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A comparative study to assess neurocognitive functions between off pump and on pump coronary artery bypass surgery patients

Renu Khamesra^{1,*}¹Dept. of Neurology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India

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ABSTRACT

Background: Coronary artery bypass grafting (CABG) for reducing angina and stabilizing ventricular dysfunction is performed with two primary techniques: “On-pump” or “Off-pump”. The present study was planned to compare neurocognitive assessment in patients undergoing “off pump” CABG and “on pump” CABG through neuropsychological tests.

Materials and Methods: All consenting CABG patients meeting inclusion criteria underwent neurocognitive testing through battery of tests at baseline and 6-12 weeks after surgery. Various standardized neuropsychological tests were used 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 in all the groups.

Results: Forty four patients underwent off-pump (OPCABG) and twenty two patients underwent on-pump (CCPB) surgery during study period. On all the neuropsychological tests in pre operative assessment both the groups were comparable except OPCABG group had significantly improved visuoconstruction ability over CCPB group ($p=0.035$). There was no significant difference in mean postoperative scores for the two groups in any of the neuropsychological tests. ($p>0.05$) Mild cognitive decline (one or two tests) was observed in 31(75.6%) of 41 OPCABG and 13(81.3%) of 16 CCPB group. A moderate or severe degree of neuropsychological dysfunction (≥ 3 tests) was seen in 7(17%) of 41 OPCABG, 3(18.7%) of 16 CCPB group.

Conclusions: The lack of significant differences in the longitudinal test performance postoperatively between the CCPB and OPCABG group in present study suggests that the use of cardiopulmonary bypass is not the sole source of cognitive change after surgery.

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1. Introduction

Coronary artery disease (CAD) causes severe disability and is the most common cause of mortality in the developed and developing world. Coronary artery-bypass graft surgery (CABG), introduced by Rene Favalaro¹ in 1967 for myocardial revascularization, is the most frequently performed cardiac surgery.

Coronary artery bypass grafting (CABG) for reducing angina and stabilizing ventricular dysfunction is performed with two primary techniques: “On-pump” or “Off-pump”.

Off-pump procedures, though more technically complex, are thought to be less invasive and only appropriate for a subgroup of CABG candidates.^{2,3} Due to advancement in surgical techniques it has resulted in older patients, and severe CAD patients with comorbid medical conditions being treated with CABG surgery. The cardiac surgery exposes brain to ischemic injury and following CABG, type II complications like deterioration in cognitive function, confusional state, memory deficit, or seizure without a stroke are more frequent than type I (death due to stroke or hypoxic encephalopathy, nonfatal stroke, transient ischemic attack, stupor or coma) and considerable variation in their rates is reported (3-79%).^{4,5} In recent years CABG surgery

* Corresponding author.

E-mail address: renu1674@gmail.com (R. Khamesra).

using off-pump technique has been shown to be a reliable and reproducible technique, and both short and medium term results have been favorable. Post-operative cognitive impairment and decline are associated with CABG.⁶ The researchers have also reported that the off-pump CABG might be causing fewer cognitive declines than conventional on-pump CABG.⁷ Whether a participant is classified as having decline or improvement in cognitive functions depends critically on the number of tests required to change from baseline, the amount each must change, and the total number of tests administered. As the number of tests decreases, the fraction that meets criteria for “change” increases dramatically in all of the study groups. There are continuing reasons to monitor the association of CABG with possible postoperative cognitive change as the technology associated with CABG is constantly changing, and the efficacy of these changes in terms of cognitive outcomes should be determined. The expression of both decline and improvement in cognition should be included, along with comparison with appropriate control groups. 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. Without these comparisons, estimates of cognitive decline are greatly overestimated, and virtually uninterpretable.⁸

There is substantial evidence that the use of OPCABG is associated with fewer emboli to the brain^{9,10} but the benefits in cognitive outcome are less obvious. In a large randomized study there was no difference in the incidence of decline between patients having CCPB versus OPCABG surgery at 3-12 months.¹¹ Previous studies have suggested that OPCABG surgery is associated with a lower risk of stroke.^{12,13} To date, there is no randomized trial evidence to suggest a lower incidence of stroke after OPCABG. Very few studies^{7,14} regarding neurocognitive assessment post CABG were found in literature search in India and could not find a single study which has compared cognitive assessment in two “off pump” and “on pump” technique of CABG. The present study, therefore, has been undertaken to compare neurocognitive assessment in patients undergoing “off pump” CABG and “on pump” CABG through neuropsychological tests.

2. Materials and Methods

The present prospective study was conducted in tertiary care teaching hospital, Bangalore only after taking approval from Institutional Review Board. This hospital is a tertiary level leading cardiac care centre in South India. Informed written consent was obtained from patients selected for participation in this study. In the cardiac groups, participants scheduled to undergo isolated on-pump or off-pump CABG based on standard clinical indications for CABG were screened during one year study period. All right-handedness

male patients between 30-65yrs old who can read and write, native speakers of English, Hindi or Kannada were included in study. The patients who were undergoing isolated, primary CABG procedure scheduled within one week were included. All patients who showed potential inability to successfully complete neurocognitive assessments in patients undergoing isolated, primary CABG procedure were excluded out. In control groups, controls having CAD and not undergoing CABG (non surgical cardiac controls-NSCC) and heart healthy controls (HHC-without specific evidence by history of cardiac, cerebrovascular or neurologic disease) were included from inpatient or outpatient of hospital.

Demographic data included age, income, education, and employment were noted. BMI (height, weight), smoking, alcohol, hypertension, diabetes mellitus, IHD, CHF, dyslipidemia, dysarrhythmias, valvular stenosis, left ventricular clot, medications (acetylsalicylic acid, beta blockers, calcium blockers), vascular disease, 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)¹⁵ for psychiatric morbidity and Edinburgh Handedness Inventory¹⁶ questionnaire for quantitative measure of handedness were used.

All consenting CABG patients 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. The following cognitive domains were assessed: fine motor dexterity (finger tapping - dominant and non-dominant hands); mental processing speed (digit symbol); sustained attention (digit vigilance); fluency or language (category and phonemic fluency); working memory (verbal); planning; set-shifting; response inhibition; and learning and memory (verbal and visual). Some of these are paper-pencil tests. The tests used for the present study have been standardized for use in the Indian population.¹⁷

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,

Table 1: Demographic characteristics of the OPCABG and CCPB patients and control groups

Parameters	OPCABG (N = 44)	CCPB (N = 22)	NSCC (N = 24)	HHC (N = 30)	p value
Age (yrs)	54.48 ± 7.13	54.73 ± 7.17	53.17 ± 8.35	52.40 ± 9.24	0.640
BMI(kg/m ²)	24.47 ± 2.03	25.83 ± 4.17	24.45 ± 2.79	26.25 ± 3.25	0.035 *
Duration of IHD less than 1 year (no. of patients)	28 (63.6%)	15(71.4%)	18(75.0%)	-	>0.05
Duration of surgery (min)	144.1 ± 31.45	124.6 ± 35.58	-	-	<0.01*
Time duration for presurgery cognitive assessment (days)	2.48 ± 1.81	2.41 ± 1.62	2.45 ± 1.73	-	0.40
Follow up assess (wk)	8.52 ± 2.62	8.34 ± 1.99	8.13 ± 2.28	7.37 ± 1.38	0.153

*p< 0.05 significant

complex figure test for assessing speed, attention, executive functions, auditory comprehension, learning, construction ability, memory were used.

CABG surgery with CPB (CCPB) and CABG surgery without CPB (OPCABG) 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, Ill) for Windows. Differences were considered to be statistically significant at p-value <0.05. The raw scores were compared with the NIMHANS normative data.¹⁷ Both continuous and categorical forms of the distribution variables were used in the analysis. Differences between continuous variables and categorical variables were assessed using the Student t-test and the chi-square test respectively. Univariate analysis techniques were used to find out the mean difference. 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. The procedure computes the differences between values of the two variables for each case and tests whether the average differs from 0.

3. Results

Forty four patients underwent off-pump (OPCABG) and twenty two patients underwent on-pump (CCPB) surgery. Age, body mass index (BMI) was comparable in OPCABG and CCPB but it was significantly high in HHC control group. The time duration of surgery was significantly more in OPCABG and CCPB groups. (p<0.01) Duration of presurgery cognitive assessment, pre post assessment (6-12

weeks) was comparable in all the groups. (Table 1)

41(93%) OPCABG patients, and 16(72%) CCPB patients were assessed pre and post cardiac surgery. Post surgery neuropsychological assessment in 3 OPCABG and 6 CCPB patients could not be carried out due to the following reasons: nonresponders (2 patients), death (1 patient), health problem (1 patient), lack of interest (3 patients), and lack of transportation (2 patients).

On all the neuropsychological tests in pre operative assessment both the groups were comparable except OPCABG group had significantly improved visuoconstruction ability over CCPB group (p=0.035). There was no significant difference in mean postoperative scores for the two groups in any of the neuropsychological tests. (p>0.05)

In present study, OPCABG patients had significantly improved from baseline for motor speed, mental speed, sustained attention, verbal fluency, set shifting, verbal learning, verbal memory, visual memory tests. (p< 0.05) In CCPB group, patients improved from baseline in few tests like set shifting, response inhibition, verbal learning, visual memory (p< 0.05) and did not show difference in rest of the tests. In NSCC group significant change found in comprehension and visual memory only and HHC group it was significant in set shifting, sustained attention and visual memory. (Tables 2 and 3)

Mild cognitive decline (one or two tests) was observed in 31(75.6%) of 41 OPCABG and 13(81.3%) of 16 CCPB group. A moderate or severe degree of neuropsychological dysfunction (≥3 tests) was seen in 7(17%) of 41 OPCABG, 3(18.7%) of 16 CCPB group. (Table 4)

4. Discussion

Cognitive dysfunction after CABG is characterized by impairment of attention, concentration, and memory with possible long-term implications.¹⁸ In present study fourteen tests assessed the six important domains of cognitive function. Number of tests used was much higher than other comparable studies where usually only 4-5 domains of cognitive function were studied using 6 to 10 tests.^{19,20} We also attempted to measure motor function (finger tapping test) as suggested by 1995 Consensus on assessment

Table 2: Pre and post operative neuropsychological test score in OPCABG, CCPB group and control groups

Domain	Test		OPCABG	CCPB	P value	NSCC	HHC
Motor Speed	Finger Tapping Right	pre	52.9±6.4	51.53±7.44	0.490	52.13±5.8	54.53±6.17
		post	55.63±6.79	52.83±8.34	0.194	53.34±5.26	56.37±5.15
	Finger Tapping Left	pre	47.72±5.6	47.09±5.25	0.698	47.96±6.23	49.7±6.09
		post	49.48±6.25	48.94±5.8	0.766	47.43±5.87	51.56±5.56
Mental Speed	Digit Symbol Substitution	pre	302±93.13	364.56±147.34	0.060	340.74±135.8	232.27±80.64
		post	268±80.75	315.5±128.78	0.100	296.78±108.2	237.87±77.54
	Digit Vigilance Time	pre	590.12±175.38	602.06±183.76	0.821	657.83±219.02	482±104.46
		post	516.02±120.64	577.13±163.67	0.127	570.48±201.06	477.77±101.46
Sustained Attention	Digit Vigilance Error	pre	8.02±9.51	14.88±18.89	0.074	9.91±7.13	10.1±9.18
		post	6.0±5.36	9.5±11.93	0.130	6.78±6.49	5.37±5.9
	Controlled Oral Word Association	pre	8.95±3.36	8.25±3.27	0.478	8.96±3.75	12.6±3.19
		post	9.92±3.43	8.87±3.22	0.297	10.46±3.72	13.03±3.78
Category Fluency	Animal Names	pre	12.32±3.42	11.69±2.82	0.516	12.09±3.64	13.43±3.07
		post	13.27±2.82	12.31±3.05	0.266	13.3±2.9	14.47±3.21
	Verbal N-Back 1-Back Hits	pre	8.76 ± 0.54	8.44 ± 1.09	0.146	8.78±0.67	9.00
		post	8.83 ± 0.44	8.75 ± 0.77	0.629	8.91±0.29	9.00
Working Memory	Verbal N-Back 2-Back Hits	pre	7.1±1.22	6.38 ±2	0.102	6.13±1.94	7.17±1.09
		post	6.8±1.57	6.81±1.64	0.987	6.91±1.31	7.47±0.82
	Tower of London	pre	8.83±2.39	8.75±1.65	0.904	8±1.57	8.73±1.72
		post	9.34±1.93	9.25±1.34	0.863	9±1.41	8.57±1.81
Planning	Total no. of problems solved with minimum moves	pre	96.56±19.44	101.5±19.93	0.396	94.7±20.29	89.9±15.35
		post	89.68±20.65	94.25±22.01	0.464	87.96±18.8	83.77±8.89
	Wisconsin Card Sorting Test Total trials	pre	24.78±9.57	26.1±9.06	0.636	24.75±13.29	25.02±13.79
		post	20.19±10.8	20.46±7.23	0.928	19.37±8.17	18.73±4.33
Set Shifting	% of errors	pre	15.72±7.39	17.81±9.57	0.382	16.48±8.63	14.56±5.88
		post	13.11±8.04	12.11±5.71	0.652	13.24±5.49	13.33±5.77
	% Perseverative responses	pre	14.25±6.2	15.2±6.71	0.614	14.55±7.17	12.93±4.57
		post	11.72±6.25	11.14±4.69	0.735	11.92±4.62	11.52±3.87
	% Non-Perseverative error	pre	10.52±5.43	10.79±4.99	0.866	10.19±7.85	8.42±4.84
		post	8.9±5.89	9.48±4.71	0.728	7.36±4.87	7.15±2.44
	% Conceptual responses	pre	66.33±12.92	64.55±12.5	0.640	66.32±16.62	70.39±9.35
		post	71.58±14.39	70.5±10.91	0.787	72.91±11	74.8±5.76

Table 3: Continue (Table 2)

Response Inhibition	Stroop effect	pre	177.98±74.94	194±72.82	0.468	171.96±59.11	165.77±60.16
		post	154.95±73.56	148.25±59.25	0.746	169.26±48.76	149.83±55.92
			0.052	0.028*		0.853	0.112
Comprehension	Token	pre	32.61±2.37	33.44±2	0.222	32±2.28	33.57±2.19
		post	33.41±2.63	34.06±2.17	0.385	33.52±2.09	34.07±1.76
			0.081	0.343		0.022*	0.113
Verbal Learning	Auditory Verbal Learning	pre	49.73±7.84	47.06±11.89	0.325	50.39±13.76	55.47±7.3
		post	56.83±8.03	53.13±11.82	0.178	51.91±8.54	56.2±8.13
	Total		<0.0001*	0.012*		0.682	0.562
	Immediate recall	pre	10.29±2.75	9.06±3.75	0.178	10.57±3.12	12.47±2.01
		post	12.12±2.56	10.63±2.87	0.060	10.22±2.76	12.47±2.13
			<0.0001*	0.08		0.663	1
Verbal Memory	Delayed recall	pre	10.32±2.72	9.69±3.44	0.470	10.09±3.32	12.2±1.99
		post	12.34±2.1	11.25 ± 2.91	0.121	10.74±2.78	12.43±2.22
			<0.0001*	0.073		0.491	0.527
	Long term percent retention	pre	85.28±18.72	84.4±19.59	0.876	83.61±19.77	88.97±10.34
		post	94.85±10.11	91.65±16.58	0.379	86.26±19.01	90.52±11.24
			0.003*	0.207		0.677	0.404
	Recognition hits	pre	14.12±1.36	13.19±2.9	0.103	14.09±1.47	14.67±0.99
		post	14.54±1.0	14.19±1.56	0.320	14.26±1.39	14.73±0.94
			0.033*	0.052		0.707	0.536
Visuocon Struction Ability	Complex Figure Test – Copy	pre	34.88±1.6	33.13±4.57	0.035*	33.87±4.56	35.8±0.81
		post	34.83±2.13	33±6.77	0.120	35±2.97	36±0
			0.865	0.92		0.168	0.184
	Immediate recall	pre	20.29±7.55	16.31±8.05	0.085	18.48±7.79	21.4±5.01
		post	24.39±7.14	20.44±7.58	0.070	21.74±7.10	24.63±6.01
			<0.0001*	0.012*		0.082	0.001*
Visual Memory	Delayed recall	pre	19.93±7.08	16.38±7.69	0.102	17.83±7.66	21.27±5.19
		post	23.83±7.79	21.06±8.57	0.246	21.04±7.37	24.67±6.38
			<0.0001*	0.006*		0.08	0.001*

*p< 0.05significant

Table 4: Postoperative neuropsychological deficits in OPCABG and CCPB

≥ 20% decline	No. of domain	OPCABG (N = 41)	CCPB (N = 16)
None	0	3 (7.3%)	0 (0)
Mild	1 - 2	31 (75.6%)	13 (81.3%)
Moderate	3 - 4	6 (14.6%)	2 (12.5%)
Severe	≥ 5	1 (2.44%)	1 (6.25%)
Total	≥ 3	7 (17.0%)	3 (18.7%)

of neurobehavioral outcomes²¹ and visual memory functioning - reproduction of drawing, an important area of cognitive function, often not evaluated in other comparable studies.

In present study OPCABG patients' cognitive performance before surgery was largely within the normal range when compared to normative data¹⁷ for age, gender and education. Patients who underwent CCPB had reduced scores in most of the domains compared with normative data.¹⁷ Similar findings were found by Ernest et al.²² This shows the importance of control for medical and demographic factors because even after excluding patients at high risk for brain dysfunction, cognitive impairment is found in patients with CAD before surgery.

There were no significant differences between OPCABG and CCPB groups in cognitive performance at baseline except OPCABG group which had significantly improved visuoconstruction ability over CCPB group (p=0.035). Postoperatively neuropsychological assessment showed no significant decrease in mean scores after OPCABG or CCPB surgery.

In the present study, clear improvement / advantage was observed for the short-term effect of the off-pump procedure. OPCABG patients showed significant improvement in 8 tests. The CCPB showed significant improvement in 4 tests, mean score improvement in 3 and remained stable in rest 7 tests. Studies reveal similar changes of either OPCABG showing better performance²³

or no change with CCPB^{11,24} on 6–12 weeks follow-up assessment. Zamvar et al²³ found that patients undergoing OPCABG had less neurocognitive impairment at 1 and 10 weeks than did patients in the CCPB group. van Dijk et al¹¹ also found no differences between the two procedures in terms of cognitive decline in 3-month and 12-month follow-ups. The findings of improvement in cognition after CABG in the present study are consistent with several recent studies.^{25–27}

The present study results showed improvement in response inhibition (Stroop test) as well as in motor and mental speed, attention / concentration, verbal fluency, executive functions and learning and memory both verbal and visual in both the group of the CABG patients at 6–12 weeks follow-up. The mean change in Stroop effect score of 23 in OPCABG, 46 in CCPB corresponds improvement from their baseline ($p=0.052$, $p=0.028$).

More specifically, longitudinal models in the present study showed that the digit symbol (processing speed), digit vigilance, verbal fluency, verbal learning and memory and visuoconstruction ability and visual memory recall being significantly different in both the groups at 6–12 weeks follow-up.

Intra-individual variations were analyzed in all subjects in all tests comparing baseline to follow-up scores. Our results of more than 20% decline on 3 or more tests at 6–12 weeks were seen in 17% OPCABG and 18.7% CCPB patients. The cognitive decline in present study at 6–12 weeks in OPCABG was comparable to results of meta-analysis of nine trials.²⁸ However, in our study cognitive decline in the CCPB group was significantly less than other RCT.

Researchers have reported early transient and reversible cognitive decline after CABG, mild but non-significant trend toward late postoperative decline for all study groups with CAD but no significant differences of late postoperative cognitive decline after CCPB or OPCABG. This suggests, as also reported earlier that CAD and the presumed coexisting cerebrovascular disease may be associated with mild decline in performance for some cognitive domains even in the absence of surgery.^{29,30} Sweet and colleagues³¹ also concluded no clear pattern of group differences or change in neuropsychological outcomes at follow-ups and that CABG surgery does not create cognitive decline.

From a neurological standpoint, CABG as currently practiced is a safe and effective procedure for the great majority of patients. Nonetheless, a subset of patients with pre-existing risk factors for cerebrovascular disease is at high risk for stroke or encephalopathy. In addition, before surgery, very little is known about the status of not only the vasculature of the brain but also the existence of previous underlying cerebrovascular disease. We suggest that neurologists have a role in assisting their colleagues in cardiology and cardiac surgery to identify

those at risk for adverse neurological outcomes. In addition, they need to be involved in evaluating patients after surgery for change in neurological condition, both by examination and interpretation of imaging studies. Most important, neurologists should be involved in the design and interpretation of studies comparing different intervention techniques, modification of existing procedures, and trials of neuroprotective agents.

Limitations: Studies with large sample size of both OPCABG and CCPB and long term follow up with neurocognitive assessment should be conducted in future.

5. Conclusions

The lack of significant differences in the longitudinal test performance postoperatively between the CCPB and OPCABG group in present study suggests that the use of cardiopulmonary bypass is not the sole source of cognitive change after surgery.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Author biography

Renu Khamesra Assistant Professor

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