ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH



# CORRELATION OF BRAIN MAGNETIC RESONANCE IMAGING INCLUDING DIFFUSION-WEIGHTED IMAGING WITH NEUROCOGNITIVE OUTCOME IN CORONARY ARTERY BYPASS GRAFTING (CABG) PATIENTS

## **RENU KHAMESRA\***

Department of Neurology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India. \*Corresponding author: Renu Khamesra; Email: renu1674@gmail.com

#### Received: 18 April 2023, Revised and Accepted: 02 June 2023

#### ABSTRACT

**Objectives:** This study aims to evaluate the new lesions on magnetic resonance imaging including diffusion-weighted imaging (MRI-DWI) in patients undergoing coronary artery bypass grafting (CABG) and its relationship with neurocognitive outcome.

**Methods:** In this prospective study, bilateral carotid and vertebral Doppler study was done before CABG surgery and the brain MRI protocol including fluid attenuation inversion recovery and DWI was applied 1–4 days before surgery and 6–12 weeks after surgery. Neuropsychological examinations were administered to both groups before and 6–12 weeks after surgery.

**Results:** A total of 66 patients were included in the study. On pre-operative angiogram, CABG had less double-vessel (31.8%) and more triple-vessel disease (65.15%). MRI brain with DWI was performed preoperatively in 50 (75.75%) of 66 CABG patients. Before surgery, no diffusion abnormalities were found on DW images. In those who underwent MRI, no lesions were found in 21 (31.82%) CABG patients. Bilateral small vessel ischemic disease (SVID) or periventricular lucencies was seen in 23 (34.85%) CABG patients. Bilateral SVID with lacunar infarct was seen in 4 (6.06%) CABG patients. Lacunar infarct and wedge infarct were seen in 1 (1.52%) patient each. At follow-up, MRI brain with DWI was performed only in 54 (81.82%) CABG patients. There was no significant change found postoperatively on brain MRI imaging. There was also no significant difference before and after CABG patients in cognitive function.

Conclusion: This study concluded that CABG has no relation in the form of brain MRI changes with the cognition function of the patients.

Keywords: Magnetic resonance imaging, Diffusion-weighted imaging, Coronary artery bypass grafting, Cognition.

© 2023 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (http://creativecommons.org/ licenses/by/4.0/) DOI: http://dx.doi.org/10.22159/ajpcr.2023v16i10.48118. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

#### INTRODUCTION

The etiology of cognitive deficits after coronary artery bypass grafting (CABG) surgery has multifactorial etiology including pre-existing risk factors such as old age, cerebral, cardiac and vascular diseases, alcohol abuse, and low educational level but the most likely etiology involves cerebral microcirculation and macrocirculation [1,2]. Three major mechanisms are thought to contribute to cerebral injury: Macroembolization of air, particulate material derived from aortic atheroma, valve debris, or the left ventricular thrombus; microembolization of gas, fat aggregates of blood cells, platelets, and fibrin, or particles of silicone or polyvinylchloride tubing; and reduction of cerebral perfusion, which may result from reduced flow, low arterial pressure, loss of the pulsatile component of flow, or incorrect placement of the aortic cannula [3-6].

There is general agreement that the incidence of post-operative cognitive dementia (POCD) early after cardiac surgery is high [7], but that cognitive performance returns nearly to baseline in 6–12 weeks for most patients [8]. Newman *et al.*, suggest that early POCD may herald further long-term cognitive decline [8]. The association of long-term POCD with cardiopulmonary bypass has recently been disputed [9]. There may nonetheless be a subpopulation in which long-term cognitive deterioration, and even dementia [10], may be accelerated, such as in those suffering from perioperative stroke or silent ischemic events. In the non-surgical arena, frank clinical stroke syndromes are accompanied by dementia in up to 25–30% of individuals [11].

Some studies [12,13] have revealed a weak association between emboli and short-term cognitive outcomes but not in others [14,15]. One study using diffusion-weighted imaging (DWI) on brain magnetic resonance imaging (MRI) with DWI has reported clinically undetected new ischemic brain lesions in 45% of patients after cardiac surgery [4]. Studies using DW-MRI have shown new ischemic lesions on post-operative MRI which are consistent with showers of emboli but their relation to neuropsychological function remains unclear [16-18].

Silent brain infarctions are commonly seen in MRI of neurologically asymptomatic elderly people, which may be associated with cognitive decline or dementia [19]. Although the particular neuropsychological effects of such lesions vary, they often result in a slowing of both psychomotor and motor speed. Patients with single or multiple infarctions had lower pre-operative cognitive performance and were more likely to have post-operative decline than the patients without infarctions [20]. Thus, silent ischemic cerebral disease is common in candidates for CABG and is associated with an increased risk for cognitive decline.

This study was planned to evaluate the new lesions on MRI-DWI in patients undergoing CABG and its relationship with neurocognitive outcomes.

#### METHODS

This prospective study was conducted in patients undergoing CABG based on standard clinical indications for CABG at a tertiary care teaching hospital in Bengaluru. Institutional review board approval was obtained and informed written consent was obtained from patients selected for participation in this study. Patients' age between 30 and 65 years, scheduled for primary CABG within 1 week were included in this study. Patients with a history of stroke with or without

residual neuropsychological deficit or symptomatic carotid artery disease, dementia, mental retardation or other psychotic disorder, substance abuse, and any current MRI contraindication (cardiac pacemaker or defibrillator, insulin pump, aneurysmal clip, implanted neural stimulator, cochlear implant, metal shrapnel or bullet, etc) were excluded from the study. All patients underwent bilateral carotid Doppler study.

#### Procedure

Bilateral carotid and vertebral Doppler study was done before surgery and brain MRI protocol including fluid attenuation inversion recovery (FLAIR) and DWI was applied 1-4 days (median 2 days) before surgery and 6-12 weeks after surgery (median 10.3 weeks); symptomatic patients (two) underwent MRI during the hospital stay. All measurements were performed on a 1.5-T device (Achieva; Philips, Best, the Netherlands). The MRI scan included an axial T2-weighted double-echo spin-echo sequence and FLAIR axial (repetition time, 4449 ms; echo time, 100 ms; and slice thickness, 5 mm, gap 1 mm, ACQ matrix 372×240) and an axial DW sequence (using echoplanar imaging) (orthogonal axis DW images: repetition time, 3182 ms; echo time, 88 ms; and slice thickness, 5 mm, gap 1 mm, matrix 192×113). The timing of the assessment (baseline and o follow-up) and the clinical and neuropsychological data were kept a secret from the MRI analysis team. The neurologist and radiologist independently evaluated the MRI scans for diffusion abnormalities on DW images and pre-existing vascular abnormalities and brain atrophy on T2 and FLAIR images. Neuropsychological examinations were administered to both groups before and 6-12 weeks after surgery.

#### Statistical analysis

All the data were expressed in numbers or percentages. Statistical analysis was performed using the Chi-square test wherever applicable. A p<0.05 was considered to be statistically significant.

#### RESULTS

A total of 66 patients were included in the study. CABG had less double-vessel (31.8%) and more triple-vessel disease (65.15%) on pre-operative angiogram. Pre-operative carotid and vertebral Doppler was performed by a trained radiologist in all CAD patients. No carotid disease was observed in 45.45% of CABG patients. Only three patients had unilateral high-grade stenosis (Table 1).

MRI brain with DWI was performed preoperatively in 50 (75.75%) of 66 CABG patients. Before surgery, no diffusion abnormalities were found on DW images. In those who underwent MRI, no lesions were found in 21 (31.82%) CABG patients. Bilateral small vessel ischemic disease (SVID) or periventricular lucencies (PVL) was seen in 23 (34.85%) CABG patients. Bilateral SVID with lacunar infarct was seen in 4 (6.06%) CABG patients. Lacunar infarct and wedge infarct were seen in 1 (1.52%) patient each (Table 2).

At follow-up, MRI brain with DWI was performed only in 54 (81.82%) CABG patients. There was no significant change was found postoperatively on brain MRI imaging. Postoperatively, during the hospital stay, one patient who had transient unilateral visual sensory neglect had one new lesion on DWI (small right thalamic infarct). This lesion was not seen at the follow-up MRI-DWI. The left eye cortical blindness in another patient did not reveal any new lesion on MRI-DWI (Table 2).

New ischemic brain lesions on FLAIR were detected in five patients at 6–12 weeks. The lesions were distributed evenly among the CABG; none of the patients had multiple lesions. The size was less than 5 mm for three lesions, 5–10 for two lesions, and none more than 10 mm.

Moderate or severe degree of neuropsychological dysfunction ( $\geq$ 3 tests) was seen in 9 (13.64%) patients preoperatively and it was also seen in 10 (15.15%) patients postoperatively. There was no significant difference before and after CABG patients in cognitive function.

Table 1: Baseline imaging characteristics of the patients undergoing coronary artery bypass grafting (n = 66)

Coronary artery disease	n (%)	
Coronary angiography		
Single vessel disease	2 (3.03)	
Double vessel disease	21 (31.82)	
Triple vessel disease	43 (65.15)	
Carotid and vertebral Doppler		
Normal	30 (45.45)	
Diffuse	27 (40.91)	
Mild (<50%)	4 (6.06)	
Moderate (50-69%)	2 (3.03)	
High (70-99%)	3 (4.55)	

Table 2: Comparison of imaging characteristics in patients before and after CABG (n = 66)

Imaging characteristics	MRI brain (before CABG)	MRI brain (after CABG)	p-value
Normal	21 (31.82)	24 (36.36)	0.713
Bilateral SVID/PVL	23 (34.85)	21 (31.82)	0.854
Bilateral SVID and lacunar infarct	4 (6.06)	6 (9.09)	0.742
Lacunar infarct	1 (1.52)	2 (3.03)	1.00
Wedge infarct	1 (1.52)	1 (1.52)	0.476

SVID: Small vessel ischemic disease, PVL: Periventricular lucencies, MRI: Magnetic resonance imaging, CABG: Coronary artery bypass grafting

#### DISCUSSION

MRI studies indicate that CNS abnormalities resulting from the patients' chronic cardiac disease may underlie pre-existing intellectual impairments [21-23].

In the present study, moderate-to-high grade stenosis was found in 7.58% of CABG patients. In this study, MRI brain with DWI was performed preoperatively in cardiac patients who revealed detectable bilateral SVID and PVL with or without lacunar infarcts. Goto and Nakamura reported evidence of ischemic brain abnormalities (50% and 97% of subjects, respectively) before surgery [20,24]. One patient in the present study had the right thalamic infarct with transient clinical (unilateral visual sensory neglect) correlate.

At follow-up, MRI with DWI was performed on CABG patients. The objective evidence of acute cerebral ischemia was obtained by DW-MRI. Six (9.09%) patients showed new post-operative SVID or cerebral infarction. In the present study, the incidence of new cerebral lesions was 6 (9.09%) of 66 CABG patients at 6–12 weeks follow-up which was less in comparison to other studies (26%, 23%, and 32%, respectively) [17,21,25]. The principal finding in our study was the absence of a correlation between post-operative cognitive dysfunction and objective evidence of structural ischemia as detected by DW-MRI. This has an important implication both for the understanding of the mechanisms of cognitive dysfunction postoperatively and for the design of trials of techniques, technologies, and pharmacological agents directed toward reducing cerebro-embolic injury or improving cognitive outcomes.

Some possible explanations for the lack of correlation between post-operative cognitive dysfunction and the presence of cerebral ischemic lesions were suggested by Knipp *et al.* [26]. The largest study that applied conventional MRI with DWI after CABG comprised 39 patients [26]. Using DW-MRI other series included 35226 and 50 patients, respectively [25]. However, in the latter, only 27 of the patients had CABG. Thus, to date, the present study of 66 CABG patients represents the largest that was administered DW-MRI and cognitive assessment before and after surgery for as long as 6–12 weeks.

Pre-operative cognitive raw scores of neuropsychological assessment were compared with the NIMHANS normative data [27]. It was found that a moderate or severe degree of neuropsychological dysfunction ( $\geq$ 3 tests) was seen in 9 (13.64%). Postoperatively, a moderate or severe degree of neuropsychological dysfunction ( $\geq$ 3 tests) was seen in 10 (15.15%). There was no significant difference before and after CABG patients in cognitive function.

The present study had shown no significant difference in the form of ischemic change on MRI after follow-up and also no significant change in the form of cognitive function. Few other studies have also not proved this association of cognition with the MRI changes [12,13,16-18].

#### CONCLUSION

This study concluded that CABG has no relation in the form of brain MRI changes with the cognition function of the patients.

#### **AUTHORS' CONTRIBUTION**

All the authors contributed to the preparation of the final manuscript.

#### **CONFLICTS OF INTEREST**

None.

#### FINANCIAL SUPPORT

Nil.

### REFERENCES

- Yuan SM, Lin H. Postoperative cognitive dysfunction after coronary artery bypass grafting. Braz J Cardiovasc Surg 2019;34:76-84. doi: 10.21470/1678-9741-2018-0165, PMID 30810678
- Selnes OA, Goldsborough MA, Borowicz LM Jr., Enger C, Quaskey SA, McKhann GM. Determinants of cognitive change after coronary artery bypass surgery: A multifactorial problem. Ann Thorac Surg 1999;67:1669-76. doi: 10.1016/s0003-4975(99)00258-1, PMID 10391273
- Wei S, Cao YR, Liu DX, Zhang DS. Cerebral infarction after cardiac surgery. Ibrain 2022;8:190-8. doi: 10.1002/ibra.12046
- Hogue CW, Gottesman RF, Stearns J. Mechanisms of cerebral injury from cardiac surgery. Crit Care Clin 2008;24:83-98. doi: 10.1016/j. ccc.2007.09.004, PMID 18241780
- Andersen K, Waaben J, Husum B, Voldby B, Bødker A, Hansen AJ, et al. Nonpulsatile cardiopulmonary bypass disrupts the flow-metabolism couple in the brain. J Thorac Cardiovasc Surg 1985;90:570-9. doi: 10.1016/S0022-5223(19)38571-X, PMID 4046623
- Watson BG. Unilateral cold neck. A new sign of misplacement of the aortic cannula during cardiopulmonary bypass. Anaesthesia 1983;38:659-61. doi: 10.1111/j.1365-2044.1983.tb12158.x, PMID 6346933
- Berger M, Nadler JW, Browndyke J, Terrando N, Ponnusamy V, Cohen HJ, *et al.* Postoperative cognitive dysfunction: Minding the gaps in our knowledge of a common postoperative complication in the elderly. Anesthesiol Clin 2015;33:517-50. doi: 10.1016/j. anclin.2015.05.008, PMID 26315636
- Newman MF, Kirchner JL, Phillips-Bute B, Gaver V, Grocott H, Jones RH, *et al.* Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. N Engl J Med 2001;344:395-402. doi: 10.1056/NEJM200102083440601, PMID 11172175 [published correction in N Engl J Med 1876;344:2001].
- Selnes OA, Grega MA, Borowicz LM Jr., Barry S, Zeger S, Baumgartner WA, *et al.* Cognitive outcomes three years after coronary artery bypass surgery: A comparison of on-pump coronary artery bypass graft surgery and nonsurgical controls. Ann Thorac Surg 2005;79:1201-9. doi: 10.1016/j.athoracsur.2004.10.011, PMID 15797050
- Lee TA, Wolozin B, Weiss KB, Bednar MM. Assessment of the emergence of Alzheimer's disease following coronary artery bypass graft surgery or percutaneous transluminal coronary angioplasty. J Alzheimers Dis 2005;7:319-24. doi: 10.3233/jad-2005-7408, PMID 16131734

- Kalaria RN, Akinyemi R, Ihara M. Stroke injury, cognitive impairment and vascular dementia. Biochim Biophys Acta 2016;1862:915-25. doi: 10.1016/j.bbadis.2016.01.015, PMID 26806700
- Fearn SJ, Pole R, Wesnes K, Faragher EB, Hooper TL, McCollum CN. Cerebral injury during cardiopulmonary bypass: Emboli impair memory. J Thorac Cardiovasc Surg 2001;121:1150-60. doi: 10.1067/mtc.2001.114099, PMID 11385383
- Clark RE, Brillman J, Davis DA, Lovell MR, Price TR, Magovern GJ. Microemboli during coronary artery bypass grafting. Genesis and effect on outcome. J Thorac Cardiovasc Surg 1995;109:249-57, discussion 257. doi: 10.1016/S0022-5223(95)70386-1, PMID 7853878
- 14. Braekken SK, Reinvang I, Russell D, Brucher R, Svennevig JL. Association between intraoperative cerebral microembolic signals and postoperative neuropsychological deficit: Comparison between patients with cardiac valve replacement and patients with coronary artery bypass grafting. J Neurol Neurosurg Psychiatry 1998;65:573-6. doi: 10.1136/ jnnp.65.4.573, PMID 9771790
- Browndyke JN, Moser DJ, Cohen RA, O'Brien DJ, Algina JJ, Haynes WG, et al. Acute neuropsychological functioning following cardiosurgical interventions associated with the production of intraoperative cerebral microemboli. Clin Neuropsychol 2002;16:463-71. doi: 10.1076/clin.16.4.463.13910, PMID 12822055
- Restrepo L, Wityk RJ, Grega MA, Borowicz L Jr., Barker PB, Jacobs MA, et al. Diffusion-and perfusion-weighted magnetic resonance imaging of the brain before and after coronary artery bypass grafting surgery. Stroke 2002;33:2909-15. doi: 10.1161/01.str.0000040408.75704.15, PMID 12468790
- Bendszus M, Reents W, Franke D, Müllges W, Babin-Ebell J, Koltzenburg M, *et al.* Brain damage after coronary artery bypass grafting. Arch Neurol 2002;59:1090-5. doi: 10.1001/archneur.59.7.1090, PMID 12117356
- Knipp SC, Matatko N, Wilhelm H, Schlamann M, Massoudy P, Forsting M, et al. Evaluation of brain injury after coronary artery bypass grafting. A prospective study using neuropsychological assessment and diffusion-weighted magnetic resonance imaging. Eur J Cardiothorac Surg 2004;25:791-800. doi: 10.1016/j.ejcts.2004.02.012, PMID 15082284
- Vermeer SE, Prins ND, den Heijer T, Hofman A, Koudstaal PJ, Breteler MM. Silent brain infarcts and the risk of dementia and cognitive decline. N Engl J Med 2003;348:1215-22. doi: 10.1056/ NEJMoa022066, PMID 12660385
- Goto T, Baba T, Honma K, Shibata Y, Arai Y, Uozumi H, et al. Magnetic resonance imaging findings and postoperative neurologic dysfunction in elderly patients undergoing coronary artery bypass grafting. Ann Thorac Surg 2001;72:137-42. doi: 10.1016/s0003-4975(01)02676-5, PMID 11465168
- Toner I, Hamid SK, Peden CJ, Taylor KM, Smith PL, Newman SP, et al. Magnetic resonance imaging and P300 (event-related auditory evoked potentials) in the assessment of postoperative cerebral injury following coronary artery bypass graft surgery. Perfusion 1993;8:321-9.
- Deshields TL, McDonough EM, Mannen RK, Miller LW. Psychological and cognitive status before and after heart transplantation. Gen Hosp Psychiatry 1996;18 (6 Suppl):62S-9. doi: 10.1016/ s0163-8343(96)00078-3, PMID 8937924
- Millar K. The effects of anesthetic and analgesic drugs. In: Smith AP, Jones DM, editors. Handbook of Human Performance. Vol. 2. London: Academic Press; 1992. p. 337-85.
- Nakamura Y, Kawachi K, Imagawa H, Hamada Y, Takano S, Tsunooka N, *et al.* The prevalence and severity of cerebrovascular disease in patients undergoing cardiovascular surgery. Ann Thorac Cardiovasc Surg 2004;10:81-4. PMID 15209548
- 25. Cook DJ, Huston J 3<sup>rd</sup>, Trenerry MR, Brown RD Jr., Zehr KJ, Sundt TM 3<sup>rd</sup>. Postcardiac surgical cognitive impairment in the aged using diffusion-weighted magnetic resonance imaging. Ann Thorac Surg 2007;83:1389-95. doi: 10.1016/j.athoracsur.2006.11.089, PMID 17383345
- 26. Knipp SC, Matatko N, Wilhelm H, Schlamann M, Thielmann M, Lösch C, *et al.* Cognitive outcomes three years after coronary artery bypass surgery: Relation to diffusion-weighted magnetic resonance imaging. Ann Thorac Surg 2008;85:872-9. doi: 10.1016/j. athoracsur.2007.10.083, PMID 18291160
- Rao SL, Subbakrishna DK, Gopukumar K. NIMHANS Neuropsychology Battery-2004 Manual. Bangalore, India: NIMHANS Publication; 2004.