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The Effect of Cross Clamp Time on Neurocognitive Function in Coronary Artery Bypass Surgery

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Abstract

Objective: This study evaluates the importance of cross clamp time (CCT) on neurocognitive function in coronary artery bypass graft at an early postoperative period.

Methods: The standardized mini mental state examination (SMMSE) is used to determine the neurocognitive function. This is a prospective study on 100 consecutive patients within a certain time interval in a single clinic.

Results: During the study period 100 participants are analysed by SMMSE, preoperatively and postoperatively. The CCT under 120 min had no significant impact on neurocognitive function ($p>0.05$). Mean age (57.8±9.7). 82% men, 18% women. Median SMMSE point: 29±0.8 (preoperative), 29.2±0.8 (postoperative) ($p>0.05$). CCT is 62.6±27.8 min and cardiopulmonary bypass time is 82.3±32.4 min in this study.

Conclusion: We have found no correlation between CCT (median: 62±27 min) and neurocognitive function. The study implies that surgeons can relax in CCT under 120 min in terms of neurocognitive disorder.

Keywords: Aortic cross clamp, neurocognitive function, standardized mini mental state examination, coronary artery bypass graft surgery

INTRODUCTION

Cardiopulmonary bypass (CPB) support during cardiac surgery is unique because blood is exposed to the foreign surface and continuously recirculated throughout the body (1).

This inflammatory response to CPB initiates a powerful thrombotic stimulus. Circulation of vasoactive and cytotoxic substances affects every organ and tissue within the body (1).

The technological advances -arterial filter systems, perfusion monitors, oxygenators, tubings- have decreased the mortality and morbidity related to coronary artery bypass graft (CABG) since modern extracorporeal circulation was first used by Gibbon (2,3). Nevertheless, neurological issues are still part of serious problems. The great majority of neurological disorders related to CABG are CPB and manipulation of the aorta (4). Hypoperfusion and systemic inflammation response can occur during CPB. Cerebral microemboli may have occurred because of manipulation and cross clamping of the aorta (5).

There are two types of neurological injury after CABG. Type 1: Transient ischemic attack, encephalopathy, stroke, and coma. Type 2: Neurocognitive decline.

The duration of cross clamping of the aorta affects the neurocognitive function because the extracorporeal CPB activates the coagulation cascade and inflammatory response (6). Neurocognitive decline impresses the daily life of the patient that is detectable by relatives (7).

Neurocognitive decline related to CABG is enhanced by aortic cross clamp (8). Although some studies observe small neurocognitive benefits in off-pump CABG, most RCTs prove the advantage of using an aortic clamp (8).

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Reducing the aortic manipulation is the main concept of the single cross-clamp CABG strategy. It minimizes cerebral embolic events, so does neurocognitive descent (9).

Bucerius et al.'s (10) study remarked that 10% of stroke events occurring in CABG have a CPB duration over 120 min. cross clamp time (CCT) >88 min was a risk factor for neurological complications in an other study (11).

This study was designed to determine the effect of CCT on neurocognitive function. We analyzed cross clamp duration for understanding whether it affects the neurocognitive function of individuals or not.

METHODS

A prospective study was chosen. Single clinic Dr. Siyami Ersek Thoracic Cardiovascular Surgery Training and Research Hospital-attended to this research.

One hundred consecutive individuals who underwent CABG surgery between February 2015-July 2015 were enrolled in the investigation and approved by the University of Health Sciences Turkey, İstanbul Dr. Siyami Ersek Thoracic Cardiovascular Surgery Training and Research Hospital institutional Ethics Committee (BŞH.FR.40, decision date: 11.02.2015). Written informed consent was obtained from the patients before the inclusion of the study. Demographic and clinical datas were obtained for each patient. Standard assessments, including physical examinations, chest X-ray, laboratory tests were performed. The criteria for selecting individuals: Non-concomitant surgery, non-carotid artery disease, non-valve disease, non-cardiomyopathy.

The primary inclusion criterion was using aortic cross clamp in coronary artery bypass surgery.

Conventional CABG surgeries were performed using either left internal mammarian artery (LIMA) as the bypass conduit or reversed saphenous vein grafts from the legs. Pedicled LIMA graft to the LAD and reversed saphenous vein grafts to other coronary arteries were anastomosed. Proximal anastomoses were done using a single clamp technique. Operations are carried out by many different surgeons with similar techniques in the same clinic.

CPB was instituted with a single, two-stage right atrial cannula, an ascending aortic perfusion cannula, and an ascending aortic cardioplegia cannula. Arterial line filters, membrane oxygenators, moderate hemodilution (hematocrit, 20-24%) techniques, α-stat acid-base balance were used in all operations. Pulsatile flows (2-2.4 L/min/m^2) were used. Mean arterial pressures were 60-80 mmHg. Target systemic temperatures were 28-32 °C.

Warm blood cardioplegia was delivered. Initially high-potassium cardioplegia (KCl 100 mmol/L, 1000 mL) was administered at 300 mL/min into the aortic root at an aortic pressure of 100 mmHg to achieve cardiac arrest. During cross clamp, intermitant (20 min) perfusion was used. The same anesthetist group was enrolled in all operations. Premedication was administered with midazolam (3 mg intramuscular). Anesthesia was induced with either fentanyl (500 µg), propofol (0.5 to 1.0 mg/kg) or rocuronium (0.6 mg/kg). Sevoflurane and propofol were used for maintenance of anesthesia.

Age, gender, education status were registered. Ejection fractions <40% and were excluded. Respiratuar function tests of individuals were normal. Participants who had abnormal blood test results preoperatively were excluded.

Because preoperative renal deficiency is an independent risk factor for neurological disorders (12), we excluded these patients from the current study. Simões et al. (13) remarked in their study that chronic kidney disease is the most potent risk factor for neurocognitive disorder.

Neurocognitive function has been assessed by measuring standardized mini mental state examination (SMMSE). SMMSE is one of the most well-known tests for assessing neurocognitive function (14).

The SMMSE was developed to provide scoring instructions and clarify indistinct MMSE to raise trusty and lower variability. The SMMSE assesses neurocognitive function, including orientation, memory, attention, calculation, remembrance, language.

Statistical Analysis

Number Cruncher Statistical System 2007 program was used for statistical analysis. Descriptive statistical methods such as mean, standard deviation, median, frequency, ratio, and Student's t-test, Mann-Whitney U test, Wilcoxon test were used for evaluating study datas.

Spearman correlation analysis was performed for assessing measurement relations ($p<0.05$).

The subjects who had aortic calcification seen on chest X-ray and have carotid stenosis >50% preoperatively were excluded. Such as urgent surgeries were excluded. Urgent cardiac surgery is an independent risk of stroke (10).

Redo CABG is an independent risk factor for stroke (10). Native structure deteriorates in the first surgical intervention, so that the manipulation gets more difficult in redo surgery. Because of these, the surgery gets longer and embolic events get more. The current study did not evaluate redo participants.

RESULTS

The mean age of individuals is 57.8±9.7. 82% men, 18% women. The mean CCT is 62.6±27.8 (Table 1).

Table 2 compares the results obtained from the SMMSE score of individuals pre and post-operatively according to cross clamp duration. Also the results of the correlation analysis are shown. What stands out in Table 2: There is no significant difference between CCT and neurocognitive function when the cross clamp duration was 62.6±27.8 min, mean standard deviation.

The CPB time is 82.3±32.4 min.

We analyzed the difference in age, CCT, pre-op and post-op SMMSE scores between men and women. Table 3 shows that no significant differences were found between men and women.

No significant correlation was found between CCT and the age of the individuals [r (Spearman correlation parameter): 0.02 and $p<0.05$].

DISCUSSION

Although the improvement in open heart surgery especially in heart lung machines, neurocognitive function disorders are still one of the most affective problems for patients with both morbidity and mortality.

Neurocognitive complications are multifactorial. Micro and macroembolic injury, abnormal cerebral perfusion, inflammatory, and neurohumoral response, premorbid disease, fragility are all influential factors related to neurocognitive function. No matter what the reason, the result is the same: Neuronal hypoxia and ischemia. Of course, CPB duration is powerful for neurocognitive function however our study is focusing on the CCT effect. Furthermore the greater CCT is the greater CPB duration. Technological advances protect the neuronal system as pointed out in the text. Although filter systems protect most majority of emboli, we should not manipulate aorta more not to provoke mobilizing microembolism and hypoperfusion of brain. Evidence suggests that off-pump CABG is associated with reduced perioperative stroke in higher-risk patients, including those with atheromatous disease of the ascending aorta.

Emboli during on-pump CABG can occur from a variety of sources such as aortic cannulation, aortic clamp removal, or bypass circuit. Therefore each source need further research. Our study is about one of them.

Dissimilar pulsatile perfusion during CPB may account for the appearance of diffuse brain edema. Systemic inflammation is an other influential factor on cerebral function.

No neuroprotective substances for cardioplegic solutions were used, as mentioned in the methods section. We could not have any further decisions about the effect of neurocognitive function related to content of cardioplegia.

Preoperative renal dysfunction is an important independent predictor of in-hospital and late mortality in adult patients undergoing cardiac surgery (12). Excluding such patients from our study made the study clearer. So that we could better focus on XCT effect on neurocognition.

CCT over 120 min, several reports have shown that there is a correlation between CCT and postoperative cerebral disfunction. In our study there were 4 individuals who have cross clamp duration over 120 min and 3 of them a little bit more than 120 min (121, 123, 132). One of them 157 min. So, we could not have a conclusion about individuals who are over 120 min cross clamp duration.

Previous studies in the literature have shown that there is no significant correlation between CCT and neurocognitive function disorder under 120 min as in our study. Beside this, a strong relationship between CCT and neurocognitive function over 120 min has been reported in the literature.

Table 1. Shows the descriptive feature distribution

n=100	Min-max	Mean ± SD
Age (year)	39-77	57.8±9.7
Cross clamp time (min)	19-157	62.6±27.8

Min: Minimum, max: Maximum, SD: Standard deviation

Table 2. Assessing the SMMSE relating to cross clamp time

		Cross clamp time	
		r	p
SMMSE point	Pre-op	-0.117	0.246
	Post-op	-0.027	0.787
	Difference (preop-postop)	-0.160	0.111

r: Spearman correlation parameter, SMMSE: Standardized mini mental state examination

Table 3. Assessing the results for gender

	Men (n=82)	Women (n=18)	p
	Mean ± SD	Mean ± SD	
Age (year)	57.6±9.6	58.8±10.5	0.617[a]
CCT (min)	62.1±26.7	65.2±33.2	0.98[b]
Pre-op SMMSE	29.1±0.83	29.4±0.62	0.156[b]
Post-op SMMSE	29.4±0.85	29.3±0.77	0.415[b]

[a]Student's t-test, [b]Mann-Whitney U test, SD: Standard deviation, CCT: Cross clamp time, SMMSE: Standardized mini mental state examination

Although the current study is based on a small sample of participants, the findings suggest that CCT should be lower than 120 min in CABG not to a neurocognitive disorder. These results match with those observed in earlier studies.

Study Limitations

A limitation of this study is that it is a single center study and the sample size over 120 min CCT is inadequate for the conclusion. An other limitation of this study is that some comorbidities such as tobacco use or diabetes mellitus are not evaluated.

A key strength of this work is being a prospective study and assessing the neurocognitive function face-to-face manner with a common reliable test.

Further study could assess the long-term effects of the cross clamp duration. Our study was limited to one week period starting on the day before surgery.

This experiment did not detect any evidence of CCT over 120 min.

The current study pointed out that there is no significant difference between young and elderly participants and women and men.

CONCLUSION

The study confirmed that CCT under 120 min has no significant impact on neurocognitive function.

The principal theoretical implication of this study: CCT <120 min is a safety zone for neurocognitive function.

Ethics

Ethics Committee Approval: Approved by the University of Health Sciences Turkey, İstanbul Dr. Siyami Ersek Thoracic Cardiovascular Surgery Training and Research Hospital institutional Ethics Committee (BŞH.FR.40, decision date: 11.02.2015).

Informed Consent: Written informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.A., M.E.E., B.K., C.U.K., Concept: E.A., M.E.E., B.K., C.U.K., Design: E.A., M.E.E., B.K., C.U.K., Data Collection or Processing: E.A., M.E.E., A.O., M.A.K., Analysis or Interpretation: E.A., M.E.E., A.O., M.A.K., Literature Search: E.A., M.E.E., A.O., M.A.K., Writing: E.A., M.E.E., A.O.

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