Original article

Pulsatile versus non-pulsatile flow to reduce cognitive decline after coronary artery bypass surgery: A randomized prospective clinical trial

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ABSTRACT

Background: In this prospective study, we aimed to compare the effect of pulsatile and non-pulsatile flow on the cognitive functions in patients undergoing coronary artery bypass surgery.**Methods:** Patients scheduled for their first coronary artery bypass surgery ($n = 148$) were randomly assigned to the pulsatile flow group (Group A, $n = 75$) or non-pulsatile group (Group B, $n = 73$). Cognitive performance was assessed with (MoCA) montreal cognitive assessment test performed by psychologists before coronary artery bypass surgery and 1 month after the operation.**Results:** Mild cognitive impairment was seen in 12 (16%) patients and serious cognitive impairment was seen in 1 (1.33%) patient in the pulsatile flow group. In the other group, mild cognitive impairment was detected in 23 (31.50%) patients and serious cognitive decline was found in 3 (4.10%) patients. Mean MoCA scores were 25.86 ± 2.62 in group A and 22.12 ± 2.20 in group B. The difference between two groups was statistically significant ($P = 0.041$).**Conclusions:** We suggest that pulsatile flow has beneficial effects to decrease cognitive dysfunction in patients undergoing on-pump coronary artery bypass surgery.

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1. Introduction

Coronary artery bypass grafting (CABG) is a type of surgery, which is known to be associated with adverse neurological outcomes. With improvements in cardiac surgery, anesthesia and cardiopulmonary bypass (CPB) techniques, stroke and mortality rates significantly decreased. Unfortunately, the cognitive decline is still frequent. Almost 60% of the patients who undergo CABG experience cognitive impairment.^{1,2} Three major mechanisms have been proposed to explain cognitive dysfunction after open-heart surgery; hypoperfusion, intraoperative cerebral microembolism and the systemic inflammatory response.^{3,4} Pulsatile CPB is considered to be more physiological than non-pulsatile flow as it provides a lower systemic vascular resistance and higher oxygen consumption. The pulsatile energy ensures the patency of the vascular bed, improves microcirculation and enhances diffusion.^{5–7}

In this prospective study, we aimed to compare the effect of pulsatile and non-pulsatile flow on cognitive functions in the

patients undergoing coronary artery bypass surgery. Montreal cognitive assessment (MoCA) test was used to evaluate the cognitive functions of these patients.⁸

2. Methods

Patients scheduled for their first CABG surgery ($n = 148$) were randomly assigned to pulsatile flow group (Group A, $n = 75$) or non-pulsatile group (Group B, $n = 73$).

2.1. Surgical procedure

After premedication, anesthesia was induced with midazolam (70 mg/kg) and fentanyl (10 µg/kg). Muscle relaxation was achieved with pancuronium bromide (0.1–0.2 mg/kg). Anesthesia was supported by inhalation of isoflurane 0.5–1% (Abbot Laboratories, North Chicago, IL, USA). The extra corporeal circuit consisted of a roller pump (Stöckert Instrumente, Munich, Germany) with a non-pulsatile and pulsatile running mode, a hollow fiber membrane oxygenator (D 708 simplex III, Dideco, Mirandola, Italy). Patients were heparinized before initiation of CPB with 300 IU/kg, and additional doses were given to maintain an ACT (Activated clotting time) of more than 480 s. Extra-corporeal circulation was initiated

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with a flow of 2.4 L/m²/min–2.6 L/m²/min. Surgery was performed in mild hypothermia (32–34 °C).

Cognitive performance was assessed with MoCA test performed by psychologists 1 day before and 1 month after the surgery.

The MoCA test is a one-page 30-point test administered in approximately 10 min. It assesses several cognitive domains [Table 1]. The short-term memory recall task (5 points) involves two learning trials of five nouns and delayed recall after approximately 5 min. Visuospatial abilities are assessed using a clock-drawing task (3 points) and a three-dimensional cube copy (1 point). Multiple aspects of executive functions are assessed using an alternation task adapted from the trail-making B task (1 point), a phonemic fluency task (1 point), and a two-item verbal abstraction task (2 points).

Attention, concentration and working memory are evaluated using a sustained attention task (target detection using tapping; 1 point), a serial subtraction task (3 points), and digits forward and backward (1 point each).

Language is assessed using a three-item confrontation naming task with low-familiarity animals (lion, camel, rhinoceros; 3 points), repetition of two syntactically complex sentences (2 points), and the aforementioned fluency task. Finally, orientation to time and place is evaluated (6 points).

The patients who scored more than 25 points were considered to have no cognitive impairment. A MoCA score between 19 points and 25 points shows mild cognitive impairment. The patients with a score less than 19 points are considered to have serious cognitive impairment. Carotid Doppler ultrasound was performed to all patients before the surgery. Serious carotid stenosis, age more than 80 years old, preoperative neurological disease, digitally palpable calcification of the aortic wall, porcelain aorta and post-operative stroke were the exclusion criteria for the study.

The statistical package for social sciences (SPSS) for Windows version 17.0 (SPSS Inc, Chicago, IL) was used for the statistical evaluation. Characteristics of the first and second groups of patients were compared using the Mann–Whitney *U* test. Mean values were compared with the aid of a 1-way analysis of variance test. The χ^2 test was used for nominal variables, and *P* 0.05 was considered significant.

The trial was approved by the institutional research and ethical committee at our institution. Informed consent was obtained from each patient.

3. Results

Demographic profile and the risk factors of the study groups were similar [Table 2]. In pulsatile flow group (Group A) 69 patients scored more than 25 points, in group B (non-pulsatile flow group) 68 patients succeeded to get more than 25 points before the surgery. They were all considered to have no cognitive decline. There were 6 patients in group A and 5 patients in group B that could score between

Table 2
Demographic profile and the risk factors of the patients.

	Group A	Group B
No. of patients	75	73
Mean age (years)	60.2 ± 8.4	58.6 ± 6.4
Female (%)	38 (50.6)	42 (57.5)
Smoking (%)	45 (60.0)	43 (58.9)
COPD* (%)	3 (4.0)	4 (5.4)
Diabetes mellitus (%)	30 (40)	28 (38.3)
Renal failure (%)	3 (4)	5 (6.8)
Hypertension (%)	50 (66.6)	48 (65.7)
LIMA harvest* (%)	69 (92.0)	66 (90.4)
Mean no. of bypass grafts	3.05 ± 0.7	3.12 ± 1.1
Mean CPB time	71.7 ± 9.0	74.2 ± 8.9
Left ventricle EF (%)*	52.4 ± 3.6	48.1 ± 5.6

LIMA = Left internal mammarian artery, *COPD = Chronic obstructive pulmonary disease, CPB = Cardiopulmonary bypass, EF = Ejection fraction.

19 points and 25 points. They were considered to have mild cognitive impairment before the coronary artery bypass surgery [Table 3]. These patients were not excluded as the number of patients were similar for both groups and there was no statistically significant difference. Furthermore, some of them were lower educated and it's well-known that education can easily affect the results of the cognitive tests. In addition, neurological examination revealed normal findings in all patients in this study before and after the surgery.

One month after the operation, cognitive performance of the patients was assessed again with MoCA test. In group A, mild cognitive impairment was found in 12 (16%) patients, only 1 (1.33%) patient had serious cognitive impairment. The other 62 (82.67%) patients were considered to have no cognitive decline.

In group B, the number of the patients with no cognitive impairment was 48 (68.40%). Unfortunately, 3 patients experienced serious problems (4.10%). 23 patients had mild cognitive impairment (31.50%). It was statistically different from the other group (0.038).

Mean MoCA score was 25.86 ± 2.62 in group A, and it was 22.12 ± 2.20 in the latter group. The means of two groups were statistically significant (*P* = 0.041) [Table 4].

4. Discussion

Every year, there are approximately one million coronary artery bypass procedures performed worldwide. Cognitive impairment is a well-known and bothersome complication of this surgery. It causes prolongation of hospitalization resulting in additional costs. The decrease in cognitive capacity can persist over many years.¹

Understanding the mechanisms that lead to cognitive decline following CABG may yield possible targets for prevention. While hypothermia has been found to be neuroprotective in several animals and human models due to reduction in glutamate release and slowing of the ischemic cascade, hyperthermia is associated with worsening of neurologic outcomes in those same models slower rewarming was associated with better neurocognitive function 6

Table 1
Montreal cognitive assessment test scoring.

Assessment	Points
Visuospatial/executive	5
Naming	3
Memory/delayed recall	5
Attention	6
Language	3
Abstraction	2
Orientation	6
Total	30
(26–30: No CI	19–25: Mild CI
	<19: Serious CI*)

CI* = Cognitive impairment.

Table 3
Comparison of the degree of cognitive impairment between two groups before the surgery.

	Group A	Group B	<i>P</i> value
No. of patients	75	73	
Mild CI*	6 (8%)	5 (6.8%)	0.654
No. CI	69 (92%)	68 (93.2%)	0.782
Mean MoCA score (points)	26.72 ± 1.76	26.89 ± 1.62	0.533

MoCA = Montreal cognitive assessment, *CI = Cognitive impairment.

Table 4

Comparison of the degree of cognitive impairment between two groups after the surgery.

	Group A	Group B	P value
No. of patients	75	73	
Mild CI (mean MoCA score)	12 (16%) 23.86 ± 2.34	23 (31.50%) 20.86 ± 1.82	0.038
Serious CI (mean MoCA score)	1 (1.33%) 17.63 ± 1.58	3 (4.10%) 16.24 ± 1.45	0.542
No. CI	62 (82.67%)	48 (64.40%)	0.226
Mean MoCA score (all patients)	25.86 ± 2.62	22.12 ± 2.20	0.041

MoCA = Montreal cognitive assessment, CI = Cognitive impairment.

weeks following surgery.⁹ Hemodynamic management during cardiopulmonary bypass is also important. Gold et al randomized 248 patients undergoing primary, nonemergency CABG to either low (50–60 mmHg) or high (80–100 mmHg) mean arterial pressure. The rates of both neurologic and cardiac complications were lower in patients maintained at higher arterial pressures.¹⁰

Pulsatile CPB is considered to be more physiological than non-pulsatile flow as it provides a lower systemic vascular resistance and higher oxygen consumption. Thus, it ensures the patency of the vascular bed, improves microcirculation and enhances diffusion.^{5–7}

A relationship between atherosclerotic load in the aorta and perioperative stroke risk has been firmly established. The use of epiaortic scanning and transesophageal echocardiography may be helpful to reduce the cognitive decline.¹¹

MoCA test assesses different types of cognitive abilities, including orientation, short-term memory, executive function, language abilities, and visuospatial ability. Since the MoCA assesses multiple cognitive domains, it may be a useful cognitive screening tool for several neurological diseases, such as Parkinson's disease, vascular cognitive impairment, Huntington's disease, brain metastasis, primary brain tumors (including high and low grade gliomas), and multiple sclerosis, and other conditions, such as traumatic brain injury, depression, schizophrenia and heart failure.^{12–14}

In our study, the overall post-operative cognitive decline was 17.33% in the pulsatile flow group and 35.60% in non-pulsatile flow group. Especially, mild cognitive impairment was observed more in the non-pulsatile flow group than the other group. The difference was statistically significant (0.038).

Thus, we suggest that pulsatile flow during CPB has beneficial effects to reduce post-operative cognitive impairment in patients undergoing on-pump coronary artery bypass surgery.

Conflicts of interest

All authors have none to declare.

References

- Newman MF, Kirchner JL, Phillips-Bute B, et al. Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. *N Engl J Med*. 2001;344:395–402.
- Selnes OA, Goldsborough MA, Borowicz LM, McKhann GM. Neurobehavioural sequelae of cardiopulmonary bypass. *Lancet*. 1999;353:1601–1606.
- Ho PM, Arciniegas DB, Grigsby J, et al. Predictors of cognitive decline following coronary artery bypass graft surgery. *Ann Thorac Surg*. 2004;77:597–603.
- Pugsley W, Klinger L, Paschalis C, Treasure T, Harrison M, Newman S. The impact of microemboli during cardiopulmonary bypass on neuropsychological functioning. *Stroke*. 1994;25:1393–1399.
- Dunn J, Kirsh MM, Harness J, Carroll M, Straker J, Sloan H. Hemodynamic, metabolic, and hematologic effects of pulsatile cardiopulmonary bypass. *J Thorac Cardiovasc Surg*. 1974;68:138–147.
- Mandelbaum I, Burns WH. Pulsatile and nonpulsatile blood flow. *JAMA*. 1965;191:657–660.
- Taylor KM, Bain WH, Davidson KG, Turner MA. Comparative clinical study of pulsatile and non-pulsatile perfusion in 350 consecutive patients. *Thorax*. 1982;37:324–330.
- McLennan SN, Mathias JL, Brennan LC, Stewart S. Validity of the Montreal Cognitive Assessment (MoCA) as a screening test for mild cognitive impairment (MCI) in a cardiovascular population. *J Geriatr Psychiatry Neurol*. 2011;24:33–38.
- Dietrich WD, Busto R, Globus MY, Ginsberg MD. Brain damage and temperature: cellular and molecular mechanisms. *Adv Neurol*. 1996;71:177–194.
- Gold JP, Charlson ME, Williams-Russo P, et al. Improvement of outcomes after coronary artery bypass. A randomized trial comparing intraoperative high versus low mean arterial pressure. *J Thorac Cardiovasc Surg*. 1995;110:1302–1314.
- Davila-Roman VG, Barzilai B, Wareing TH, Murphy SF, Kouchoukos NT. Intraoperative ultrasonographic evaluation of the ascending aorta in 100 consecutive patients undergoing cardiac surgery. *Circulation*. 1991;84:47–53.
- Videnovic A, Bernard B, Fan W, Jaglin J, Leurgans S, Shannon KM. The Montreal Cognitive Assessment as a screening tool for cognitive dysfunction in Huntington's disease. *Mov Disord*. 2010;25:401–404.
- Pendlebury ST, Cuthbertson FC, Welch SJ, Mehta Z, Rothwell PM. Underestimation of cognitive impairment by Mini-Mental State Examination versus the Montreal Cognitive Assessment in patients with transient ischemic attack and stroke: a population-based study. *Stroke*. 2010;41:1290–1293.
- Olson RA, Chhanabhai T, McKenzie M. Feasibility study of the Montreal Cognitive Assessment (MoCA) in patients with brain metastases. *Support Care Cancer*. 2008;16:1273–1278.