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Single Aortic Clamping in Coronary Artery Bypass Surgery Reduces Cerebral Embolism and Improves Neurocognitive Outcomes

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ABSTRACT

Aortic manipulation releases embolic material, thereby enhancing the probability of adverse

neurologic outcomes following coronary artery bypass grafting (CABG). We prospectively evaluated

59 patients undergoing CABG. Patients in the single (SC, n=37) and multiple clamp (MC, n=22)

groups were comparable in relation to age and operative risk (P>0.05). Neurocognitive evaluation

consisted of the auditory verbal learning test (AVLT), color-trail test A, grooved pegboard and the

mini-mental state examination. Data acquisition was performed preoperatively, early postoperatively

and at 4-month follow-up (F-U). Intraoperative transcranial Doppler (TCD) monitoring was used to

quantify the embolic load in relation to different aortic clamping strategies. Preoperative

neurocognitive results were similar between the groups (*P*>0.05). The incidence of postoperative

delirium was greater in the MC group but this failed to reach statistical significance (23% vs. 8%,

P=0.14). SC patients had fewer embolization signals (270±181 vs. 465±160, P<0.0001). Early

postoperative neurocognitive results were depressed in comparison to preoperative values in both

groups (*P*<0.05 for multiple comparisons). The magnitude of this cognitive depression was greater in

the MC group (*P*<0.05 for multiple comparisons). Preoperative levels of neurocognition were restored

at F-U in the SC group in all tests except the AVLT. A trend towards improvements in neurocognitive

performances at F-U was also observed in the MC group. Residual attention, motor skill and memory

deficits were, however, documented with multiple tests. In conclusion, the embolic burden was

significantly lower in the SC group. This TCD imaging outcome translated into fewer early cognition

deficits and superior late restoration of function.

INTRODUCTION

Loss of neurological integrity following cardiac surgery may become evident as either a new onset

motor deficit or a reduction in neurocognitive performance. While the former is relatively rare it

constitutes one of the most dreaded complications following coronary artery bypass grafting (CABG).

In contrast to the relative rarity of stroke, postoperative cognitive dysfunction (POCD) is common in

this setting and may present itself as a combination of deficits in fine motor function, attention,

memory consolidation and psychomotor dexterity (1). The etiology of POCD is not clearly defined,

but a multifactorial genesis has been postulated. Embolic events, inflammation, hypoperfusion,

cerebral edema and hyperthermia all likely play a role in the decline in neurocognitive performance

that is seen in as many as 50%-70% of cardiac surgical patients (1,2,3,4,5).

Transcranial Doppler ultrasound (TCD) detects embolic events via enhancement of ultrasound

reflection in comparison to the background signal caused by blood flow (6). High intensity transient

signals (HITS) are the TCD equivalents of cerebral embolism. Contradictory observations on the

correlation between HITS and POCD have been published. While certain publications enforce the

notion that embolic signals detected on TCD exert an adverse impact on neurocognitive performance,

others refute these findings (1,4,6,7,8,9). A major drawback of TCD is its inability to discriminate

between solid particular emboli and micro-cavitational phenomena (8). While the former harbor

potential for inducing neurological impairment, the latter are clinically benign. This lack of specificity

of transcranial Doppler ultrasound may account for the fact that high intensity transient signals (HITS) have not been unequivocally linked to inferior neurocognitive performances. A variety of different aspects of initiating and maintaining cardiopulmonary bypass (CPB) have been implicated in the generation of embolic material (7,8). Aortic manipulation plays a pivotal role in the release of showers of embolic material, which are visualized on TCD (8).

The mechanism by which emboli induce cerebral injury surpasses simple mechanical obstruction to involve activations of the inflammatory, complement and coagulation cascades (10).

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

METHODS

Following the approval from our institutional ethics committee, 59 patients scheduled to undergo

elective coronary artery bypass grafting using cardiopulmonary bypass (CPB) were enrolled into our

prospective observational study from July 2010 to May 2011. Exclusion criteria were concomitant

valvular pathology that required surgery, emergent CABG, ejection fraction <35%, atrial fibrillation,

prior stroke or transient ischemic attack, significant carotid disease, inability or refusal to provide

informed consent, poor TCD bone window and significant anxiety. While preoperative brain imaging

was not a part of the study protocol, all patients underwent non-invasive carotid imaging. Patients in

whom CABG was performed following a single aortic cross-clamp (SC) strategy comprised the SC

group, whereas patients in whom a side-biting clamp was used for the construction of proximal

anastomoses were included into the multiple clamp (MC) group. Patient recruitment into either group

was based on surgeon discretion. All patients participating in this study signed an informed consent

form prior to enrollment.

Perioperative management

The patients received diazepam and morphine 30 minutes prior to induction of anesthesia.

Endotracheal tube, urinary catheter, as well as radial artery and pulmonary artery catheters were

inserted. The anesthetic protocol included induction and maintenance of anesthesia with midazolam,

fentanyl and pancuronium bromide. This was coupled with sevoflurane inhalation. The ascending

aorta and right atrium were cannulated for cardiopulmonary bypass. Myocardial protection consisted

of both antegrade and retrograde cardioplegia. Systemic heparinization aiming at an ACT > 480

seconds was used, followed by full reversal with protamine after decannulation. Tepid CPB was

employed, targeting the flow at 2.2 $L/min/m^2$. The target mean arterial pressure during CPB was 60

mmHg. If necessary, norepinephrine was employed to reach the aimed blood pressure. The distal

coronary anastomoses were performed on an arrested heart, during a single period of aortic cross-

clamping. Patients in the SC group had their proximal aortic anastomoses constructed during the

period of aortic cross-clamping. The aortic cross-clamp was universally applied at the distal ascending

aorta, below the level of the innominate artery. Conversely, the proximal anastomoses were

constructed with the aorta partially occluded with a side-biting clamp in the MC group. The side-

clamp was applied to the right lateral aspect of the ascending aorta, with the CPB flows temporarily

reduced during the actual clamp placement. Patients in the SC group suffered less aortic manipulation,

at the expense of prolonging the cross-clamp time. Weaning from CPB was initiated once the

patient's rhythm had stabilized and normothermia had been achieved. Inotropic support was initiated

in order to maintain a cardiac index greater than 2.2 $L/min/m^2$.

Transcranial Doppler ultrasound

Transcranial Doppler ultrasound was used for the bilateral detection of embolic signals in both middle cerebral arteries (Sonara TCD System, Viasys Healthcare, Inc, Conshohocken, PA, USA). Two 2 MHz probes were used for bilateral data acquisition. Both middle cerebral arteries were insonated at the depth of 55 mm with a sample volume of 7 mm. An offline analysis and quantification of the high intensity transient signals was performed by an independent vascular neurologist blinded to the patient group allocation. Every effort was made to visually and audibly differentiate between artifacts and true HITS phenomena according to pre-specified criteria with an intensity threshold of 7 dB (11,12). Data acquisition started before aortic cannulation and ended 5 minutes after aortic decannulation. All aortic manipulation events within that time interval were recorded.

Neurocognitive testing

A uniform battery of neurocognitive tests was utilized to quantify each individual patient's performance preoperatively (PRE), at postoperative day 7 (POD 7) and a 4-month follow up (F-U). It consisted of the Rey auditory verbal learning test (AVLT), color trail test A (CTT), grooved pegboard test (GP) and mini–mental state examination (MMSE). In order to reduce the impact of anxiety on a patient's neurocognitive performance the State Trait Anxiety Inventory Test (STAI) was employed (13,14). STAI is an instrument designed to assess the level of anxiety, which may be an

independent confounder when evaluating neurocognitive outcomes. Patients with a STAI score

greater than 40 were excluded from the study.

AVLT is a commonly used instrument for testing the individual's capacity to assess short-term

memory, resistance to interference and memory consolidation (15,16). In brief, it involves a five trial

presentation of a 15-noun list of words, followed by a single presentation of a 15-noun interference

list and concluded with a 2 trial post-interference recall. Patients are expected to repeat as many items

as they can remember at different time intervals and after hearing an interfering list. Deficits in

attention, psychomotor speed and mental flexibility were monitored with the CTT. The test requires

the participant to connect numbered colored circles in as short a time interval as possible. GP test is

designed to assess fine motor skills, and requires complex visual-motor coordination. Bilateral manual

dexterity is determined by the time it takes to complete the designated task (17). The neurocognitive

evaluation was completed with the mini-mental state examination (MMSE). It is a questionnaire-

based test aimed to evaluate arithmetic problem resolution, language comprehension and basic motor

skills. Clinicians blinded to patient group assignment performed all neurocognitive tests.

Statistical analysis

The data are presented as mean values ± standard deviation or medians followed by the interquartile

range for variables with a distribution that is not normal. Longitudinal comparisons among samples of

the same subject were analyzed using the Wilcoxon matched pairs test. Analyses between different

groups of patients were performed using the Mann-Whitney U-test. A P<0.05 was considered to be of

statistical significance. The differences in categorical variables between the two groups were

processed using Fisher's exact test. The data were processed using the Statistica software package

(StatSoft Inc., Tulsa, USA).

RESULTS

The patient demographic data and preoperative characteristics are presented in Table 1. The two

studied patient cohorts were well matched with respect to the severity of their cardiac pathology as

well as to the commonly observed comorbidities. Patients with hypertension had inferior GP scores

preoperatively in comparison to normotensive ones (right hand: 118±24 vs. 96±21, P=0.007, left

hand: 130±29 vs. 99±22, P=0.002). Similarly, 4-month follow up testing revealed that hypertensive

patients retained inferior motor skills in comparison to normotensive patients (right hand: 123±28 vs.

96±23, P=0.003, left hand: 136±34 vs. 102±25, P=0.002). Furthermore, inferior follow-up CTT

results were noted in hypertensive patients (93±31 vs. 74±20, P=0.04). The studied groups were well

matched with regard to hypertension (84% in SC group vs. 77% in MC group, P=0.73). The effect of

hyperlipidemia on neurocognitive function was less pronounced in our study. The only statistically

significant comparison between patients with and without hyperlipidemia was in the preoperative

CTT (89±27 vs. 73±16, P=0.05). Again, the distribution of hyperlipidemic patients was uniform

among the groups (81% in the SC group vs. 77% in the MC group, P=0.75). Perioperative data are

summarized in Table 2. Patients in the SC group had longer aortic cross-clamp times, consistent with

the strategy of performing proximal anastomoses during one period of aortic occlusion (67±23 vs.

44±15, P<0.0001). Discharge medications included beta-blockers, aspirin and 3-hydroxy-3-methyl

coenzyme A reductase inhibitors in all patients. Postoperative delirium was defined in accordance to

the Society of Thoracic Surgeons definition as an acute state characterized by illusions, confusion, cerebral excitement, and having a comparatively short course (18). Its incidence was greater in the MC group, and while this difference trended towards statistical significance it failed to reach it (8% vs. 23%, *P*=0.14). There was one stroke in the MC group. The motor deficit in this patient correlated with the computed tomographic brain imaging data. No other patient was found to have neurologic symptoms requiring brain imaging. One patient in the SC group died. The cause of death was massive pulmonary embolism despite adequate anticoagulation in a patient with antiphospholipid syndrome who had two preoperative episodes of pulmonary embolism. The total number of high intensity transient signals on TCD representative of embolic events was statistically significantly higher in the MC group of patients (465 ± 160 vs. 270 ± 181, P<0.0001). The increase in total number of embolic events in patients in the MC group is reflective of the cumulative effect of multiple aortic manipulations. Each such aortic manipulation harbors potential to release embolic showers. A more detailed description of the embolic potential of various manipulations during the revascularization procedure is given in Table 3. A number of interventions unrelated to aortic manipulation also have the potential to provoke embolic signals on TCD. These include defibrillation, heart manipulation, blood sampling and drug infusions (19,20). Embolic events related to these types of interventions, in addition to those of unknown origin, were also accumulated and presented in Table 3.

The adverse impact of cardiac surgery on the early postoperative neurocognitive performance was seen in both groups on almost all evaluators (Tables 4 and 5). The amplitude of the relative reduction

in early neurocognitive performance, however, was observably greater in the MC group (Table 6; $P<0.05$ for multiple comparisons). More specifically, early cognitive outcomes were worse in the MC group, when compared to the SC group, in multiple trials of the Rey AVLT, as well as CTT, bilateral GP tests and MMSE. At 4-month follow up a universal trend toward improvement of cognitive performance was seen in both groups. This restoration of neurocognition reached preoperative levels in the SC group of patients as evaluated by the CTT, GP test and MMSE (Table 4). Residual deficits at 4-month follow up in the SC group were noted only in the Rey AVLT indicating a persistent problem with memory consolidation (Table 4). Conversely, three of the four neurocognitive tests employed in the current study showed significant residual depression of performance in memory acquisition, attention and fine motor skills in the MC cohort of patients (Table 5).

The correlation of the number of HITS with neurocognition is depicted in Table 7. The strongest correlation between the number of embolic signals and inferior cognitive performances was seen in the attention and fine motor skill domains.

DISCUSSION

Postoperative neurocognitive dysfunction following cardiac surgical procedures is a commonly seen

problem affecting as many as 50-70% of patients (1). While neurocognitive impairment remains much

less feared than the motor deficits associated with stroke, it still significantly prolongs hospitalization

and impacts the quality of life (1). Neurologic sequelae following cardiac surgery stem from a variety

of possible culprits, and these include embolism, hypoperfusion, inflammation and cerebral edema.

Reducing mortality and improving neurologic outcomes remain the two most important benchmarks

in the contemporary cardiac surgical practice. Our study focused on the dissimilar embolic potentials

of two different aortic manipulation strategies during surgical myocardial revascularization. We

hypothesized that the strategy of aortic manipulation during CABG is paramount to postoperative

neurocognitive outcomes. The single clamp CABG strategy has shown capacity to improve

neuropsychological results and reduce the incidence of motor deficits (21,22). We have demonstrated

that every form of surgical trauma to the aorta led to a systemic release of embolic material that

produced microembolic signals on transcranial Doppler. Reducing aortic manipulation consistently

reduced the amount of embolic showers detected on TCD. The pivotal disadvantage of the multiple

clamping strategy of coronary revascularization lies in the fact that individual aortic manipulations

produce a cumulative embolic effect. The present study showed that cardiac surgery adversely

influenced early neurocognitive performance in both groups of patients. The magnitude of the early

cognitive depression was invariably greater in the MC group, and likely parallels the increased amount of aortic trauma inherent to that type of revascularization. We have found a statistically significant correlation between the number of embolic events on TCD and inferior neurocognitive outcomes. Patients in whom a single clamp strategy of revascularization was pursued demonstrated better early postoperative results in learning and memory consolidation domains, and had fewer attention deficits coupled with significantly better fine motor skills. The cognitive performance significantly improved in both groups of patients, across almost the entire spectrum of tests utilized in this study, at 4-month follow up when balanced against the early postoperative results.

Cognitive dysfunction after cardiac surgery stems from multiple factors. In addition to embolic events, cerebral edema, hyperthermia and cardiopulmonary bypass duration are likely contributors to the problem. Isolated reports notwithstanding, off-pump coronary bypass surgery (OPCAB) has failed to reliable reduce the incidence of neurocognitive impairment in comparison to the conventional method utilizing cardiopulmonary bypass (23). Conventional OPCAB does not eliminate aortic manipulation as the proximal anastomoses are still created to the aorta in most cases. The dogma that any surgical trauma to the aorta influences the embolic burden of the procedure may lead to a more liberal use of techniques that completely avoid aortic manipulation. One procedure that may rise to the challenge is total arterial OPCAB revascularization utilizing the aortic no-touch strategy. This technique, however, is not likely to ever become universally applicable to all patient populations nor is it without it's own specific shortcomings.

The limitations of the study stems from its non-randomized design, which may bring into focus

surgeon bias as a factor. This is, however, unlikely to be of major concern since the surgeons pursuing

single clamp revascularization perform it unselectively to all their patients. The same holds true for

surgeons who prefer multiple clamping of the aorta. Each individual surgeon invariably used only one

of the techniques. The other limitation of the study stems from an important TCD drawback.

Transcranial Doppler cannot reliably dichotomize embolic signals into those that bear clinical

relevance and those that do not.

In summary, minimizing aortic manipulation is the principal idea of the single cross-clamp CABG

strategy and is reflected in our study by a lower incidence of cerebral embolic events. The clinical

correlate of pursuing this surgical technique is the improvement in early neurocognitive outcomes and

more complete restoration of cognitive function at mid-term follow up.

FUNDING

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Table 1. Preoperative patient characteristics presented as mean values ± standard deviation

	SC group	MC group	*P*
N	37	22	
Age (years)	65±9	66±8	0.70
Male (n/%)	31 (84)	18 (82)	1.0
EuroScore	2.9±3.2	2.2±1.2	0.68
Ejection fraction	56±9	58±11	0.42
Body mass index	31±5	29±3	0.19
Hyperlipidemia (n/%)[*]	30 (81)	17 (77)	0.75
Preop. LDL-cholesterol (mmol/L)	3.1±1.0	2.8±1.0	0.26
Preop. triglyceride (mmol/L)	2.3±1.1	1.7±0.8	0.01
Hypertension (n/%)[†]	31 (84)	17 (77)	0.73
Diabetes mellitus (n/%)	11 (30)	5 (23)	0.76
Preop. MI (n/%)	22 (59)	13 (59)	1.0
Three-vessel disease (n/%)	26 (70)	19 (86)	0.21
Preoperative medication (n/%)			
Beta-blocker	37 (100)	21 (95)	0.37
Statin	34 (92)	22 (100)	0.29
Aspirin	35 (95)	21 (95)	1.0

SC, single clamp; MC, multiple clamp; MI, myocardial infarction

[*]Hyperlipidemia was defined as any of the following: history of hypercholesterolemia (LDL-cholesterol>3.4 mmol/l or total cholesterol>5.2 mmol/l), hypertriglyceridemia (>1.7 mmol/L), hyperchylomicronemia or use of lipid-lowering medications to achieve target lipid/lipoprotein values

[†]Hypertension was defined as 2 or more diastolic blood pressure (BP) measurements ≥90 mmHg, or systolic BP readings on 2 or occasions ≥140 mmHg, or use of anti-hypertensive medications to achieve the desired BP values in patients with a history of high BP

Table 2. Perioperative summary of data for patients in both the single clamp (SC) and multiple clamp

(MC) groups. Data are presented as mean values ± standard deviation unless otherwise indicated

	SC group	MC group	*P*
X-clamp	67±23	44±15	<0.0001
CPB	94±30	87 ± 29	0.35
M. ventilation (hours)	7 [6/10]	8 [6/9]	0.51
Inotropes (n/%)	7 (19)	7 (32)	0.35
ICU	1 [1/2]	1 [1/3]	0.58
No. of grafts	2.6±0.5	2.9±0.3	0.07
Total HITS	270±181	465±160	<0.0001
Postop. AF	9 (24)	4 (18)	0.75
Stroke (n/%)	0 (0)	1 (5)	0.37
Postop. delirium	3 (8)	5 (23)	0.14
Mortality (n/%)	1 (2.6)	0 (0)	1.0

X-clamp, aortic cross clamp; CPB, Cardiopulmonary bypass, M. ventilation, duration of mechanical ventilation (data as medians and interquartile range); ICU, intensive care unit stay (data as medians and interquartile range); HITS, High intensity transient signals; AF, atrial fibrillation

Table 3. Microembolic signals detected on transcranial Doppler examination at various stages of

CABG. The number of microembolic signals summarized in the table is an aggregate from both the

left and right TCD probes. Data are presented as mean values ± standard deviation

	HITS recorded
Aortic cannulation	41±26
Initiation of CPB	28±27
Aortic cross clamp placement	33±32
Cross clamp removal	38±35
Average HITS per side-clamp positioning	43±47
Average HITS per side-clamp removal	35±37
Aortic decannulation	12±14
Other[*]	138±120

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HITS, High intensity transient signals; CPB, Cardiopulmonary bypass

[*]Includes HITS unrelated to aortic manipulation that were recorded during defibrillation, drug infusion during

CPB, blood sampling and all other embolic signals of unknown origin during the data acquisition period

Table 4. The neurocognitive outcome of the single clamp (SC) cohort of patients. Data are presented

as mean values and their respective standard deviations. Wilcoxon matched paired analysis was

performed to evaluate the statistical significance of the observed changes

	Preop	POD 7	4 mo F-U	P^*	$P^\dagger$
Rey AVLT					
Trial 1	4.4±1.3	4.2±1.4	4.2±1.2	0.33	0.24
Trial 2	6.3±1.5	6.0±1.5	5.9±1.2	0.04	0.004
Trial 3	7.7±1.4	7.4±1.6	7.4±1.4	0.02	0.07
Trial 4	9.1±1.5	8.4±1.8	8.6±1.6	0.0005	0.003
Trial 5	10.9±2.6	9.8±2.4	10.5±2.4	0.0004	0.09
Trial 6	4.9±1.7	4.4±1.6	4.8±1.9	0.0006	0.24
Trial 7	4.3±1.7	2.9±1.7	3.8±1.9	<0.0001	0.005
CTT	85.5±28.4	93.1±35.1	88.2±33.9	0.0001	0.34
GP test					
left	122.4±30.6	136.2±43.5	126.1±35.2	0.0004	0.09
right	112.1±26.5	124.3±37.1	114.8±30.0	<0.0001	0.23
MMSE	28.6±1.7	27.7±2.2	28.6±1.4	0.004	0.64

[*]Comparison between postoperative day 7 and preoperative data

[†]Comparison between 4-month follow up and preoperative data

AVLT, auditory verbal learning tests; CTT, color trail test A; GP, grooved pegboard; MMSE, mini-mental state examination

Table 5. The neurocognitive outcome of the multiple clamp (MC) cohort of patients. Data are

presented as mean values and their respective standard deviations. Wilcoxon matched paired analysis

was used to evaluate the observed changes

	Preop	POD 7	4 mo F-U	P^*	$P^\dagger$
Rey AVLT					
Trial 1	4.2±1.3	3.6±1.3	4.0±1.0	0.005	0.33
Trial 2	5.7±1.5	5.5±1.8	5.6±1.2	0.50	0.72
Trial 3	7.7±1.1	7.1±1.8	7.3±1.1	0.05	0.05
Trial 4	9.2±1.4	8.1±1.5	9.0±1.6	0.0004	0.20
Trial 5	11.3±2.0	9.2±2.2	10.7±2.1	0.001	0.05
Trial 6	5.8±1.5	4.4±1.2	5.1±1.3	0.0004	0.005
Trial 7	4.5±1.4	2.2±1.3	4.2±1.3	<0.0001	0.11
CTT	85.9±21.6	100.7±25.8	90.3±23.5	<0.0001	0.02
GP test					
left	126.8±30.6	153.6±46.3	134.8±33.2	<0.0001	0.01
right	116.5±21.9	133.5±27.5	122.3±27.4	<0.0001	0.03
MMSE	29.1±1.6	27.2±2.3	28.6±1.3	0.0007	0.08

[*]Comparison between postoperative day 7 and preoperative data

[†]Comparison between 4-month follow up and preoperative data

AVLT, auditory verbal learning tests; CTT, color trail test A; GP, grooved pegboard; MMSE, mini-mental state examination

Table 6. The relative reductions in postoperative neurocognitive outcomes in comparison to

preoperative values for the single clamp (SC) and multiple clamp (MC) groups. Data are expressed as

percentages. A negative algebraic sign is indicative of deterioration in neurocognitive performance on

the Rey AVLT and MMSE, whereas the opposite is true for the GP and CTT.

	Relative reduction (SC)		Relative reduction (MC)		P^*	$P^\dagger$
	POD 7	4 mo F-U	POD 7	4 mo F-U		
Rey AVLT						
Trial 1	-1.6 %	-0.7 %	-13.6 %	-1.7 %	0.03	0.83
Trial 2	-5.2 %	-6.1 %	-2.6 %	-0.5 %	0.65	0.08
Trial 3	-4.9 %	-3.9 %	-7.5 %	-4.9 %	0.29	0.53
Trial 4	-7.8 %	-5.5 %	-11.8 %	-2.6 %	0.14	0.49
Trial 5	-8.6 %	-1.9 %	-17.3 %	-4.4 %	0.002	0.26
Trial 6	-11.5 %	-2.6 %	-23.3 %	-10.7 %	0.005	0.07
Trial 7	-34.0 %	-9.5 %	-54.2 %	-3.3 %	0.008	0.65
CTT	+8.1 %	+2.7 %	+17.6 %	+5.4 %	0.007	0.20
GP test						
left	+10.6 %	+2.9 %	+21.1 %	+6.6 %	0.009	0.17
right	+11.0 %	+3.1 %	+14.7 %	+4.8 %	0.04	0.26
MMSE	-3.0 %	+0.4 %	-6.5 %	-1.4 %	0.02	0.17

[*]Comparison of postoperative day 7 data between the SC and MC groups

[†]Comparison of 4-month follow up data between the SC and MC groups

AVLT, auditory verbal learning tests; CTT, color trail test A; GP, grooved pegboard; MMSE, mini-mental state

examination

Table 7. The Spearman correlation analysis between the total number of embolic signals and various aspects of neurocognition.

Correlation of HITS with:	Spearman R	P
Rey AVLT		
Trial 1 (POD 7)	-0.07	0.60
Trial 1 (4 mo f/u)	-0.09	0.50
Trial 2 (POD 7)	-0.15	0.28
Trial 2 (4 mo f/u)	-0.14	0.29
Trial 3 (POD 7)	-0.17	0.21
Trial 3 (4 mo f/u)	-0.21	0.12
Trial 4 (POD 7)	-0.09	0.50
Trial 4 (4 mo f/u)	-0.08	0.56
Trial 5 (POD 7)	-0.09	0.51
Trial 5 (4 mo f/u)	-0.03	0.85
Trial 6 (POD 7)	0.02	0.90
Trial 6 (4 mo f/u)	0.06	0.67
Trial 7 (POD 7)	-0.29	0.03
Trial 7 (4 mo f/u)	-0.04	0.75
CTT (POD 7)	0.36	0.01
CTT (4 mo f/u)	0.35	0.01
GP-L (POD 7)	0.29	0.03
GP-L (4 mo f/u)	0.25	0.07
GP-R (POD 7)	0.31	0.02
GP-R (4 mo f/u)	0.24	0.08
MMSE (POD 7)	-0.10	0.46
MMSE (4 mo f/u)	-0.05	0.71

HITS, high intensity transient signal; AVLT, audio verbal learning test; POD, postoperative day; 4 mo f/u, 4-month follow up; CTT, color trail test A; GP-L, grooved pegboard test – left arm; GP-R, grooved pegboard test – right arm; MMSE, mini mental state examination