JAMDA 16 (2015) 263.e9–263.e11

JAMDA

journal homepage: www.jamda.com

Brief Report

Assessment of Long-Term Cognitive Impairment After Off-Pump Coronary-Artery Bypass Grafting and Related Risk Factors

Luis M. Pérez-Belmonte MD, PhD [a,b,*], Carlos M. San Román-Terán MD, PhD [c], Manuel Jiménez-Navarro MD, PhD [a], Miguel A. Barbancho MD, PhD [b], José M. García-Alberca MD, PhD [d], José P. Lara MD, PhD [b]

[a] CMU (Clinical Management Unit) of Heart Department, Virgen de la Victoria University Hospital, Málaga, Spain
[b] Unit of Cognitive Neurophysiology, Research Medical Center of Málaga University, ICE (International Campus of Excellence) Andalucía Tech, BRIM (Biomedical Research Institute of Málaga), Málaga, Spain
[c] Department of Internal Medicine, Axarquía County Hospital, Vélez-Málaga, Málaga, Spain
[d] Department of Psychiatry, Unit of Dementia, Andalusia Institute of Neuroscience and Conduct, Málaga, Spain

Keywords:
Postoperative cognitive impairment
cognitive domain
risk factors
predictors of cognitive impairment
off-pump
coronary-artery bypass grafting

A B S T R A C T

Objectives: To assess cognitive impairment after off-pump coronary-artery bypass grafting, with a particular emphasis on long-term follow-up and related risk factors.
Design: Prospective study.
Setting: Virgen de la Victoria University Hospital, Málaga, Spain.
Participants: Participants were 36 patients undergoing off-pump coronary-artery bypass grafting.
Measurements: Changes in the neuropsychological test battery administered from before to after surgery (1, 6, and 12 months). Postoperative cognitive impairment was defined by a significant decrease.
Results: A significantly multidomain (attention-executive functions, $P < .01$; immediate and delayed memory, $P < .001$; and verbal fluency, $P < .05$) postoperative cognitive impairment was shown, being maximum at 6 months (more than 50% of patients) and still presented at 12 months (more than 30% of patients), but partially recovered. Related risk factors as smoking ($P < .01$), diabetes mellitus ($P < .01$), peripheral arteriopathy ($P < .01$), obesity ($P < .05$), lower hematocrit ($P < .01$), and hemoglobin ($P < .05$) levels and diastolic blood pressure ($P < .05$) were identified as predictors of cognitive impairment. Better New York Heart Association class ($P < .01$) and less severity of angina ($P < .01$) were associated with partial postoperative recovering.
Conclusion: A multidomain long-term postoperative cognitive impairment and a partial neurocognitive recovering were detected after off-pump coronary-artery bypass grafting and were associated with several nonspecific surgery factors. These findings may be useful when counseling patients before surgery and suggest the importance of long-term neurocognitive evaluation.

Coronary-artery bypass grafting (CABG) is one of the most commonly performed procedures in patients with extensive coronary-artery disease.[1] Postoperative cognitive impairment (PCI) may be an important complication after this surgery. It is defined as a decline in performance on neuropsychological tests relative to preoperative levels and important cognitive domains (execute functions, attention, memory, and visuospatial perception) could be affected.[2,3] The incidence ranges of PCI varies from 20% to 80%,[3,4] and these defects are not always transient but may remain months or years after surgery.[2,4]

Specific factors of cardiac surgery and anesthesia have been shown to be associated with PCI,[2,4,5] but much is still unknown with respect to other potential risk factors and mechanisms of cognitive dysfunction after cardiac surgery.[5,6] The purposes of this study were to determine the presence of PCI after off-pump CABG, with a particular emphasis on long-term follow-up and involved risk factors.

Materials and Methods

Thirty-six patients scheduled for elective off-pump CABG at Virgen de la Victoria University Hospital were prospectively enrolled between May 2012 and October 2013. The study was approved by the institutional research ethics committee and all patients gave written informed consent. A wide range of sociodemographic, clinical, and

The authors declare no conflicts of interest.

* Address correspondence to Luis M. Pérez-Belmonte, MD, PhD, Centro de Investigaciones Médico-Sanitarias (CIMES), Calle Marqués de Beccaria, número 3, Código postal: 29010, Málaga, Spain.
E-mail address: luismiguelpb@hotmail.com (L.M. Pérez-Belmonte).

http://dx.doi.org/10.1016/j.jamda.2014.12.001
1525-8610/

Table 1
Sociodemographic, Clinical, and Surgical Data

Age	65.9 (1.4)	Male	69.4%	Smoking	27 (75%)
Hypertension	26 (72.2%)	Dyslipidemia	24 (66.7%)	DM	19 (52.8%)
Obesity	14 (38.9%)	HF	8 (22.2%)	NYHA ≥3	9 (25%)
PA	5 (13.9%)	CKD	6 (16.7%)	Stroke	3 (8.3%)
AF	2 (5.6%)	Years of CAD	4.6 (1.4)	3-vessels CAD	26 (72.2%)
LVEF	57 (5%)	EuroSCORE	3.8 (1)	Operation time	235 (21)
Intubation time	537 (55)	Graft/Patient	2.5 (0.4)	IOS	97 (3)

AF, atrial fibrillation; CAD, coronary-artery disease; CKD, chronic kidney disease; DM, diabetes mellitus; EuroSCORE, European System for Cardiac Operative Risk Evaluation; HF, heart failure; IOS, intraoperative oxygen saturation; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PA, peripheral arteriopathy.
Continuous data are shown as means (SDs) and qualitative data as absolute value and percentage.

operative-anesthetic variables was collected and all patients had a neuropsychological examination with a battery of 6 standardized neuropsychological tests preoperatively (6 [SD 1] days) and at 1, 6, and 12 months after CABG. The neuropsychological evaluation included measures of attention-executive functions (Trail Making Test [TMT] and Stroop Color-Word Interference Test [SCWIT]), memory (Free and Cued Selective Reminding Test [FCSRT]), verbal fluency (Semantic and Phonological Tests [SVFT and PVFT]) and visuospatial perception (Judgment of Line Orientation Test [JLOT]). Patients' raw cognitive scores were converted to age and education-adjusted co-normative reference values according to The NEURONORMA project.[7] The presence of PCI was determined by a significant worsening in the performance of any test related to the preoperative value. Percentile ranks of test performance were obtained defining the presence of mild cognitive impairment (MCI) (percentile rank equal or less than 10%), inferior normal (percentile rank 11%–18%), normal (percentile rank 19%–81%), or superior (percentile rank >82%).[7,8]

Continuous data were shown as means (SDs) and qualitative data as absolute value and percentage. The postoperative performance with respect to the preoperative levels was assessed by repeated measures analysis of variance. Multiple linear regression models were used to identify independent predictors of PCI and cognitive recovering (CR). Statistical analysis was performed with SPSS for Windows statistical software package version 15.0 (IBM SPSS Statistics, IBM Corporation, Chicago, IL).

Results

Sociodemographic, clinical, and surgical data are listed in Table 1. Preoperative and postoperative test scores (raw data and percentile ranks), including statistical comparisons, and the percentage of patients who presented MCI, inferior normal performance, and its sum (percentile rank ≤18%) are presented in Table 2. The postoperative evaluations showed a significant worsening in the performance of the TMT, SCWIT, FCSRT, SVFT, and PVFT, being maximum at 6 months but partially recovered at 12 months. JLOT remained unchanged. MCI percentage had a significant increase in the TMT Part A, Stroop Part A and Part C, and FCSRT Delayed Free Recall and Total Delayed Recall, also maximum at 6 months. At 12 months, only the FCSRT Delayed Free Recall and Stroop Part C were significant. In addition, the inferior normal performance increased postoperatively in TMT Part B and Stroop Part B. SVFT, PVFT, and JLOT had a percentile rank greater than 18%.

Cardiovascular risk factors, such as the history of smoking, the presence of diabetes mellitus, peripheral arteriopathy, and obesity, and noncardiovascular risk factors, such as anemia (lower hematocrit and hemoglobin) and lower diastolic blood pressure, were identified as independent cardiovascular predictors of PCI. At 12 months, a partial CR was observed and was associated with better NYHA class and lower presence, number, and severity of angina. These results are presented in Table 3. Other clinical and operative/anesthetic variables were not significant.

Table 2
Test Scores (Raw Data and Mean Percentile Ranks)

Test	Preoperative	1-Month Follow-Up	6-Month Follow-Up	12-Month Follow-Up
TMT Part A	71 (4.5)/19–28	78 (5)*/11–18	85 (5)‡/11–18	76 (5)*/11–18
TMT Part B	156 (11)/19–28	159 (11)/19–28	174 (11)‡/19–28	163 (11)/19–28
Stroop Part A	76 (3.8)/19–28	70 (3.2)*/11–18	68 (3)‡/11–18	72 (3.4)†/19–28
Stroop Part B	51 (2.5)/29–40	48 (2.4)*/19–28	47 (2.2)†/11–18	49 (2.4)†/19–28
Stroop Part C	26 (1.1)/29–40	23 (1.1)†/19–28	20 (0.9)‡/11–18	23 (1)†/19–28
FCSRT DFR	7 (0.2)/19–28	6.2 (0.2)†/11–18	5.6 (0.2)‡/6–10	5.9 (0.2)‡/11–18
FCSRT TDR	12.5 (0.3)/19–28	11.6 (0.29)*/11–18	10.6 (0.3)‡/6–10	11.4 (0.2)‡/11–18
SVFT	21.4 (0.9)/60–71	19.3 (0.8)/41–59	18.5 (0.7)†/41–59	18.9 (0.7)†/41–59
PVFT	13.8 (0.6)/41–59	13 (0.7)/41–59	12.7 (0.6)*/41–59	13.1 (0.5)/41–59
Percentage of patients with MCI, inferior normal performance, and its sum				
TMT Part A	20/3.9/23.9	29.4*/8.8*/38.2*	42.2‡/12.2†/54.4*	21.2/8.2*/29.4*
TMT Part B	16.7/5.6/22.3	11.8/24.7‡/36.5†	18.2/35.2‡/53.4‡	9.1/18.2‡/27.3*
Stroop Part A	11.1/16.7/27.8	17.6*/17.7/35.3*	15.2*/25.2*/40.4*	12.1/18.2/30.3
Stroop Part B	19.4/8.3/27.7	17.6/17.8†/35.4*	18.2/22.1‡/40.3†	21.1/9.1/30.2
Stroop Part C	0/23.9/23.9	5.9*/25.5/31.4*	18.2‡/27.3/45.5†	9.1†/21.2/30.3*
FCSRT DFR	8.3/11.1/19.4	11.8/23.5†/35.3†	33.3‡/21.2†/54.5‡	21.2‡/17.3*/38.5†
FCSRT TDR	5.6/14.3/19.9	14.7†/18.8/33.5†	27.3‡/26.1†/53.4‡	6.1/22.2†/28.3*

DFR, delayed free recall; FCSRT, Free and Cued Selective Reminding Test; MCI, mild cognitive impairment; TDR, total delayed recall; TFR, total free recall; TMT, Trail Making Test; VFT, Verbal Fluency Test; SCWIT, Stroop Color-Word Interference Test; SVFT, Semantic Verbal Fluency Test; PVFT, Phonologic Verbal Fluency Test.
Continuous data are shown as means (SDs) and qualitative data as absolute value and percentage. Statistical significance was established comparing preoperative and postoperative scores. Only statistically significant data are shown. TMT score derived for each trail is the number of seconds required to complete the task. SCWIT, FCSRT, SVFT, and PVFT are based on the number of successes.

*$P < .05$.

†$P < .01$.

‡$P < .001$.

Table 3
Predictors of Postoperative Cognitive Impairment and Recovering

	Cognitive Impairment $R^2 = 0.6$ B coefficient	
History of smoking	12 (2.9–54)†	0.667
Diabetes mellitus	1.7 (1.1–2.5)†	0.466
Peripheral arteriopathy	1.7 (1.1–2.1)†	0.718
Obesity	1.6 (1.2–3.8)*	0.562
Hematocrit $\leq$ 30%	2.9 (1.6–4.3)†	−0.533
Hemoglobin $\leq$10 g/dL	2.3 (1.3–4.5)*	−0.401
Diastolic blood pressure $\leq$ 50 mm Hg	1.6 (1.3–3.1)*	−0.455
	Cognitive Recovering $R^2 = 0.57$ B coefficient	
NYHA degree $\leq$ 2	2.5 (1.6–4.5)†	−0.567
Presence of angina†	2.8 (1.6–4.0)	−0.522
Angina/year† $\leq$ 5	2 (1.3–3.8)	−0.433
CCS degree† $\leq$ 2	3.8 (1.8–5.8)	−0.648

CCS, Canadian Cardiovascular Society; NYHA, New York Heart Association; OR, odds ratio; R^2, coefficient of determination; 95% CI, 95% confidence interval.
Multiple linear regression analyses for postoperative cognitive performance and partial CR. OR (95% CI) and B coefficient are shown.
*$P < .05$.
†$P < .01$.

Discussion

The present study found a multidomain long-term PCI after off-pump CABG, with a significant deterioration in attention-executive functions, immediate and delayed memory, and verbal fluency, and even reaching levels of MCI (executive functions and memory), maximum at 6-month follow-up (more than 50% of patients) and still presented at 12 months (more than 30% of patients) but with a partial CR. Cardiovascular and noncardiovascular risk factors were associated with PCI and CR and not with specific procedural effects.

In previous reports, the incidence of long-term neuropsychological sequelae (at least 3 months after surgery[6,9]) ranged from 6% to 30%,[6,10,11] lower than our results at 6 months but similar at 12 months. This variation may be because of an inadequate evaluation of the effect of surgery on global cognitive performance, and as a possible cause of the unstable and usually underestimated values of the incidence of cognitive deficits in cardiac patients.[2,4,10]

The mechanisms leading to PCI are increasingly debated. Specific effects of cardiac surgery (microembolic cerebral injury) or anesthesia have been classically associated with cognitive impairment after surgery.[4,5] Little is known about patient-related risk factors or predictors of PCI. Data from Ho et al[6] and the review by Rundshagen[12] found association between long-term PCI and cardiovascular factors, such as older age, diabetes mellitus, cerebrovascular disease, and peripheral arteriopathy. In addition, the degree of atherosclerosis of ascending aorta was associated with neurobehavioral changes after CABG by Hammon et al.[13] Nevertheless, history of smoking and obesity have not been previously described as risk factors, although both have been associated with vascular cognitive impairment.[14,15] Noncardiovascular risk factors, such as anemia and lower diastolic blood pressure, have contributed significantly to PCI. All these factors, cardiovascular and noncardiovascular, are probably related to the health of the brain vessels and central nervous system hypoperfusion, which would alter the cerebral hemodynamic.[16,17] These mechanisms behind PCI may explain the impairments in several cognitive domains, including attention and executive functions (domain classically affected in vascular cognitive impairment), memory, verbal fluency, and visuospatial processing.[14]

On the other hand, data from our cohort provided evidence for a benefit of improving NYHA class and angina, producing a partial CR. Eggermont et al[18] reported in a systematic review the importance of an integrated treatment to improve cognitive function in cardiac patients.

No measures of cognitive performance have yet become established as part of routine clinical practice, because the appropriate instruments are time- and labor-intensive.[6] However, some manageable neuropsychological evaluation of attention-executive functions and/or memory could be implemented, particularly in high-risk cardiovascular patients.

This study is limited by several factors, including the small number of recruited patients and the lack of neuroimaging correlation. However, it also has strengths, such as the prospective design, the robustness of the multiple linear regression results, and the uniformity of both surgical technique and neurocognitive evaluation. Further research could be helpful to confirm these results and to provide other risk factors.

Conclusions

A multidomain long-term PCI and a partial CR were identified after off-pump CABG and were associated with several nonspecific surgery factors. These findings suggest the importance of long-term neurocognitive evaluation to adopt preoperative preventive measures, trying to improve the preoperative medical situation or to adopt other therapeutic options as far as possible, and counseling patients about risks.

References

1. Lamy A, Devereaux PJ, Prabhakaran D, et al. Effects of off-pump and on-pump coronary-artery bypass grafting at 1 year. N Engl J Med 2013;368:1179–1188.
2. Rudolph JL, Schreiber KA, Culley DJ, et al. Measurement of post-operative cognitive dysfunction after cardiac surgery: A systematic review. Acta Anaesthesiol Scand 2010;54:663–677.
3. Zamvar V, Williams D, Hall J, et al. Assessment of neurocognitive impairment after off-pump and on-pump techniques for coronary artery bypass graft surgery: Prospective randomized controlled trial. BMJ 2002;325:1268–1272.
4. McDonagh DL, Berger M, Mathew JP, et al. Neurological complications of cardiac surgery. Lancet Neurol 2014;13:490–502.
5. Kneebone AC, Luszcz MA, Baker RA, et al. A syndromal analysis of neuropsychological outcome following coronary artery bypass graft surgery. J Neurol Neurosurg Psychiatry 2005;76:1121–1127.
6. Ho PM, Arcienagas DB, Grigsby J, et al. Predictors of cognitive decline following coronary artery bypass graft surgery. Ann Thorac Surg 2004;77:597–603.
7. Peña-Casanova J, Quiñones-Úbeda S, Quintana-Aparicio M, et al. Spanish Multicenter Normative Studies (NEURONORMA Project): Norms for verbal span, visuospatial span, letter and number sequencing, trail making test, and symbol digit modalities test. Arch Clin Neuropsychol 2009;24:321–341.
8. Sánchez-Benavides G, Peña-Casanova J, Casals-Coll M, et al. Cognitive and neuroimaging profiles in mild cognitive impairment and Alzheimer's disease: Data from the Spanish Multicenter Normative Studies (NEURONORMA Project). J Alzheimers Dis 2014;41:887–901.
9. Baumgartner WA. Neurocognitive changes after coronary bypass surgery. Circulation 2007;116:1879–1881.
10. Di Carlo A, Perna AM, Pantoni L, et al. Clinically relevant cognitive impairment after cardiac surgery: A 6-month follow-up study. J Neurol Sci 2001;188:85–93.
11. Kozora E, Kongs S, Collins JF, et al. Cognitive outcomes after on- versus off-pump coronary artery bypass surgery. Ann Thorac Surg 2010;90:1134–1141.
12. Rundshagen I. Postoperative cognitive dysfunction. Dtsch Arztebl Int 2014;111:119–125.
13. Hammon JW Jr, Stump DA, Kon ND, et al. Risk factors and solutions for the development or neurobehavioral changes after coronary artery bypass grafting. Ann Thorac Surg 1997;63:1613–1618.
14. Rincon F, Wright CB. Vascular cognitive impairment. Curr Opin Neurol 2013;26:29–36.
15. Willeumier K, Taylor D, Amen D. Elevated BMI is associated with decreased blood flow in the prefrontal cortex using SPECT imaging in healthy adults. Obesity 2011;19:1095–1097.
16. Selnes OA, Gottesman RF, Grega MA, et al. Cognitive and neurologic outcomes after coronary-artery bypass surgery. N Engl J Med 2012;366:250–257.
17. Marshall RS. Effects of altered cerebral hemodynamics on cognitive function. J Alzheimers Dis 2012;32:633–642.
18. Eggermont LH, de Boer K, Muller M, et al. Cardiac disease and cognitive impairment: A systematic review. Heart 2012;98:1334–1340.