Cognitive Function after Coronary Artery Bypass Graft Surgery: A Prospective Study in Northern Iran

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Abstract: Neurocognitive dysfunction is still considered as a well-recognized complication of coronary artery bypass graft (CABG) surgery. Cognitive decline after cardiac surgery is frequent. However, its reported incidence varies widely. The aim of this study was to evaluate cognitive function of patients after CABG surgery in Mazandaran Heart Center, Sari, northern Iran. In a cross-sectional study from September 2011 to April 2012, a total of 161 consecutive cases of elective CABG at Mazandaran Heart Center were included. Cognitive brain function of eligible individuals was evaluated by the Mini Mental State Examination (MMSE) before CABG and at 10-day and 2-month follow-up. The results were analyzed using repeated measures analysis of variance, Pearson's correlation test, and linear regression analysis. Out of 161 patients, 98 were male (60.9 %) and 63 were female (39.1%). The mean age of patients was 58.83 ± 8.02 years. The mean total scores of MMSE before CABG surgery and 10 and 60 days after it were 25.42, 24.89, and 25.48 respectively ($P < 0.001$). Scores of two areas of cognitive function, i.e. orientation (at 10 days and 2 months after surgery) and language-praxis (at 10 days after surgery) decreased significantly in patients ($P < 0.05$). MMSE scores 10 days after CABG surgery were significantly related with age and blood transfusion ($P < 0.05$). This study highlighted the incidence of early (10 days after surgery) cognitive dysfunction in patients undergoing CABG surgery. It also suggested cognitive function to be correlated with age and blood transfusion. Therefore, interventions for prevention or reduction of this complication after CABG are warranted.

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1. Introduction

Coronary artery bypass graft (CABG) surgery is one of the most expensive and frequently performed surgical procedures in the world. It intends to treat ischemic heart disease and reduce angina pectoris (1-3). Despite technological advances in the surgical procedure, anesthesia, and cardiopulmonary bypass (CPB) which resulted in a steady decrease in the mortality and morbidity associated with these procedures over the past four decades, neurocognitive dysfunction is still recognized as a well-recognized complication of CABG (4,5). Cognitive decline is a frequent complication after cardiac surgery whose reported incidence varies widely. Its incidence rate has been estimated as 50-80% at discharge, 20-50% at 6 weeks, and 10-30% at 6 months after operation (5-9). Intraoperative cerebral microembolism and hypoperfusion have been proposed as the two major mechanisms involved in the occurrence of cognitive dysfunction after cardiac surgery (6). Neurocognitive dysfunction after CABG is associated with reduced quality of life and can threaten a patient's independence, work performance and daily living skills after hospital discharge. It can also increase the

demand for healthcare resources (10). In spite of the importance of cognitive dysfunction and its consequences, few studies have been carried out in this regard so far. Therefore, this study was conducted to evaluate cognitive function in patients undergoing CABG surgery in Mazandaran Heart Center, Sari, northern Iran.

2. Material and Methods

In a cross-sectional study from September 2011 to April 2012, a total of 161 consecutive cases of elective CABG at Mazandaran Heart Center entered the study. After the approval of the Ethics Committee of Mazandaran University of Medical Sciences, informed consents were obtained from 161 patients who aged 20-70 years old and were scheduled for elective CABG using CPB (cardiopulmonary bypass). The exclusion criteria were other simultaneous cardiac surgeries (e.g. valve replacement), symptomatic cerebrovascular disease, alcoholism (more than 2 drinks/day), psychiatric illnesses (any clinical diagnosis requiring therapy), drug abuse (any illicit drug abuse in the previous three months), hepatic insufficiency (liver function tests > 1.5 times the upper limit of normal), severe pulmonary insufficiency (requiring home oxygen therapy), renal failure (serum creatinine > 2 mg/dl), reluctance to do cognitive test performance, previous heart surgery, and preoperative left ventricular ejection fraction (LVEF) < 30%. In addition, only patients who completed the 2-month follow-up were included.

All patients received standardized anesthesia. They were premedicated with promethazine (25 mg) and morphine (5 mg) intramuscular injections one hour before entering the operating room. In all cases, anesthesia was based on moderate doses of fentanyl (20-30 µg/kg) and midazolam (0.05-0.15 mg/kg) supplemented with isoflurane (< 1%) or propofol (2.5-4.0 mg/kg/h) during CPB. Muscle relaxation was maintained with cisatracurium. Median sternotomy was performed in all patients and CPB was instituted through cannulation of the ascending aorta and the right atrium. Aortic palpation was used to detect atherosclerosis and, if present, to select an appropriate site for cannulation and clamping. In all patients, a blood based St. Thomas' Hospital cardioplegic solution was used at 12°C for myocardial protection. Distal coronary anastomoses were completed with the proximal aorta cross-clamped and the heart arrested. For proximal aortic anastomoses, the aorta was partially clamped while the heart was beating. The CPB circuit included a roller pump (Stockert Instruments, Munich, Germany), a hollow fiber membrane oxygenator (Medtronic Inc, Minneapolis, MN, USA), and an arterial filter with a 34-µm screen (Medtronic Inc.). Moderate hypothermia (32°C) was used during CPB. During rewarming, the maximum allowed blood temperature (at the heat exchanger) was 37.5°C and the maximum allowed nasopharyngeal temperature was 37°C. The warming rate was approximately 1°C and the core temperature increased per 3-5 minutes during the bypass time. Perfusion was non-pulsatile with indexed flows set at 2.4 L/m/min during cooling and rewarming and at 2.0 L/m/min during stable CPB. The mean arterial blood pressure was maintained between 60 and 80 mmHg. Alpha-stat acid-base management was used for all patients.

Cognitive brain function was evaluated before CABG and at 10-day and two-month follow-up using the Mini Mental State Examination (MMSE) or Folstein test. The test comprised five areas of cognitive functions and was applied individually for each patient by an experienced and well-educated nurse. MMSE was also used to estimate the severity of cognitive impairment at a given point of time and to follow the course of cognitive changes in an individual over time. The five areas of the test were orientation (10 points), registration (3 points), attention and calculation (5 points), recall (3 points), and language and praxis (9 points). The maximum score was 30 and scores greater than or equal to 25 were considered as normal (intact). Scores ≤ 9, 10-20, and 21-24 indicated severe, moderate, and mild cognitive impairment, respectively (11). This test has been previously used by Iranian researchers on patients undergoing CABG surgery (12, 13).

Statistical analyses were performed with SPSS software (Statistical Package for Social Sciences, version 16.0, SSPS Inc., Chicago, IL, USA). Differences between preoperative neurocognitive scores and scores on the 10^{th} and 60^{th} days after the operation were tested by repeated measures analysis of variance. Pearson's correlation test and linear regression analysis were used to evaluate the relationships between variables and MMSE scores 10 days after the surgery. The statistical significance was set at a $P < 0.05$.

3. Results

Out of 161 patients, 98 were male (60.9%) and 63 were female (39.1%). The mean age of patients was 58.83 ± 8.02 years (range: 44-70). The mean LVEF was 48.68 ± 7.37%. In addition, 15 subjects (71.4%) had hypertension and 65 (40.4%) had diabetes mellitus. Other baseline and clinical characteristics are shown in Table 1.

Table 1. Basic and clinical characteristics of patients

Variable	Mean ± SD	95% confidence interval
Body mass index (kg/m^2)	26.1 ± 4.7	18.7-39.3
Serum creatinine (mg/dL)	1.01 ± 0.24	0.60-1.96
Intubation time (hour)	7.33 ± 2.60	4.10-22.00
Cardiopulmonary bypass time (min)	81.5 ± 17.4	44.0-150.0
Cross-clamp time (min)	42.6 ± 10.3	26.0-91.0
Minimum hemoglobin (g/dL)	7.6 ± 1.1	5.1-10.5
Minimum temperature (°C)	30.7 ± 1.5	28.0-34.0
Minimum mean arterial pressure (mmHg)	50.5 ± 6.1	37.0-75.0

The mean total score and scores of all five areas of MMSE at baseline and 10 and 60 days after the surgery are shown in Table 2.

Table 2. The mean total scores and scores of the five areas of Mini Mental State Examination at baseline and 10 and 60 days after coronary artery bypass graft surgery

Test	Baseline	10th day	60th day	P
Orientation (10 points)	8.95	8.78	8.86	**0.045**
Registration (3 points)	2.99	2.97	2.98	0.640
Attention and calculation (5 points)	2.53	2.50	2.54	0.720
Recall (3 points)	2.97	2.95	2.98	0.550
Language and praxis (9 points)	8.19	8.06	8.22	**0.001**
Total (30 points)	25.42	24.89	25.48	**< 0.001**

As shown in Table 2, there were significant differences between the mean total scores of MMSE at baseline and on the 10th and 60th postoperative days (P < 0.0001). Moreover, scores of orientation and language-praxis significantly decreased as time passed (P < 0.05). Pearson correlation coefficient showed statistically significant negative correlations between MMSE scores on the 10th day and age (r = -0.26; P = 0.001) and blood transfusion (r = -0.25; P = 0.001). Based on the adjusted regression model, every one-year increase in age was associated with 0.13 reduction in the MMSE score (on average) (95% confidence interval: -0.21 to -0.05; P = 0.002). On the other hand, every one-unit increase in blood transfusion decreased the MMSE score by 1.14 (95% confidence interval: -1.55 to -0.04; P = 0.03) (Table 3).

Table 3. Linear regression analysis of Mini Mental State Examination (MMSE) scores on the 10th day after coronary artery bypass graft surgery

Linear regression	Crude model			Adjusted Model		
Variable	**B**	**P**	**95% confidence interval**	**B**	***P***	**95% confidence interval**
Age (years)	-1.5	0.001	-0.24 to -0.06	-0.13	0.002	-0.21 to -0.05
Blood transfusion (units)	-1.38	0.001	-2.19 to -0.56	-1.14	0.030	-1.55 to -0.04

Variables were analyzed using mixed linear regression models with MMSE scores on the 10th postoperative day as a random effect with adjustment for age, sex, and blood transfusion.

4. Discussions

The results of this study demonstrated that cognitive function of patients after CABG surgery in our institution had significantly differences before, after 10 days and 2 month after surgery. In fact, the mean total MMSE score apparently decreases 10 days after the surgery. Previous studies have suggested that cognitive dysfunction after CABG occurred in 3-80% of patients (5,8,14). In our study, the mean preoperative total score of MMSE was 25.42 which was categorized as normal cognitive function. Farhudi et al. reported the mean total scores of MMSE before and after surgery as 23.82 and 24.52, respectively (12). The results of our study showed that cognitive function of patients apparently decreases 10 days after CABG surgery. Likewise, Kadoi et al. reported that 7 days after CABG surgery, cognitive impairment occurred in 55% of patients without diabetes mellitus and in 68% of patients with diabetes mellitus (15). Farhoudi et al. compared the impacts of on-pump and off-pump CABG on neurocognitive impairment in low risk patients. Based on MMSE scores, cognitive impairment was detected in 21.2% of the cases in the on-pump group and 23.1% of the off-pump (16). In a retrospective, descriptive, cross-sectional study, Hassani et al. evaluated the documents of 514 patients with neurologic complication after open heart surgery. They found that cognitive disorders had developed in 12 patients (2.33%) (17). Adverse neurological outcomes of cardiac surgery are the result of damage to the brain, spinal cord, or peripheral nerves. Central nervous system injury ranges in severity from subtle changes in personality, behavior, and cognitive function to fatal brain injury (18). Taban et al. used MMSE to compare cognitive dysfunction in elderly patients before and after surgeries. As they reported, cognitive dysfunction occurred in 29.1% of the participants (19). Boodhwani et al. indicated that 59% of patients developed cognitive deficits after CABG surgery (20).

The reported incidence of cognitive decline varies widely (9). This variability is partly caused by methodological problems since a multitude of definitions of cognitive decline are used and a large number of neuropsychological tests exist to assess various cognitive domains (21). In this study, we found a statistically significant inverse correlation between age and cognitive function 10 days after CABG surgery. Kadoi et al. suggested that age was associated with cognitive impairment at 7 days after CABG surgery (15). Other studies by Ganavati et al.[13] and Taban et al. showed that scores of cognitive function decreased with aging (19).

On the other hand, we found a statistically significant inverse correlation between blood transfusion and cognitive function 10 days after CABG surgery. In a study on CABG patients in three Finnish hospitals, Mikkola et al. indicated that transfusion of blood products after CABG had a strong, dose-dependent association with the risk of stroke after surgery (22). Stone et al. showed that transfusion of more than three units of red blood cells after CABG was strongly associated with subsequent mortality (23). Similarly, Bahrainwala et al. (24) and Whitson et al. (25) showed that the use of blood products to restore coagulation and correct anemia may contribute to the development of neurological events after cardiac operation. The present study had some limitations. First, we only used one neuropsychological test (MMSE) to assess cognitive function. Second, MMSE is a simple screening tool which might not be reliable in detection of delicate cognitive impairments. Therefore, in further investigations, a more rigorous set of neuropsychological tests is required.

In conclusion, this study highlighted early (10 days after surgery) cognitive dysfunction after CABG surgery. It also suggested cognitive function to be associated with age and blood transfusion. Therefore, interventions for prevention or reduction of this complication after CABG are warranted.

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References

1. Yoon BW, Bae HJ, Kang DW, Lee SH, Hong KS, Kim KB, et al. Intracranial cerebral artery disease as a risk factor for central nervous system complications of coronary artery bypass graft surgery. Stroke 2001; 32 (1):94–99.
2. Farhoudi M, Afrasiabi A, Tarzamni MK, Khoshnan M, Arami MA. Transcranial and carotid Doppler study in coronary artery bypass graft patient. Neurosciences 2004; 9:186–189.
3. Farhoudi M, Parvizi R, Bilehjani E, Tarzamni MK, Mehrvar K, Safaiyan A. Preoperative transcranial and carotid Doppler study in coronary artery bypass graft patients. Neurosciences 2007; 12: 42–45.
4. Wang D, Wu X, Li J, Xiao F, Liu X, Meng M. The effects of lidocaine on early postoperative cognitive dysfunction after coronary artery bypass surgery. Anesth Analg 2002; 95: 1134–1141.
5. Sun JH. Wu XY, Wang WJ. Jin LL. Cognitive Dysfunction after Off-pump versus On-pump Coronary Artery Bypass Surgery: a Meta-analysis. The Journal of International Medical Research 2012; 40: 852- 858.
6. Selnes OA, Goldsborough MA, Borowicz LM, McKhann GM. Neurobehavioural sequelae of cardiopulmonary bypass. Lancet 1999; 353:1601–6.
7. Sotaniemi KA, Mononen H, Hokkanen TE. Long-term cerebral outcome after open-heart surgery: a five-year neuropsychological follow-up study. Stroke 1986; 17:410–6.
8. 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.
9. Mahanna EP, Blumenthal JA, White WD, Croughwell ND, Clancy CP, Smith LR, et al. Defining neuropsychological dysfunction after coronary artery bypass grafting. Ann Thorac Surg 1996; 61:1342-7.
10. Ghafari R, Gholipour Baradari A, Firouzian A, Nouraei M,Aarabi M, Zamani A, Emami Zeydi A. Cognitive deficit in first time coronary artery bypass graft patients: A randomized clinical trial of lidocaine versus procaine hydrochloride. Perfusion 2012; 27: 320-325.
11. Crum RM, Anthony JC, Bassett SS, Folstein MF (May 1993). Population-based norms for the Mini-Mental State Examination by age and educational level. JAMA 1993; 269(18): 2386–2391.
12. Farhudi M, Mehrvar K, Parvizi R, Tarzmani M, Bilejani I, Safaiyan A. Correlation of cognitive complications with Doppler findings in selected coronary artery bypasses graft patients. Iranian journal of neurology 2009; 8 (25) :419-426
13. Ganavati A, Forooghi M, Esmaeili S, Hasantash SA, Blourain AA, Shahzamani M, et al. The Relation between Post Cardiac Surgery

Delirium and Intraoperative Factors. Iranian Journal of Surgery 2009; 17(3).
14. Roach GW, Kanchuger M, Mangano CM, Newman M, Nussmeier N, Wolman R, et al. Adverse cerebral outcomes after coronary bypass surgery. Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation Investigators. N Engl J Med. 1996; 335(25):1857-63.
15. Kadoi Y, Saito S, Fujita N, Goto F. Risk factors for cognitive dysfunction after coronary artery bypass graft surgery in patients with type 2 diabetes. J Thorac Cardiovasc Surg. 2005; 129(3):576-83.
16. Farhoudi M, Mehrvar K, Afrasiabi A, Parvizi R, Khalili AA, Nasiri B, et al. Neurocognitive impairment after off-pump and on-pump coronary artery bypass graft surgery - an Iranian experience. Neuropsychiatr Dis Treat 2010; 6:775-8.
17. Hassani E, Mahoori A, Noroozinia H, Mehdizadeh H, Sepasi N. Evaluation of risk factors for adverse neurologic outecome after cardiac surgery. URMIA MEDICAL JOURNAL 2010; 21 (2):249-253.
18. Arrowsmith JE, Grocott HP, Reves JG, Newman MF. Central nervous system complications of cardiac surgery. Br J Anaesth 2000; 84 (3): 378-393.
19. Taban H, Ahmadzadeh GH, Tavassoli MH. Cognetive dysfunction in elderlies, before and after of surgery. Hormozgan Medical Journal 2003; 7(2): 135-139.
20. Boodhwani M, Rubens FD, Wozny D, Rodriguez R, Alsefaou A, Hendry PJ, et al. Predictors of early neurocognitive deficits in low-risk patients undergoing on-pump coronary artery bypass surgery. Circulation 2006; 114(1 Suppl):I461-6.
21. Blumenthal JA, Mahanna EP, Madden DJ, White WD, Croughwell ND, Newman MF. Methodological issues in the assessment of neuropsychologic function after cardiac surgery. Ann Thorac Surg 1995; 59:1345-50.
22. Mikkola R, Gunn J, Heikkinen J, Wistbacka JO, Teittinen K, Kuttila K, Lahtinen J, Juvonen T, Airaksinen JK, Biancari F. Use of blood products and risk of stroke after coronary artery bypass surgery. Blood Transfus. 2012 Feb 22:1-12.
23. Stone GW, Clayton TC, Mehran R, Dangas G, Parise H, Fahy M, Pocock SJ. Impact of major bleeding and blood transfusions after cardiac surgery: analysis from the Acute Catheterization and Urgent Intervention Triage strategY (ACUITY) trial. Am Heart J. 2012 Mar; 163(3):522-9.
24. Bahrainwala ZS, Grega MA, Hogue CW, et al. Intraoperative hemoglobin levels and transfusion independently predict stroke after cardiac operations. Ann Thorac Surg 2011; 91: 1113-8.
25. Whitson BA, Huddleston SJ, Savik K, Shumway SJ. Bloodless cardiac surgery is associated with decreased morbidity and mortality. J Card Surg 2007; **22**: 373-8.

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