

Reduction of Microembolic Signals with a Single-Clamp Strategy in Coronary Artery Bypass Surgery: A Pilot Study

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ABSTRACT

Background: Neurologic deficits are perhaps the most feared form of adverse outcome following cardiac surgery. Aortic trauma generates emboli and hence harbors the potential for neurocognitive injury. The single aortic clamp strategy of coronary artery bypass grafting (CABG) aims at reducing aortic manipulation. We hypothesized that this strategy will lead to a reduction in the number microembolic signals (MES) evaluated by transcranial Doppler (TCD), a surrogate measure of cerebral embolism.

Methods: This pilot study was based on a prospective analysis of 22 patients in whom CABG was performed either with a single aortic clamp (SC group) or with a conventional multiple aortic side-clamp technique (MC group). The 2 groups did not differ with respect to mean age (60 ± 6 years versus 65 ± 8 years, not statistically significant [NS]) or EuroSCORE (2.1 ± 1.5 versus 2.9 ± 2 , $P = \text{NS}$). The neurocognitive evaluation was based on the mini-mental state examination (MMSE). The preoperative MMSE values for the SC and MC groups were similar (29.5 ± 0.5 and 29.2 ± 1 , respectively; $P = \text{NS}$).

Results: The total number of solid-particle embolization signals secondary to aortic manipulation was lower in the SC group than in the MC group (72 ± 28 versus 127 ± 69 , $P = .02$). Neurocognitive performance was moderately reduced in both groups compared with preoperative values. This reduction was more pronounced in the MC group than in the SC group (22.2 ± 4.1 versus 25.3 ± 1.6 , $P = .02$). One patient in the MC group had a reversible ischemic neurologic deficit ($P = \text{NS}$). There were no deaths or perioperative myocardial infarctions in either group.

Conclusions: The single-clamp CABG strategy led to a reduction in MES, indicating a less pronounced embolic burden than with the conventional side-clamp CABG strategy. This strategy translated into a better

performance in postoperative neurocognitive testing in the SC group of patients.

INTRODUCTION

Neurologic injury remains a significant source of major morbidity and mortality following surgical coronary revascularization. The fraction of elderly and severely comorbid patients in the contemporary population of cardiac surgical patients has risen progressively over the past decade. This fact underscores the importance of cerebral protection, because the risk of cerebral injury following cardiac surgery is proportional to patient age [Bar-El 1992]. The spectrum of post-procedural neurologic symptoms ranges from neurocognitive impairment to overt stroke. The etiology remains multifactorial and includes embolic events, inflammation, hypoperfusion, cerebral edema, and hyperthermia [Blauth 1992; Hoffman 2006; Abu-Omar 2006; Grocott 2007; Ghogwala 2008]. The incidence of stroke ranges from 1.5% to 5%, whereas neurocognitive impairment is detected in as many as 20% to 30% of patients [Hogue 2008]. The timing of neuronal injury does not directly overlap with the surgical procedure in as many as 20% of patients [Hogue 2008]. Hence, the entire immediately postoperative period should be considered one of cerebral vulnerability [Hogue 2008]. Although the etiology of brain damage is complex and the various factors associated with it act in concert to produce a cumulative effect, embolism should be singled out as the most important cause [Hogue 2008]. The clinical repercussions of microembolic signals (MES) depend on their origin. MES secondary to solid particles originating from atherosclerotic disease carry a much more ominous prognosis than do those related to cavitation [Dittrich 2008]. Patients with mechanical heart valves may be subjected to several hundred microemboli per hour, which remain clinically asymptomatic [Russell 2002]. The vast majority are gaseous emboli [Russell 2002]. The generation of MES is closely related to aortic clamping and declamping [Dittrich 2008]. The showers of embolic signals detected during aortic manipulation are due to the mobilization of solid particles, whereas gaseous bubbles predominate during perfusion maneuvers, such as blood sampling or drug administration [Dittrich 2008]. The mechanism by which emboli induce injury involves mechanical obstruction, as well as activation of the inflammatory, complement, and coagulation cascades [Lynch 2008].

Presented at the 6th Annual Meeting of the Euro-Asian Bridge, Dubrovnik, Croatia, April 27-28, 2009.

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The mechanism of emboli detection with transcranial Doppler (TCD) is enhancement of ultrasound reflection compared with the background signal caused by blood flow [Russell 2002]. The clinical impact of embolic signals is evident in reductions in neurocognitive test performances by individuals in whom large numbers of MES have been documented [Russell 2002]. The histopathologic equivalent of cerebral microemboli has been known as small capillary and arteriolar dilatations. Microembolic signals documented by TCD have previously been shown to correlate with neurologic outcome in the patient population undergoing coronary artery bypass grafting (CABG) [Barbut 1997; Abu-Omar 2006]. Reducing aortic manipulation while performing surgical myocardial revascularization has previously been shown to improve neurologic outcomes [Grega 2003].

We hypothesized that the recognition and quantification of the microembolic burden with TCD may serve as a guide for improving the surgical technique of on-pump coronary revascularization.

MATERIALS AND METHODS

Following the approval from our institutional ethics committee, 22 patients scheduled to undergo elective CABG with cardiopulmonary bypass (CPB) were enrolled in our study from February 2009 to April 2008. Exclusion criteria were concomitant valvular pathology that required surgery, emergent CABG, significant carotid disease, and a poor bone window for TCD sonography. Patients who underwent CABG with a single aortic cross-clamping (SC) strategy were included in the SC group, whereas patients in whom a side-biting clamp was used for the construction of proximal anastomoses were included in the multiple-clamp (MC) group. The process of patient enrollment in the groups was not randomized; rather, it was based solely on surgeon preference. Informed consent was obtained from all patients. The study was conducted in a prospective observational fashion.

Perioperative Management

The patients received diazepam and morphine 30 minutes prior to induction of anesthesia. An endotracheal tube, a urinary catheter, and radial artery and pulmonary artery catheters were inserted. The anesthesia regimen included induction and maintenance of anesthesia with midazolam, fentanyl, and pancuronium bromide. This regimen was coupled with sevoflurane inhalation. The initial ventilator settings included a tidal volume of 8 mL/kg and a respiratory rate of 12 breaths/minute. The fraction of inspired oxygen was typically set at 50%. The critical components of the cardiopulmonary circuit used were the Medtronic Affinity Trilium membrane oxygenator, venous reservoir, and polyvinylchloride tubing (Medtronic, Minneapolis, MN, USA) as well as a Stoekert III roller pump (Stoekert, Munich, Germany). The ascending aorta and right atrium were cannulated for CPB. Myocardial protection consisted of both antegrade and retrograde cardioplegia. Systemic heparinization targeted at an activated clotting time >480 seconds was used, followed by full reversal with protamine after decannulation. Tepid

Table 1. Preoperative Patient Characteristics*

	SC Group (n = 16)	MC Group (n = 6)	P
Age, y	60 ± 6	65 ± 8	NS
Male, n (%)	13 (81)	5 (83)	NS
EuroSCORE	2.1 ± 1.5	2.9 ± 2	NS
Ejection fraction, %	57 ± 8	59 ± 9	NS
Hyperlipidemia, n (%)	4 (25)	3 (50)	NS
Hypertension, n (%)	11 (69)	5 (83)	NS
Diabetes mellitus, n (%)	14 (88)	1 (17)	NS
Preoperative AMI, n (%)	5 (31)	2 (33)	NS
3-Vessel disease, n (%)	11 (69)	5 (83)	NS
Preoperative MMSE	29.5 ± 0.5	29.2 ± 1	NS

*Data are presented as the mean ± SD. SC indicates single aortic clamp; MC, multiple aortic side-clamp; NS, not statistically significant; AMI, acute myocardial infarction; MMSE, mini-mental state examination.

CPB was used with a target flow rate of 2.2 L/min per m². The lungs were open to the atmosphere during CPB. The target mean arterial pressure during CPB was 60 mm Hg. If necessary, norepinephrine was used to reach the target blood pressure. The distal coronary anastomoses were performed on an arrested heart during a single period of aortic cross-clamping. Two distinct groups were formed according to the way the aorta was managed during the construction of proximal anastomoses. In the SC group, only a single period of aortic cross-clamping was used for both distal and proximal anastomoses. Conversely, in the MC group, the proximal anastomoses were performed after the aortic cross-clamp had been removed and the aorta was re-clamped with a side-biting clamp. Weaning from CPB was initiated once the patient's rhythm had stabilized and normothermia had been achieved. Inotropic support was initiated to maintain a cardiac index >2.2 L/min per m². The inotropic agent of choice was dobutamine. Norepinephrine was used if excessive vasodilatation was documented. Epinephrine was used if the hemodynamic performance remained inadequate with the previously mentioned catecholamines. An intra-aortic balloon pump was inserted if further support was required.

Transcranial Doppler

TCD was used for the detection of embolic signals in the middle cerebral artery. A 2-MHz probe was used for bilateral data acquisition (Sonara TCD System; Viasys Healthcare, Conshohocken, PA, USA). Rather than relying on the available software, an independent neurologist performed a manual offline analysis and quantification of the high-intensity transient signals.

Cognitive Testing

The mini-mental state examination (MMSE) was used for the quantitative evaluation of both the preoperative and postoperative neurocognitive performance of all patients. It

Table 2. Perioperative Summary*

	SC Group	MC Group	P
X-clamp time, min	65 ± 19	59 ± 20	NS
CPB, min	90 ± 27	107 ± 26	NS
MV, hours	9 (7-12)	10 (8-24)	NS
Inotropes, n (%)	5 (38)	2 (33)	NS
ICU†	2 (2-3)	3 (2-7)	NS
No. of grafts	2.4 ± 0.6	2.8 ± 0.4	NS
Postoperative MI, n (%)	0 (0)	0 (0)	NS
Mortality, n (%)	0 (0)	0 (0)	NS

*Data are presented as the mean ± SD unless otherwise indicated. SC indicates single aortic clamp; MC, multiple aortic side-clamp; X-clamp, aortic cross-clamp; CPB, cardiopulmonary bypass; MV, mechanical ventilation; ICU, intensive care unit; MI, myocardial infarction.

†Data are presented as the median (interquartile range).

is a questionnaire-based test used to evaluate neurocognitive performance. The MMSE consists of questions based on arithmetic problems, language comprehension, and basic motor skills. It provides insight into memory deficits, arithmetic problem-solving abilities, and orientation. It can be performed at various time points and thus provide longitudinal follow-up of a patient's cognitive status. A score >27 is interpreted as normal. A score between 20 and 26 corresponds to modest cognitive impairment, whereas a reduction to 10 to 19 indicates more pronounced cognitive dysfunction. A score <10 indicates severe neurocognitive impairment.

Statistical Analysis

The data are presented as the mean ± SD, or as the median (interquartile range) for variables with a nonnormal distribution. Longitudinal comparisons of sample results for the same individual were analyzed with the Wilcoxon matched-pairs test. Analyses of different groups of patients were performed with the Mann-Whitney *U* test. A *P* value <.05 was considered statistically significant. Differences in categorical variables between the 2 groups were evaluated with the Fisher exact test. The data were processed with the Statistica software package (StatSoft, Tulsa, OK, USA).

RESULTS

The patient demographic data are presented in Table 1. The spectrum of comorbidities seen in our patient population reflects the contemporary cardiac surgical practice. There were no statistically significant differences between the 2 groups of patients with respect to either the severity of their preoperative conditions or the incidence of major comorbidities. The preoperative quantification of neurocognitive status revealed a completely normal examination result in both groups of patients, as indicated by an MMSE score surpassing 27.

Table 3. Microembolic Signals (MES) Detected on Transcranial Doppler Examination at Various Stages of Aortic Manipulation*

	MES
Aortic cannulation	13 ± 11
Antegrade CP placement	9 ± 8
X-clamp placement	15 ± 13
Side-biting clamp placement	13 ± 12
X-clamp removal	16 ± 10
Side-biting clamp removal	9 ± 6
Decannulation CP	9 ± 6
Decannulate aorta	15 ± 10

*Data are presented as the mean ± SD and are accumulated from both groups. CP indicates cardioplegia; X-clamp, aortic cross-clamp.

The perioperative data are summarized in Table 2. In line with our expectations, the cross-clamping times were longer in the SC group (65 ± 19 minutes versus 59 ± 20 minutes, not statistically significant [NS]). Conversely, total CPB times were shorter in the SC group (90 ± 27 minutes versus 107 ± 26 minutes, *P* = NS). There were no differences between the 2 groups in the use of inotropic support or the duration of mechanical ventilation. The 2 groups also did not differ with respect to major complications, such as permanent stroke, perioperative myocardial infarction, or death. One patient in the SC group had an intra-aortic balloon pump placed because of hemodynamic instability coupled with very poor distal targets, which were most likely secondary to preoperative irradiation for breast cancer. This patient's postoperative course was otherwise unremarkable, and she was discharged home on postoperative day 7.

Table 3 demonstrates the occurrence of microembolic signals as detected by TCD at various times when the aorta was manipulated. These effects are cumulative in either group with respect to the total number of MES. Every form of aortic handling produced a certain amount of embolic debris reaching the cerebral circulation. The greatest numbers of MES were observed during aortic decannulation and cross-clamp removal. A similar amplitude of embolic potential was seen with the placement of either the cross-clamp or the side-biting clamp. The total number of MES related to solid-particle embolization secondary to aortic manipulation was lower in the SC group than in the MC group (72 ± 28 versus 127 ± 69, *P* = .02). This finding is a reflection of less aortic manipulation in the SC group.

Postoperative neurocognitive performance was modestly reduced in both groups compared with their respective preoperative values. This reduction in the MMSE score was less pronounced in the SC group than in the MC group (25.3 ± 1.6 versus 22.2 ± 4.2, respectively; *P* = .03). The relationships between neurocognitive performance and the incidence of neurologic deficits on the one hand and the occurrence of microembolic signals on the other are presented in Table 4.

Table 4. Relationship of Neurocognitive Outcome and Detection of Total Number of Microembolic Signals (MES)*

	SC group	MC group	P
Type I deficit, n (%)	0 (0)	1 (17)	NS
Type II deficit, n (%)	1 (6)	1 (17)	NS
MMSE postoperatively	25.3 ± 1.6	22.2 ± 4.1	.02
Total MES, n	72 ± 28	127 ± 69	.02

*SC indicates single aortic clamp; MC, multiple aortic side-clamp; X-clamp, aortic cross-clamp; MMSE, mini-mental state examination.

One patient in the MC group had a reversible focal motor deficit that produced no permanent disability ($P = NS$). Transient postoperative confusion was noted in a single patient in each group and was classified as a type II deficit. In both patients, the confusion was short-lived and resolved completely by postoperative day 5.

DISCUSSION

Neurologic complications following CABG may originate from embolic phenomena, inflammation, hypoperfusion, cerebral edema, or hyperthermia. Previous stroke, carotid disease, diabetes, and hypertension are additional contributors to the occurrence of new neuronal injury [Tsang 2003].

The strategy of aortic manipulation during surgical myocardial revascularization is paramount to postoperative neurocognition. Superior outcomes in terms of neuropsychological performance, focal motor deficits, and myocardial protection have been noted in patients undergoing CABG using single aortic cross-clamping compared with patients in whom the proximal anastomoses were performed with the use of additional aortic manipulation [Aranki 1994; Grega 2003; Hammon 2007].

Our study demonstrated that virtually any form of aortic manipulation has the potential to inflict injury sufficient to become evident as embolic signals on a TCD frequency spectrum.

The application of a side-biting clamp on a pulsatile aorta produces radial stress on the aortic wall, which is very dissimilar to the application of a cross-clamp. Although the mechanics of aortic occlusion are different with a cross-clamp than with a partially occluding clamp, this fact did not seem to influence the amount of mobilized embolic debris on TCD. The greatest potential for cerebral embolization was seen with aortic decannulation and cross-clamp removal. The pivotal disadvantage of the multiple-clamping strategy of coronary revascularization lies in the fact that all of these individual aortic manipulations produce a cumulative embolic effect. We have documented a modest decline in the cognitive status of patients in both groups, compared with their respective preoperative values. The amplitude of this decline, however, was greater in the MC group of patients and likely parallels the amount of aortic trauma needed for the completion of that procedure. Approaching the aorta in

a more conservative fashion is the principal dogma of the single cross-clamp strategy, and this view is reinforced in our findings of significantly lower occurrences of cerebral embolic events in this group of patients. Whether the use of an off-pump coronary artery bypass (OPCAB) strategy has a beneficial impact on neurocognitive performance remains a point of controversy [Newman 2007]. Hammon et al [2007] have shown fewer persistent neurobehavioral deficits in patients undergoing on-pump CABG with the single aortic cross-clamp method than in patients undergoing either OPCAB or on-pump CABG in which the creation of proximal anastomoses depended on the use of mechanical connecting devices. On the other hand, superior neurocognitive scores have been reported with OPCAB compared with the conventional multiple aortic clamping CABG strategy [Diegeler 2000].

Quantification of the embolic burden in patients undergoing different surgical myocardial-revascularization procedures offers a tool for identifying the superiority of one method over another. We believe that the observed superior neurocognitive outcomes and the reduction in the number of microembolic signals on TCD in the SC group are not independent findings, but rather stem one from the other.

There are some limitations inherent to the presented study. Patient allocation into the single-clamp and multiple-clamp groups was not randomized. This method leaves room for potential surgeon bias. Acknowledging that this is a pilot study, we stress that the groups comprised small numbers of patients, which limits the statistical power of the study.

In summary, our study suggests that the single-clamp strategy of coronary revascularization reduces cerebral embolization by reducing aortic manipulation and hence may provide a better postoperative neurocognitive outcome.

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