Assessment of Neurocognitive Functions before and after Coronary Artery Bypass Surgery

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ABSTRACT

Introduction: Coronary artery bypass grafting (CABG) is one of the most commonly performed cardiac surgeries today and impact of this on cognitive performance can be established through cognitive assessment. This study was planned to evaluate cognitive functions in patients undergoing CABG through neuropsychological tests.

Material and Methods: All consenting CABG patients and control group underwent neurocognitive testing through various standardized neuropsychological tests to compare attention, verbal memory, visual memory and visuoconstruction ability, working memory, verbal learning, delayed recall, motor and mental speed, planning, set shifting, sustained attention, verbal fluency, category fluency and comprehension. Neuropsychological tests were performed before and after 6-12 weeks of surgery in both the groups.

Results: Total 66 patients underwent CABG surgery during the study period. 54 controls were selected for the study. Both groups were similar with regard to age and gender and body mass index (BMI), education and employment status. ($p>0.05$) At baseline the neuropsychological status of both groups were comparable in 10 of 14 tests. At base line verbal fluency, verbal working memory, verbal learning and verbal memory were statistically significant in the control group in comparison to CABG group. Verbal fluency, verbal memory and visuoconstruction ability were statistically significant in the control group in comparison to CABG group at follow up. ($p<0.05$)

Conclusions: CABG procedures per se undertaken using appropriate neurocognitive "protection" techniques may not cause 6-12 weeks decline in cognitive function and the results also confirm that it is important to consider patient's pre-existing cognitive and emotional states.

Keywords: Coronary Artery Bypass Grafting, Cognitive Function, Neuropsychological Tests

INTRODUCTION

Coronary artery bypass grafting (CABG) is one of the most commonly performed cardiac surgeries today and is recognized to be a highly effective procedure for reducing angina and stabilizing ventricular dysfunction. The advancement in surgical techniques has reduced morbidity and mortality.[1] The preoperative variability in cognitive performance in candidates for CABG can be attributed in part to demographic variables, such as age and education, but in addition there is variability due to cerebrovascular disease. The majority of CABG patients have some degree of coexisting cerebrovascular disease,[2] and the impact of this on their preoperative cognitive performance can be established through cognitive assessment.

Over the past two decades studies have shown that patients experience cognitive changes such as poor concentration, problem-solving difficulties, and memory loss after cardiac surgery,[3] and the focus was mainly on short-term cognitive changes, evaluated days or weeks after the surgery. Most of the studies seem to be in agreement that short-term cognitive decline is apparent in many patients post-CABG. However, the long-term studies offer more conclusive evidence that long-term cognitive decline after CABG can be significant in some patients and cannot simply be explained by pre- existing cognitive deficits, advanced age, or comorbid conditions like diabetes and hypertension, or depression.[3,4] The preoperative baseline performance of patients on cognitive tests may show a wide variability; studies have suggested that a subset of patients for CABG may be cognitively impaired before surgery.[5] Although some[6] have reported decline in cognitive function from baseline to 2 and 5 years post-surgery, others[7] have not found notable changes in cognitive function over a 55-month period.

Moreover, changes were found in only specific cognitive domains e.g. visuoconstruction ability and psychomotor speed[6] or attention.[8] Although the cognitive deficits are usually not severe enough to meet criteria for mild cognitive impairment, they lower quality of life and add to hospitalization and out-of-hospital costs. Though the cognitive impairment after CABG is well recognized, some investigations have been limited by lack of an appropriate control group. The emphasis on healthy control group for accurate assessment of the prevalence of cognitive impairment in patients scheduled for CABG surgery is necessary if valid assumptions regarding cognitive change are to be made. Such a cognitive assessment requires the use of an individual free of cardiovascular disease. Except few,[9,10] there is paucity of literature in our country regarding neurocognitive assessment post CABG. The present study, therefore, was planned to evaluate cognitive functions in patients undergoing CABG through neuropsychological

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tests.

MATERIAL AND METHODS

The present prospective study was conducted in tertiary care teaching hospital of Bangalore, which is a leading cardiac care centre which caters the health care need of south India. In the cardiac groups, scheduled to undergo isolated primary CABG based on standard clinical indications during one year study period, were enrolled in the study only after taking approval from Institutional Review Board. All right-handed male patients between 30-65 years old who can read and write native speakers of English, Hindi or Kannada were included in study. Informed written consent was obtained from patients selected for participation in this study. All patients who showed potential inability to successfully complete neurocognitive assessments were excluded out. In control groups, both patients having CAD who were not undergoing CABG (non surgical cardiac controls) and heart healthy controls (without specific evidence by history of cardiac, cerebrovascular or neurologic disease) were included from inpatient or outpatient of hospital.

Demographic data, comorbid medical illness, previous surgeries, detailed systemic and comprehensive neurological examination (absence of focal neurological deficit including dysphasia), complete blood count (CBC), liver function test (LFT), kidney function test (KFT) including electrolytes, fasting and postprandial sugar (FBS /PPBS), lipid profile, urine complete, chest x-ray, electrocardiogram (ECG), 2D ECHO were also recorded. Medical and neurological evaluation was done before surgery and 6-12 weeks after surgery. Neuropsychological examinations were conducted by a trained evaluator 1-7 days prior and 6-12 weeks after surgery. General Health Questionnaire-12 (GHQ-12)[11] for psychiatric morbidity and Edinburgh Handedness Inventory[12] questionnaire for quantitative measure of handedness were used.

All consenting CABG patients and controls meeting inclusion criteria underwent neurocognitive testing at baseline and 6-12 weeks after surgery. Each study subject was tested on all occasions by the same experienced psychometrician in a comfortable, well-lit environment generally free from visual and auditory distractions over approximately 3 hours with adequate rest pauses. Finger tapping test, digit-symbol substitution test, digit vigilance test, verbal (phonemic) fluency cowa test, animal names test, N-back: verbal test, tower of london test, wisconsin card sorting test, stroop color-word test, verbal comprehension token test, auditory verbal learning test, complex figure test were used for assessing speed, attention, executive functions, auditory comprehension, learning, construction ability, memory. Some of these are paper-pencil tests. The tests used for the present study have been standardized for use in the Indian population.[13]

CABG surgeries were done by expert cardiothoracic surgeons. Along with a daily clinical neurological evaluation on the five first postoperative days, data from the notes were used to perform a diagnosis of delirium. Most patients were discharged by the 8th postoperative day. Data for blood chemistry, blood transfusion, use of ionotropes, medical and surgical complications and length of stay were collected. All patients were followed from the day prior to surgery until the day 84th (12 weeks) after surgery. At follow up, repeat biochemistry, ECG, chest X-ray, 2D-ECHO, MRI brain and neuropsychological assessment were performed.

Statistical analyses were performed using Statistical software package (Statistical product and services solutions version 17; SPSS Inc., Chicago, III) for Windows. Differences between continuous variables and categorical variables were assessed using the Student t-test and the chi-square test respectively. Analysis of variance is used to test the hypothesis that several means are equal. The Paired-Samples t test procedure compares the means of two variables for a single group. Differences were considered to be statistically significant at p-value <0.05.

RESULTS

Total 66 patients underwent CABG surgery during the study period. 54 controls were selected for the study. All the hundred and twenty subjects preoperatively and one hundred eleven patients with no postoperative neurological deficits underwent the same standardized 14 - part neuropsychological examination at 6-12 weeks follow-up. No differences were found between CABG group and control group with regard to age and gender and body mass index (BMI), education and employment status (table-1).

Post surgery neuropsychological assessment could not be carried out in nine patients so they were not used for final analysis. At baseline the neuropsychological status of both

Parameters	CABG-Group (N = 66)	Control Group (N = 54)	p value
Age (yrs)	54.56±7.09	52.74±8.78	0.211
BMI(kg/m2)	24.92±2.96	25.45±3.16	0.346
Education (College level)	34(51.52%)	36(66.67%)	0.569
Employed	59(89.39%)	49(72%)	0.951
Risk factors for cerebral injury			
Hypertension	41(62.12%)	17(31.48%)	0.002*
Diabetes mellitus	40(60.61%)	17(31.48%)	0.003*
Smoking	31(46.97%)	14(25.93%)	0.029*
*p<0.05 significant			

Table-1: Demographic characteristics and risk factors of the CABG group and control group groups were comparable in 10 of 14 tests. At base line verbal fluency, verbal working memory, verbal learning and verbal memory were statistically significant in the control group in comparison to CABG group. Verbal fluency, verbal memory and visuoconstruction ability were statistically significant ($p<0.05$) in the control group in comparison to CABG group at follow up (table-2).

Three patients (0.045%) developed new clinical neurologic abnormalities after CABG. None of the detectable abnormalities resulted in functional disability. Stroke developed in 2 patients (0.03%), both were not severely incapacitated. Ophthalmologic abnormalities were observed in 2 patients (0.03%) and included areas of retinal infarction and reduction in visual acuity in one (0.015%),

Domain	Test		CABG group Mean ± SD (N = 57)	Control group Mean ± SD (N = 54)	P value
Motor speed	Finger Tapping Right	pre	52.51 ± 6.67	53.49 ± 6.08	0.423
		post	54.85 ± 7.29	55.14 ± 5.34	0.809
		p	0.076	0.137	
	Finger Tapping Left	pre	47.54 ± 5.47	48.95 ± 6.16	0.209
		post	49.33 ± 6.08	49.77 ± 6.01	0.704
		p	0.101	0.485	
Mental speed	Digit Symbol Substitution	pre	319.56 ±113.2	279.34±119.89	0.073
		post	281.33 ± 97.79	263.43± 95.79	0.335
		p	0.056	0.448	
Sustained attention	Digit Vigilance Time	pre	593.47 ±176.2	558.3 ± 184.81	0.309
		post	533.18±135.42	518 ± 158.1	0.589
		p	0.043*	0.226	
	Digit Vigilance Error	pre	9.95 ± 13.03	10.02 ± 8.28	0.973
		post	6.98 ± 7.82	5.98 ± 6.14	0.459
		p	0.143	0.003*	
Verbal fluency	Controlled Oral Word Association	pre	8.76 ± 3.32	11.02 ± 3.87	0.001*
		post	9.63 ± 3.38	11.91 ± 3.94	0.001*
		p	0.168	0.239	
Category fluency	Animal Names	pre	12.14 ± 3.25	12.85 ± 3.36	0.264
		post	13 ± 2.89	13.96 ± 3.11	0.095
		p	0.138	0.078	
Working memory	Verbal N-Back 1-Back Hits	pre	8.67 ± 0.74	8.91 ± 0.45	0.045*
		post	8.81 ± 0.55	8.96 ± 0.19	0.054
		p	0.254	0.454	
	Verbal N-Back 2-Back Hits	pre	6.89 ± 1.5	6.72 ± 1.59	0.547
		post	6.81 ± 1.57	7.23 ± 1.09	0.109
		p	0.781	0.055	
Planning	Tower of London Total no. of problems solved with minimum moves	pre	8.81 ± 2.19	8.42 ± 1.68	0.298
		post	9.32 ± 1.77	8.75 ± 1.65	0.090
		p	0.174	0.305	
Set shifting	Wisconsin Card Sorting Test Total trials	pre	97.95 ± 19.53	92.02 ± 17.65	0.099
		post	90.96 ± 20.94	85.58 ± 14.07	0.119
		p	0.068	0.038*	
	% of errors	pre	25.15 ± 9.37	24.9 ± 13.45	0.911
		post	20.27 ± 9.86	19.01 ± 6.23	0.428
		p	0.008*	0.004*	
	% Perseverative responses	pre	16.31 ± 8.03	15.39 ± 7.19	0.531
		post	12.83 ± 7.42	13.29 ± 5.6	0.717
		p	0.018*	0.093	
	% Perseverative error	pre	14.51 ± 6.3	13.63 ± 5.84	0.450
		post	11.56 ± 5.82	11.7 ± 4.2	0.888
		p	0.011*	0.051	
	% Non-Perseverative error	pre	10.6 ± 5.27	9.18 ± 6.32	0.205
		post	9.06 ± 5.55	7.24 ± 3.66	0.046*
		p	0.132	0.054	
	% Conceptual responses	pre	65.83 ± 12.72	68.63 ± 13.03	0.257
		post	71.28 ± 13.42	73.98 ± 8.4	0.212
		p	0.028*	0.013*	

Domain	Test		CABG group Mean ± SD (N = 57)	Control group Mean ± SD (N = 54)	P value
Response inhibition	Stroop effect	pre	182.47± 74.05	168.45 ± 59.21	0.277
		post	153.07 ± 69.39	158.26±53.33	0.662
		p	0.031*	0.350	
Comprehension	Token	pre	32.84 ± 2.28	32.89 ± 2.34	0.919
		post	33.6 ± 2.51	33.83 ± 1.91	0.585
		p	0.093	0.024*	
Verbal learning	Auditory Verbal Learning Total	pre	48.98 ± 9.13	53.26 ± 10.78	0.026*
		post	55.79 ± 9.29	54.34 ± 8.51	0.396
		p	0.000*	0.565	
Verbal memory	Immediate recall	pre	9.95 ± 3.08	11.64 ± 2.7	0.003*
		post	11.7 ± 2.71	11.49 ± 2.65	0.681
		p	0.002*	0.771	
	Delayed recall	pre	10.14 ± 2.92	11.28 ± 2.82	0.040*
		post	12.04 ± 2.38	11.7 ± 2.6	0.480
		p	0.000*	0.423	
	Long term percent retention	pre	85.03 ± 18.8	86.64 ± 15.24	0.624
		post	93.95 ± 12.2	88.67 ± 15.09	0.045*
		p	0.003*	0.532	
	Recognition hits	pre	13.86 ± 1.94	14.42 ± 1.25	0.079
		post	14.44 ± 1.18	14.53 ± 1.17	0.690
		p	0.056	0.638	
Visuocon struction ability	Complex Figure Test – Copy	pre	34.39 ± 2.84	34.96 ± 3.17	0.317
		post	34.32 ± 4.03	35.57 ± 2	0.044*
		p	0.915	0.234	
Visual memory	Immediate recall	pre	19.18 ± 7.83	20.13 ± 6.47	0.488
		post	23.28 ± 7.42	23.38 ± 6.6	0.943
		p	0.005*	0.011*	
	Delayed recall	pre	18.93 ± 7.37	19.77 ± 6.54	0.528
		post	23.05 ± 8.04	23.09 ± 7	0.977
		p	0.005*	0.012*	

*p<0.05 significant

Table-2: Pre and post operative neuropsychological test score in CABG group and control group

and visual field defect in another (0.015%). None of the CABG group had fatal cerebral hypoxic/ischemic injury resulting from an episode of profound intra-operative hypotension, postoperative psychosis, primitive reflexes, peripheral nervous system complications, and major functional disability or signs indicative of minor focal CNS injury. The major categories of neurologic disorder (fatal cerebral hypoxia, depression of consciousness level, stroke, ophthalmologic abnormalities, and psychosis) were not found in the non surgical control group.

DISCUSSION

Cognitive impairment which is the integral part of cardiac disease is of principal concern in studying the outcome after CABG in old age patients. It is also important to be aware of potential improvements in cognitive function because of the beneficial effects of CABG surgery upon cerebral microcirculation. Improvements in CABG surgical technique that have been introduced over the past decade may have resulted in better preservation of cognitive function after cardiac surgery compared with earlier analyses.[3,14] In present study fourteen tests were used to assess the six important domains of cognitive function which were much higher than other comparable studies where up to ten tests were studied.[15,16]

In present study there were low-risk in CABG patients due to age being lesser than 65 yrs, better education, most employed, had controlled hypertension with moderate left ventricular ejection fraction. These pre surgical factors did not place subgroups of CABG candidates at increased risk for post-surgical cognitive impairment.[17,18]

In present study CABG patients were compared with control group. It was found that baseline performance in CABG group was lower than those of control group in all domains reaching statistical significance in verbal fluency, verbal working memory, and verbal learning and verbal memory. These findings were in accordance with Ernest and coworkers[19] who administered a battery of neuropsychologic tests to consecutive patients undergoing CABG (*n*=109) so as to evaluate and compare 'presurgical' cognitive functioning with that of a 'healthy control group' (*n*=25) and 'published test norms'. The conclusion was that even after excluding patients at high risk for brain dysfunction, cognitive impairment is found in patients with CAD before surgery thus highlighting the importance of control for medical and demographic factors.

Blackstone et al[20] emphasized that although using a simple "one number answer" (e.g. percentage of patients having a deficit) to address the occurrence and quantification of cognitive deficits after CABG surgery is easy and appealing; the issue of cognitive dysfunction is more complex. In this study we examined the raw scores for each test and compare them to available norms.[13] We used group mean scores based on raw scores to represent the data pre and post surgery, and we used changes in scores from pre surgery to post surgery to evaluate improvement or deterioration of cognitive performance. Blackstone et al[20] also demonstrated that simply comparing average pre post CABG cognitive performance does not accurately describe the adverse impact of CABG upon Stroop performance and the recovery of cognitive function. They concluded that mean-based analysis gave the impression of overall recovery of function at 6 months whereas the assessment of absolute impairment showed a substantial proportion of the patients still to be impaired.

Patients in CABG group improved in sustained attention, verbal working memory, set shifting, response inhibition, and both verbal and visual learning and verbal memory post-surgery at 6-12 weeks follow-up. It is similar to a prospective neuropsychological evaluation[21] of CABG patients revealing improvement at 8 weeks and then decline at 5 years. It however is in contrast to a long term prospective study on cognition pre and post CABG, which showed decline of two cognitive domains - psychomotor and visuo-construction.[22] Analysis of 5-year data suggested that long-term deficits that persist reflect damage or continuing damage of posterior parietal cortex (watershed area), which is primarily vulnerable to hypoperfusion.[23] Eight patients who showed impairment pre-CABG improved significantly to adequate functioning 6-12 weeks post-surgery. This improvement in CABG group cannot be explained as only due to "practice effect" which is typically seen in non-surgical or 'normal' subjects.[24] Given the present small sample in our study, apart from the possible practice effect such an improvement could be due to the beneficial effects of enhanced cerebral perfusion upon cognition following CABG.[25]

In the present study, evidence of cognitive improvement was seen in CABG group. Selnes et al has also speculated in their study that the short term transient declines (which disappear for most patients 3 months after surgery) may be due to the bypass procedure itself and that the cause of long term declines could be found among factors such as age-related changes and poor control of risk factors for cerebrovascular disease, such as hypertension and hypercholesterolemia. The findings of improvement in cognition after CABG in the present study are consistent with several recent studies.[27-29] Similarly Sweet and colleagues[30] gathered neuropsychological data (14 cognitive tests) at baseline, and post surgery at 3 weeks, 4 months and 1 year from 46 HHC, 42 CAD patients undergoing PCI and 43 undergoing CABG. They concluded no clear pattern of group differences or change in neuropsychological outcomes at follow-ups and that CABG surgery does not create cognitive decline.

The observed improvements in cognitive function in CABG group may be a result of the improvements in cardiac function, improved surgical and anesthesia techniques and good control of vascular risk factors. Although it could be suggested that they are due to "practice effects" as it was not practical to perform repeated training sessions before baseline. Given the time period between follow-up assessments, it is unlikely that the improvements are attributable to practice effects and more likely reflect true changes in cognition after surgery. Several studies have reported that cardiovascular risk factors predict performance on neuropsychological tests, in particular measures of processing speed and executive function.[31,32] More large-scale prospective population-based studies have also confirmed that cardiovascular risk factors are associated with incident cognitive decline,[33] and there is some evidence that treatment of the underlying cardiovascular risk factors may reduce the degree of cognitive decline over time.[34]

Large samples study are needed that allow for investigation of subgroup risk factors may lead to better identification of CABG candidates who could suffer cognitive impairment, despite the improvements in CABG techniques that have served to reduce post-surgical cognitive dysfunction.

CONCLUSION

The present study concluded that the CABG procedures per se undertaken using appropriate neurocognitive "protection" techniques may not cause 6-12 weeks decline in cognitive function, at least within the limitations imposed by the currently recommended testing battery. Overall, the results also confirm that it is important to consider patient's pre- existing cognitive and emotional states. The neuropsychological assessment in CABG candidates is essential and not optional. The presence of neuropsychological deficits warrants for neuropsychological rehabilitation which will help the patient function adequately in his day to day activities post CABG.

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