative dropouts, 237 patients remained for analysis. Patient demographics among the 3 groups were similar, with the exception of patient age (Table 1). The MAC group was significantly older than OPCAB patients and SAC patients. There was a trend toward more women in the OPCAB group and more patients with peripheral vascular disease and type 2 diabetes in the SAC group.

As would be expected, there was a significant difference in crossclamp time: SAC patients had a significantly longer time (Table 2). OPCAB patients had significantly higher temperatures during the operation than patients on bypass. SAC patients had significantly more cardiomy suction blood returned; this was paradoxical in that a previous publication from our group suggested a higher microembolism load.⁷ In our practice, the use of cardiomy suction varies widely and was not a primary or secondary end point.

TABLE 2. Operative data

Variable	Multiple clamp (n = 67)	OPCAB (n = 68)	Single clamp (n = 102)
Pump time min.	107.1 ± 27.4 103		113.2 ± 26.5 108
Cross clamp min.	61.0 ± 16.3* 61		77.1 ± 21.0 74
Lo temp °C	30.6 ± 1.6 30	35.4 ± 0.8†	30.9 ± 1.9 31
Hi temp °C	37.0 ± 0.5 37	36.6 ± 0.5†	37.0 ± 0.5 37
Re-warming time min.	41.2 ± 15.8 40		37.0 ± 12.8 38
Lo HCT%	22.7 ± 4.0 23		23.4 ± 3.2 23
Cardiotomy ml	544.2 ± 636.6** 400		824.7 ± 760.2 700
Cell saver ml	700.4 ± 241.7 660	407.9 ± 328.00† 350	709.6 ± 320.5 675
Transfused RBC units	1.0 ± 1.3 0	0.2 ± 0.6† 0	0.6 ± 1.0 0
Transfused platelets units	0.3 ± 0.5	0.0 ± 0.1	0.2 ± 0.6
Emboli total	122 ± 186.8 54	30 ± 61.4† 5	145 ± 298.6 44
Emboli gas	74.2 ± 107.2 29	10.2 ± 38.9† 0	94.6 ± 210.8 18
Emboli particulate	72.3 ± 125.2 25	8.4 ± 24.4‡ 0	79.9 ± 194.2 15

* $P < 0.001$, Multiple vs. Single. ** $P = 0.026$, Multiple vs. Single. † $P < 0.01$, OPCAB vs. Multiple, OPCAB vs. Single. ‡ $P < 0.01$, OPCAB vs. Multiple.

OPCAB patients had significantly less return through the cell salvage device and fewer transfused red blood cell units. OPCAB patients had significantly fewer total gaseous and particulate emboli. SAC patients had fewer median emboli in all 3 categories than MAC patients, but this did not reach statistical significance. Two thirds of patients in all 3 groups had aortic atherosclerosis grades 1 and 2. The remainder had higher grades, but there were no significant differences among groups.

There were more hospital deaths in the MAC group, but this did not reach statistical significance (Table 3). OPCAB patients had a shorter total length of stay, intensive care unit length of stay, and intubation time than MAC patients.

There was 1 acute stroke appearing on awakening from anesthesia in each group. Two patients in both the MAC and SAC groups had late strokes.

Neurocognitive deficit results appear in Table 4 and Figure 1. At 3 to 5 days after surgery, the incidence of deficits was high in all 3 groups, with no significant differences. By 6 weeks, however, there was a significant difference between the deficit rates in MAC versus SAC patients. By 6 months after surgery, both OPCAB and SAC patients were significantly different from MAC patients. It is obvious from looking at the percentage numbers of patients with deficits in Figure 1 that MAC patients had a high incidence of deficit at 3 to 5 days after surgery that did not significantly

TABLE 3. Post OP data

Variable	Multiple clamp (n = 67)	OPCAB (n = 68)	Single clamp (n = 102)
Hospital death	3/67-4%	1/68-1%	0/102-0%
Hospital los days	7.1 ± 6.3 6	4.9 ± 2.0* 5	6.1 ± 3.9 5
ICU los hrs.	50.3 ± 41.2 40	32.4 ± 28.0* 24	43.3 ± 33.3 30
Intubation time hrs.	14.5 ± 15.6 10	11.1 ± 22.7† 6	12.9 ± 12.1 9

* $P < 0.01$, OPCAB vs. Multiple. † $P < 0.01$, OPCAB vs. Multiple, OPCAB vs. Single.

TABLE 4. Neurocognitive deficit results

	Multiple	OPCAB	Single
3-5 days post-op			
Total enrolled	67	68	102
Total tested	42	47	74
Patients with deficit	25	33	44
Deficit rate (%)	59.5%	70.2%	59.5%
All Groups	χ^2 , $P = 0.439$		
6 weeks post-op			
Total enrolled	67	68	102
Total tested	49	51	85
Patients with deficit	25	20	27
Deficit rate (%)	51.0%	39.2%	31.8%
All groups	χ^2 , $P = 0.088$		
OPCAB vs. multiple	χ^2 , $P = 0.325$		
OPCAB vs. single	χ^2 , $P = 0.485$		
Multiple vs. single	χ^2 , $P = 0.043$		
6 months post-op			
Total enrolled	67	68	102
Total tested	42	41	74
Patients with deficit	24	13	22
Deficit rate (%)	57.1%	31.7%	29.7%
All groups	χ^2 , $P = 0.007$		
OPCAB vs. multiple	χ^2 , $P = 0.035$		
OPCAB vs. single	χ^2 , $P = 0.921$		
Multiple vs. single	χ^2 , $P = 0.005$		

* $P = 0.007$, All Groups; † $P = 0.035$, OPCAB vs. Multiple; ‡ $P = 0.005$, Multiple vs. Single.

change by 6 months. Deficit rates in SAC and OPCAB patients progressively decreased, thus suggesting less permanent injury in both groups. There was no significant difference between OPCAB and SAC patients at 6 months after surgery, thus indicating that in this study, OPCAB did not offer a significant long-term advantage in terms of neurocognitive function over patients with operations performed on pump but with reduced aortic manipulation.

Discussion

The results of this study support the hypothesis that reduced aortic manipulation during on-pump coronary bypass surgery has a significant long-term benefit by reducing cognitive deficits in a contemporary group of patients. The 6-month data confirm nonrandomized data published from our institution in 1997.¹ The 6-month result of cognitive function studies showed no difference between patients who underwent operation on pump with a single-clamp technique and those who underwent operation concurrently in a nonrandomized fashion with an OPCAB technique. It would have been preferable to include an OPCAB arm in our randomization scheme. However, surgeons in our institution believed that it would be difficult to do so because our experience with OPCAB surgery was such that we felt more comfortable selecting the best patients with the appropriate coronary anatomy and cardiac function for OPCAB operations to ensure satisfactory short- and long-term results. For this

Figure 1. This bar graph illustrates the percentage of patients tested with neurocognitive deficits at the 3 time periods. Note the significant difference between SAC and MAC at 3 to 6 weeks and 6 months. *opcab*, Off-pump coronary artery bypass surgery. * $P = .043$ from multiple clamp. ** $P = .035$ from multiple clamp. *** $P = .005$ from multiple clamp.

reason, the OPCAB group in this series was significantly younger and, in general, had a better preoperative profile.

The results with a single-clamp technique in this study are supported by several recent publications that compared the use of SAC versus MAC on patients undergoing CABG surgery and demonstrated better postoperative neurologic and neuropsychological outcomes.^{8,9} On the basis of the results of this study and those previously published, it would be safe to say that patients undergoing on pump coronary revascularization who have any risk factors for intraoperative atheroembolism should undergo operation with the single-clamp technique. We used a softer and less powerful aortic clamp in SAC patients, and because of the good results, this clamp has replaced the Fogarty clamp for most coronary bypass applications in our institution. It was impressive in our in vitro testing that the Bahnson clamp exerted less force on the aorta when clamped to the maximal extent than the Fogarty clamp when clamped to 1 click.

Although OPCAB surgery has been proposed as a safer alternative to on-pump CABG surgery in patients at higher risk for postoperative neurologic injury,¹⁰ this study failed to show a significant difference between OPCAB patients and patients who had reduced aortic manipulation. The effect of aortic manipulation has recently been carefully approached by Calafiore et al and was found to be a significant factor in postoperative neurologic outcome in patients undergoing OPCAB operations.³ Although some studies of OPCAB versus on-pump coronary surgery have demonstrated a lower incidence of stroke in patients having off-pump operations,¹¹ there have been no comparisons of an ideally performed coronary operation on pump (reduced aortic manipulation) with OPCAB that have shown significant differences in neurologic or neuropsychologic outcomes. It would thus seem reasonable that surgeons who wish to perform CABG surgery on pump can expect to have equivalent outcomes if they use a reduced aortic manipulation protocol such as that used in this study.

The number of carotid emboli was less in this study than in the previous nonrandomized protocol. There are several reasons for the difference. First, the EDAC equipment has a much greater ability to discriminate between true emboli and “noise,” which complicates Doppler ultrasound detection. In addition, many techniques that reduce particulate and gaseous emboli have been instituted in our practice. These include aortic cannulas with lower shear rates, modification of blood entry into the cardiectomy reservoir to reduce microbubble production, and better arterial and venous filtration. The final factor is the increased awareness by the entire surgical/anesthesia/perfusion team of the factors that produce emboli and how to avoid them.

Because the embolic rates are lower than previously published, why the continued 30% late cognitive deficit rates in SAC and OPCAB patients? It is clear that CABG patients

were older and had more comorbid factors leading to poorer outcomes in this series when compared with data collected a decade or more earlier.¹² We have eliminated many sources of gaseous embolism and reduced but not eliminated particulate embolism in SAC and OPCAB. It is theoretically possible that particulate emboli that occur in MAC and OPCAB patients will have a greater effect in producing brain injury because they arrive when the brain temperature is higher than in on-pump patients.¹³ We have previously demonstrated that a large percentage of total intraoperative emboli are produced when the partial occlusion clamp is applied to and released from the aorta.¹⁴ This would be late in the on-pump part of the procedure, during rewarming, when the brain is at normothermia and more susceptible to injury. Future research should be directed toward methods that further reduce intraoperative embolism and provide neuroprotection in our increasingly aged population.

There are obvious limitations of this study. Patients in the MAC group were significantly older than patients in the SAC and OPCAB groups. The reasons for these differences are related to the option in this study for patients to cross over to other groups depending on the surgeon's preference after randomization. We believed that it was important that surgeons who felt uncomfortable performing a multiclamp operation in patients who had obvious aortic atherosclerosis or other reasons for using the single-clamp technique should have no hindrance in crossing patients over. Therefore, additional analysis of the late cognitive deficit findings demonstrated that patients in the multiclamp group who were older than 65 years had a greater incidence of deficits than patients in the other 2 groups. It seemed that the use of the single-clamp or OPCAB approach tended to neutralize the effect of age on the number of neuropsychologic deficits after surgery. The other potential confounder is the unequal number of patients in each group and the nonrandomized OPCAB group. The marked differences in outcome between the MAC group and the other groups argue against these factors playing a significant role in influencing results.

In conclusion, a significant improvement in late neurocognitive outcome was demonstrated in this series by using reduced aortic manipulation in both on-pump CABG and OPCABG. Clearly, this illustrates the importance of surgical technique and reduces the emphasis on cardiopulmonary bypass as the primary cause of brain injury during cardiac operations.

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Discussion

Dr Giovanni Teodori (Novara, Italy). Dr Hammon and his co-workers analyzed the relationship between aortic manipulation and neurocognitive dysfunction. This relationship was mediated by the evaluation of cerebral emboli, particulate or gaseous, that can occur during the different phases of aortic manipulation. The field of neurocognitive modifications after coronary artery bypass is controversial. Many studies tried to find some correlation between the use of cardiopulmonary bypass and the change in the neurocognitive domain, but, again, the results were not definitive.

On the contrary, many reports, and among them one of our group, found a good correlation between aortic manipulation and incidence of stroke. In your experience, the incidence of stroke is not different among the 3 groups, but this was very likely due to the small number of patients. I have only one question for you.

In your study, there is no difference in neurocognitive outcome between OPCAB and SAC patients. Nevertheless, the number of cerebral emboli is definitely lower in OPCAB patients and is similar in SAC and in MAC patients. Evidently there is no correlation between the number of cerebral emboli and the incidence of neurocognitive deficits. In your opinion, why did SAC patients

have an outcome similar to OPCAB patients even though they had a higher number of cerebral emboli? Why did SAC patients have a better outcome than MAC patients even though they had a similar number of cerebral emboli? In other words, what is the mechanism of the neurocognitive deficits in your patients?

Dr Hammon. Thank you very much, Dr Teodori. I might mention that Dr Calafiore was invited to discuss this paper, and he worked with Dr Teodori to prepare those remarks. He could not attend. You did mention prior to your question that you did not believe that there were any differences in the incidence of stroke between the 3 patient groups because of the small number of patients. I think that is possibly true, but if you followed patients through all the way from the beginning of the study to the end, the groups followed a very similar progression, with most neurocognitive deficits disappearing after the first 3 or 4 postoperative days, except in patients having more aortic manipulation. I do believe that it is true, and this is responding to your question, that the embolus data are very confusing, and I think there are several reasons for that. Number 1, embolus data were collected only in the left carotid artery, and so any emboli that went up the innominate artery and right carotid were not measured. The technique that we used is a new technique, with a new device that actually was developed at our own institution. It is possible that we missed some emboli or that the data might be inaccurate. Nevertheless, there was a difference between the single- and multiple-clamp patients—just not statistically significant.

The small number of emboli in the OPCAB patients was puzzling, especially because the neurocognitive results were no different. On the other hand, if you look at series of patients that have been evaluated by MRI [magnetic resonance imaging] studies postoperatively comparing on-pump versus off-pump patients, particularly those patients having single aortic clamping, the number of infarcted areas in the brain by diffusion-weighted imaging is about 30% and is present in both off-pump and on-pump patients.

Dr Michael Maxwell (Mesa, Ariz). I noticed that you allowed crossover from the multiple clamp group to the single clamp group at the discretion of the surgeon based on intraoperative findings, which might include epiaortic ultrasound. Did that happen much, and did you find the epiaortic ultrasound useful in discriminating between those who would benefit from a single-clamp technique versus a multiple-clamp technique?

Dr Hammon. I do believe that the crossover techniques were necessary for ethical reasons, for the simple reason that since we had epiaortic ultrasound on our patients, if we did detect a plaque in an area where a clamp would be applied or in an area where a graft would be anastomosed to the aorta, most people would feel that it would be very unreasonable to try to place a clamp over that area. For that reason, in the patients that were to have multiple aortic clamping, over 20 patients crossed over to the single-clamp group. About 5 patients crossed over from the single clamp to the multiple clamp group because the surgeon felt like the crossclamp would be on too long.

And did I think that influenced the results? No, I do not believe it did, for the simple reason that many unfavorable patients then went to the single-clamp group, yet the results in the single-clamp group were much better.

Dr G. Hossein Almassi (Milwaukee, Wis). Specifically for the OPCAB group, could you elaborate on the construction of the

proximal anastomosis? Was a partial-occlusion clamp used, or were the proximal anastomoses done with the use of other modalities and other tools that are available now?

Dr Hammon. I believe I mentioned in the presentation that in the OPCAB group, the vast majority, 98% of the group, had anastomoses performed either with mechanical connectors or with an aortic shield device. So a partial clamp was not used in patients undergoing OPCAB surgery.

Dr William A. Baumgartner (*Baltimore, Md*). I think the strength of your study is that it was randomized and the determination of neurologic injury was made in a prospective manner. As you mentioned, our own work showed similar findings, and I have just a couple of questions for you.

At 6 months of follow-up, the neurocognitive deficit rates continued to be about 30% for the OPCAB group as well as the single-crossclamp group, suggesting that perhaps cardiopulmonary bypass is probably not the cause of late neurologic injury. I was wondering what your comments were on this particular observation?

Also, would you please comment on your laboratory clamp testing? In my own practice, I continue to use the standard Fogarty crossclamp but found that it is necessary to use just a couple of clicks that maintain occlusion despite perfusion pressures in the 70 to 80 mm Hg range.

And finally, you have commented in the past that the reinfusion of cardiomy reservoir blood may be detrimental in neurologic outcomes in patients, and I was wondering if you have changed your thoughts on that concept?

Dr Hammon. Thank you very much, Dr Baumgartner. Your group has, I think, done our profession a real service since the publication from Duke, which suggested that patients who had deficits at the time of CABG surgery that then disappeared might reappear at a later date. Dr Selnes has published data from the Hopkins study showing that patients at high risk have deficits occurring off and on throughout the rest of their lives. And so if you follow these patients long enough, they do acquire deficits not necessarily related to surgery.

I think your second question is relevant in the sense that you say you clamp your crossclamp, the Fogarty clamp, which I think is widely used in this country, only a couple of times. Well, I can

tell you from our laboratory testing that if you clamp the Fogarty clamp just 2 or 3 times, it reaches its full occlusion, and then if you clamp it any more, it doesn't achieve much more pressure on the aorta.

In terms of reinfusion of cardiomy blood, we have published from our institution that cardiomy blood does contain quite a lot of fat and other potential microemboli. In this particular study, there was a wide utilization of different techniques for reinfusion of shed blood, and so the results showed marked variability and were not statistically significant. I wish we could have made more out of that, but we didn't control for that variable, and so we really don't have anything to say about it.

Dr Paul Kurlansky (*Miami, Fla*). Just to follow up what Dr Baumgartner brought up, a certain number of studies have shown that preoperative evaluation of these patients will demonstrate an approximately 30% demonstrable neurocognitive deficit preoperatively. I noticed that all of the on-pump patients were randomized, but the OPCAB patients were concurrent but not randomized, and I was wondering if you had preoperative studies on a subgroup or on the entire cohort of patients that might help elucidate the fact that 30% of these patients had persistent deficits 6 months postoperatively? They may not have been new deficits; they may have been deficits that were present preoperatively.

Dr Hammon. Well, that is a very good comment. Our methodology would suggest that in order to accurately record a new deficit, one that occurs at the time of operation, one does a preoperative study and establishes that as a baseline, and thus any deficits that appear postoperatively must have happened during the operation. The deficits you are referring to are large population studies where some patients do more poorly on neurocognitive studies than others. Unfortunately, you can't make a lot out of that kind of data because of the small number of patients in this group.

You also wondered again why we didn't randomize our OPCAB patients. Unlike Dr Puskas, we were uncomfortable with the idea of randomizing OPCAB patients, for a couple of reasons.

First of all, we have a number of cardiologists that almost require their patients to be done on pump versus off pump. We also have a number of surgeons that have more experience with off-pump surgery than others, so to randomize OPCAB patients across our surgical group would be impractical and possibly unethical.