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Original Research Article

Prospective analysis of cerebrovascular events in patients following coronary artery bypass surgery

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ABSTRACT

Background: Cerebrovascular events are the most common cause of disability in adults and can be classified into two categories: ischemic stroke and hemorrhagic stroke. Risk factors for stroke include age, gender, race, family history of stroke, hypertension, smoking, heart disease, valvular heart disease, arrhythmias, diabetes, obesity, and dyslipidemia. Low cardiac output syndrome, myocardial infarction, and atrial fibrillation can also contribute to stroke. This study aims to investigate the incidence of stroke post-cardiac surgery and the risk factors contributing to it.
Methods: A prospective observational study with a sample size of 516 patients was conducted. Patients over the age of 40 who were undergoing CABG (both off and on pump) were included. Patients were subjected to on-pump or off-pump coronary artery bypass surgery as per requirement, but preferably off-pump.
Results: Out of 516 patients, 13 developed strokes, of which 8 (61.5%) had hypertension and 10 (76.9%) had diabetes, 4 (30.8%) were smokers, 6 (46.2%) had normal LDL values, 7 (53.8%) had high LDL levels, none had normal HDL values, 1 (7.7%) had normal LV function, 4 (30.8%) had mild LV dysfunction, 4 (30.8%) had moderate LV dysfunction, and 4 (30.8%) had severe LV dysfunction. 11 (84.6%) had COPD. 7 (53.8%) had no prior MI, 5 (38.5%) had a recent MI, and 1 (7.7%) had a prior MI that was more than ten years old. 8 (61.5%) had normal renal functions, while 5 (38.5%) had disturbed renal functions.
Conclusions: In this study, the incidence of CVE after CABG is 2.52%. All the patients who developed stroke had multiple risk factors. High LDL, low LVEF, deranged renal functions, PVD, arrhythmia pre-op, anti-coagulation pre-op, on pump surgery, Cardioplegia usage, CCF pre-op, urgent surgery, LCOS post-operatively are risk factors for post-operative stroke.

Keywords: Cerebro vascular event, Stroke, Coronary artery bypass surgery

INTRODUCTION

Cerebrovascular events are the most common cause of disability in adults. Cerebrovascular events post-cardiac surgery is a debilitating complication and contributes to prolonged hospitalization, morbidity, and mortality. A cerebrovascular event is a clinical syndrome caused by disruption of blood supply to the brain, characterized by rapidly developing signs of focal or global disturbance of cerebral functions, lasting for more than 24 hours or leading to death. A transient ischemic attack (TIA) refers to a similar presentation that resolves within 24 hours.[1]

Stroke can be classified in 2 categories, namely Ischemic stroke and hemorrhagic stroke of which ischemic stroke is most common contributing to 80% of all strokes.[2]

Risk factors for stroke include age, gender, race, family history of stroke, hypertension, smoking, heart diseases like coronary artery disease, valvular heart disease, arrhythmias, diabetes, obesity, and dyslipidemia.

In addition to these, cardiac surgery is also a risk factor for stroke. perioperative factors-

Pre-operative

Renal insufficiency, chronic obstructive pulmonary disease, peripheral vascular disease, diseased carotid arteries, hyperlipidemia, anticoagulation, recent myocardial infarction, congestive cardiac failure, arrhythmias.

Intra-operative

Urgent surgery, use of cardiopulmonary bypass, prolonged cardiopulmonary bypass time, prolonged aortic cross-clamp time, multi-vessel CABG, redo surgery, ascending aorta atherosclerosis, ascending aorta manipulations as partial clamping and cross-clamping.[3]

Post-operative

Low cardiac output syndrome, myocardial infarction, atrial fibrillation.[4]

With the emergence of off-pump CABG, the gradual switch over from venous grafts to the use of more arterial grafts leading to less number of proximal anastomoses on the aorta, and the incidence of stroke post cardiac surgery has reduced. This study aims to find out the incidence of stroke post-cardiac surgery in the present era and analyze the risk factors contributing to stroke.

The aim of this study is to examine cerebro-vascular incidents in patients who have had coronary artery bypass surgery. Study's objectives include measuring incidence of cerebrovascular events in patients after coronary artery bypass grafting surgery and analyzing the risk factors that contribute to cerebrovascular events in patients following coronary artery bypass grafting surgery.

METHODS

A prospective observational study with a sample size of 516 patients was conducted at the department of cardiovascular and thoracic surgery, Apollo Main hospital, Chennai, from June 2018 to November 2021.

Patients over the age of 40 who were undergoing CABG (both off and on pump) were included in this study. Patients with a history of stroke and other neurological abnormalities, such as epilepsy, as well as patients undergoing other cardiac surgeries such as valve replacement surgeries and congenital anomalies, were excluded from this study.

Methodology

Patients who satisfy the inclusion and exclusion criteria are admitted, a detailed history is obtained, and a detailed clinical and neurological examination is done. Patients are subjected to blood and radiological investigations namely complete blood picture, renal function tests, liver function tests, lipid profile, carotid and vertebral arterial Doppler as a part of the routine pre-operative evaluation. Patients were informed about their disease condition, and informed consent was obtained for the surgery. Patients are informed about the study in their native language by using patient information sheets and consent is taken from patients willing to participate in the study. A unique identification no. is given to each patient in the study.

Patients are subjected to on-pump or off-pump coronary artery bypass surgery as per requirement but preferably off-pump. Off-pump CABG is done using arterial and venous conduits. Anastomosis of venous conduits to the aorta is done with partial clamping of the aorta. On pump CABG is done in cases of hemodynamic instability pre-operatively or intraoperatively. A Hemo-filter, bubble detector, and membrane oxygenators are used on-pump CABG. Four mg/kg heparin is given maintaining ACT of more than 480 sec. 2 mg/kg heparin is given for off-pump CABG. Adequate ACT is maintained all through the procedure.

In cases of on-pump CABG, preference will be given to operate as on-pump- beating heart CABG than intermittent fibrillatory cross-clamp technique or cross-clamping with cardioplegic arrest.

OCTOPUS 4.3 suction stabilizer, carbon-dioxide blower-mister, and chase intra-coronary shunts are used during distal anastomosis. A partial clamp is applied over ascending aorta for proximal anastomosis of vein grafts. Heparin is reversed with protamine at the end of surgery.

Postoperatively patients are extubated on POD 1 as an institutional protocol. Patients are assessed for neurological deficits. In patients who developed neurological deficit, CT/MRI neuroimaging is done as per requirement. In patients who developed a stroke, risk factor analysis is done.

Patients are extubated on POD 1 as per our ICU protocol. For patients requiring ventilation beyond 5 days, a tracheostomy is done on POD 6. The discharge day in our institute was 7th post-operative day. Patients are followed up till the time of discharge.

Statistical analysis

Data obtained was entered into an excel sheet (MS Office 2007). All continuous variables were assessed for normality using Shapiro-Wilk's test. Continuous variables following Gaussian distribution were expressed as mean ± standard deviation (SD). Otherwise, they were

expressed as median (interquartile range). A comparison of continuous variables was done using an independent sample t test. Comparison of categorical variables was taken care of by Chi-square test or Fisher's exact test basedon the number of observations. All the $p<0.05$ were considered statistically significant. Analysis was carried out using statistical software IBM SPSS statistics for Windows, Armonk, NY IBM Corp. version 25.0.

IRB approval

IRB approval was obtained from institutional ethical committee-Bio medical research-apollo hospitals. Informed consent was obtained from all the patients who met the exclusion criteria.

RESULTS

The total number of patients included in the analysis is 516. The details of patients who developed stroke post-operatively with different categorizations are given in Table 1. Of 516 patients, 13 developed stroke, of which 9 (69.2%) were male and 4 (30.8%) were female. The number of hypertension patients in these 13 stroke patients was 8 (61.5%), while the number of diabetes patients in these 13 stroke patients was 10 (76.9%).11 (84.6%) of the 13 patients who suffered stroke did not have arrhythmia post-operatively, while 2 (15.4%) did. 9 (69.2%) of the 13 stroke patients were nonsmokers, while 4 (30.8%) were smokers. Nine (69.2%) of the 13 stroke patients did not have LVH, while 4 (30.8%) had. 6 (46.2%) of the 13 stroke patients had normal LDL values, while 7 (53.8%) had high LDL levels. None of the 13 patients who endured a stroke had normal HDL values, while all (100%) had low HDL levels. Of the 13 individuals who suffered a stroke, 11 (84.6%) had COPD. 8 (61.5%) of the 13 stroke patients had normal renal functions, while 5 (38.5%) had disturbed renal functions. 7 (53.8%) of 13 stroke patients did not have peripheral vascular disease, while 6 (45.2%) had. In carotid Doppler, 12 (92.3%) of 13 stroke patients had carotid artery disease, while 1 (2.4%) had carotid artery disease. 3 Out of 13 stroke patients, 7 (53.8%) had no post-operative low cardiac output syndrome, while 6 (46.2%) had postoperative low cardiac output syndrome (Table 2).

One (7.7%) patient had normal LV function, 4 (30.8%) patients had mild LV dysfunction, 4 (30.8%) patients had moderate LV dysfunction, and 4 (30.8%) patients had severe LV dysfunction (Table 3).

Thirteen patients out of 516 patients experienced a stroke; 7 (53.8%) of these patients had no prior MI, 5 (38.5%) had a recent MI, and 1 (7.7%) had a prior MI that was more than ten years old (Figure 1). Out of the 13 stroke patients, 11 (84.6%) had no arrhythmia prior to surgery, while 2 (15.4%) had arrhythmia prior to surgery (Figure 2), 11 (84.6%) of the 13 stroke patients did not get anticoagulation pre-operatively, while 2 (15.4%) received anticoagulation using patient information sheets, and consent is taken from patients willing to participate on-pump CABG. The 11 (84.6%) of the 13 stroke patients did not have cardioplegia, while 2 (15.4%) experienced cardioplegia during CABG (Table 4).

Table 1: Details of patients who developed stroke post-operatively (n=13).

Variables	N	Percentage (%)
Male	9	69.2
Female	4	30.8
Hypertensive patients	8	61.5
Diabetic patients	11	84.6
Arrhythmia patients	2	15
COPD patients	11	84.6
Smokers	4	30.8
LVH	7	53.8
Elevated LDL	7	53.8
Patients with disturbed renal function	5	38.5
Patients with peripheral vascular disease	6	45.2
Patients with carotid artery disease	1	2.4

Table 2: Demographic details of all the participants (n=516).

Variables	N	Percentage (%)
Male	448	86.8
Female	68	13.2
Hypertensive patients	340	65.9
Diabetic patients	351	68
Smokers	4	2.6
Patients with pre-operative arrhythmia	25	4.8
COPD patients	47	9.1
Patients with H/O MI	130	25.2

Table 3: Patients LV function status.

Variables	N	Percentage (%)
Normal LV function	1	7.70
Mild LV dysfunction	4	30.80
Moderate LV dysfunction	4	30.80
Severe LV dysfunction	4	30.80

Table 4: Number of patients received off-pump CABG, On Pump CABG and number of the patients experienced cardioplegia.

Variables	N	Percentage (%)
Off-pump CABG	10	76.9
On-pump CABG	3	23.1
Cardioplegia	2	15.4

During CABG, 1 (7.7%) of the 13 stroke patients had 1 graft while none had 2 grafts, 3 (76.9%) had 3 grafts, 2 (15.4%) had 4 grafts, and none had 5 grafts (Table 5).

Three (23.1%) of the 13 stroke patients did not have arterial grafts, while 10 (76.9%) had one arterial transplant and none had more than one. None of the 13 stroke patients developed bilateral IMA during CABG. There were no post-operative MI patients among these 13 stroke patients. None of the 13 stroke patients had previously undergone heart surgery. The 11 (84.6%) of the 13 stroke patients got elective surgery, while 2 (15.4%) underwent emergent CABG (Figure 3).

Table 5: Number of the grafts patients received.

Variables	N	Percentage (%)
Patients with 1 graft	1	7.7
Patients with 2 graft	0	0
Patients with 3 graft	3	76.9
Patients with 4 graft	2	15.4
Patients with 5 graft	0	0

Table 6: Statistical significance of variables.

Variables	P value
Sex	0.078
Hypertension	0.472
Diabetes	0.359
Arrhythmias post op	0.127
Smoking	0.564
LVH	0.409
LDL	0.002
HDL	0.053
LVEF	0.000
COPD	0.335
History of MI	0.522
Renal functions	0.033
Peripheral vascular disease	0.000
Carotid disease	0.724
Arrhythmia pre op	0.028
Anti coagulation pre op	0.002
On pump/ off pump	0.006
Cardioplegia usage	0.015
No. of grafts	0.175
No. of arterial grafts	0.311
Bilateral IMA	0.365
CCCF pre op	0.024
Prior cardiac surgery	0.880
Urgent surgery	0.003
Low cardiac output syndrome post op	0.000

Out of all the variables, the following are the risk factors (statistically significant $p<0.05$) for cerebrovascular events following coronary artery bypass surgery (Table 6).

LD, LVEF, renal functions, peripheral vascular disease, arrhythmia pre-op, anti-coagulation pre-op, on-pump/ off-pump, cardioplegia usage, CCF pre-op, urgent surgery and low cardiac output syndrome post-op.

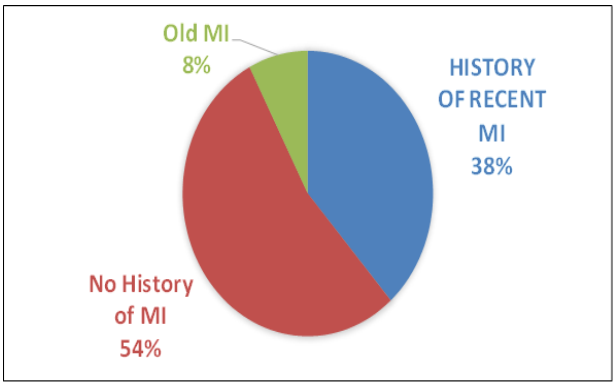

Figure 1: Patients history of MI.

Pie diagram depicting distribution of MI.

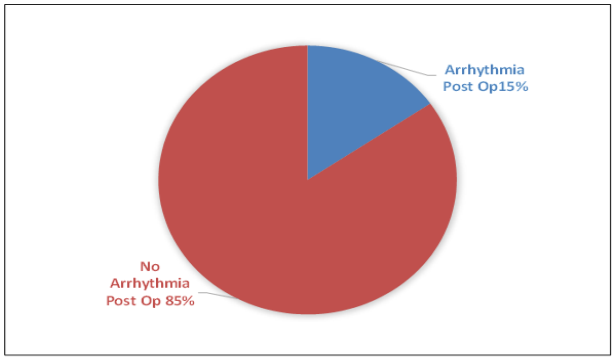

Figure 2: Patients arrhythmic status.

Pie diagram depicting distribution of arrhythmia post op.

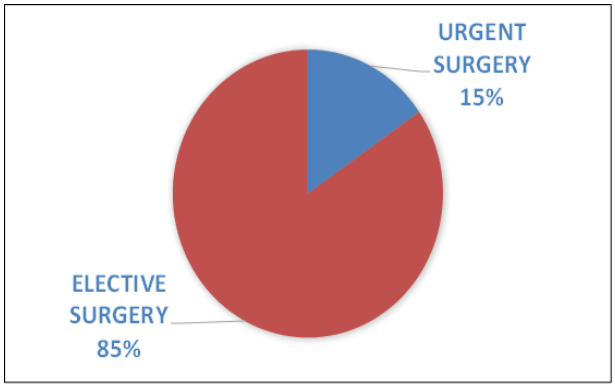

Figure 3: Distribution of urgent and elective surgery.

Pie diagram depicting distribution of urgent surgery and elective surgery.

DISCUSSION

Out of 516 patients, 448 (86.8%) patients were male of which 9 (2%) patients developed stroke post operatively, and 68 (13.2%) were female of which 4 (5.9%) patients developed stroke post operatively. The 176 (341%) patients did not have hypertension of which 5 (2.8%) patients developed stroke post operatively, while 340 (65.9%) had hypertension, of which 8 (2.4%) patients developed stroke post operatively. The 165 (32%) patients did not have diabetes of which 3 (1.8%) patients developed stroke post operatively while 351 (68%) patients had diabetes of which 10 (2.8%) patients developed stroke post operatively. The 491 (95.2%) did not have arrhythmia pre-operatively of which 11 (2.2%) patients developed stroke post-operatively, while 25 (4.8%) patients had arrhythmia preoperatively of which 2 (8%) patients developed stroke post-operatively. The 364 (70.5%) patients were nonsmokers of which 9 (2.5%) patients developed stroke post operatively while 152 (29.5%) were smokers of which 4 (2.6%) patients developed stroke post operatively. 388 (75.2%) patients did not have LVH of which 9 (2.3%) patients developed stroke post operatively while 128 (24.8%) patients had LVH, of which 4 (3.1%) patients developed stroke post operatively. The 432 (83.7%) patients had normal LDL levels, of which 6 (1.4%) patients developed stroke post operatively while 84 (16.3%) patients had elevated LDL levels, of which 7 (8.3%) patients developed stroke post operatively. The 103 (20%) patients had normal HDL levels, of which none of them developed stroke but 413 (80%) patients had low HDL levels of which 13 (3.1%) patients developed stroke post operatively. The 266 (51.6%) patients had normal LV function, of which 1 (0.4%) patient developed stroke post operatively, 116 (22.5%) patients had mild LV dysfunction of which 4 (3.4%) patients developed stroke post operatively, 100 (19.4%) had moderate LV dysfunction of which 4 (4%) patients developed stroke post operatively and 34 (6.6%) had severe LV dysfunction of which 4 (11.8%) patients developed stroke post operatively. The 469 (90.9%) patients did not have COPD of which 11 (2.3%) patients developed stroke post operatively and 47 (9.1%) had COPD, of which 2 (4.3%) patients developed stroke post operatively.

The 348 (67.4%) patients did not have a history of MI, of which 7 (2%) patients developed stroke post-operatively while 130 (25.2%) had a recent history of MI of which 5 (3.8%) patients developed stroke post operatively and 38 (7.4%) had an old history of MI, of which 1 (2.6%) patient developed stroke post operatively. Gaudino et al found that stroke after CABG is 1-2%, with elderly age, deranged real functions, chronic lung disease, emergency surgery, peripheral vascular disease, pre-operative MI, and pre-operative CCF being risk factors.[5] Pre-operative CT scan, palpation of the aorta, epi aortic scan, and trans esophageal echo are recommended.

The 438 (84.9%) patients had normal renal functions, of which 8 (1.8%) patients developed stroke post operatively and 78 (15.1%) patients had deranged renal functions, of which 5 (6.4%) patients developed stroke post operatively. The 499 (96.7%) patients did not have peripheral vascular disease, of which 7 (1.4%) patients developed stroke post operatively and 17 (3.3%) had peripheral vascular disease, of which 6 (35.3%) patients developed stroke post operatively. The 475 (92.1%) did not have the carotid disease, of which 12 (2.5%) patients developed stroke post operatively while 41 (7.9%) had carotid disease, of which 1 (2.4%) patient developed stroke post operatively. Mao et al found that elderly age, history of stroke, atherosclerosis in carotid arteries, peripheral vascular disease, and long CPB are associated with cerebrovascular events after CABG.[6] The incidence of stroke was up to 5.7%, with half occurring in the early post-operative period.

The 505 (97.9%) patients did not have arrhythmia pre operatively, of which 11 (2.2%) patients developed stroke post operatively and 11 (2.1%) patients had arrhythmia pre operatively, of which 2 (18.2%) patients developed stroke post operatively. The 513 (99.4%) patients did not receive anticoagulation preoperatively, of which 11 (2.1%) patients developed stroke post operatively while 3 (0.6%) had anticoagulation pre operatively of which 2 (66.7%) patients developed stroke post operatively. Eight (1.6%) patients received cardioplegia, of which 11 (2.2%) patients developed stroke post operatively, while 508 (98.4%) did not receive cardioplegia of which 2 (25%) patients developed stroke post operatively.

Stamou et al that stroke following CABG is linked to a significant short-term morbidity and death rate.[7] Preoperative and postoperative clinical variables can indicate increased stroke risk. 500 (96.9%) patients underwent off-pump coronary artery bypass surgery, of which 10 (2%) developed stroke post operatively. Despite the fact that current surveillance and surgical protocols have considerably decreased the incidence of stroke following CABG, their findings support OPCAB as a strategy to further minimize stroke after CABG, particularly in high-risk patients.

The 19 (3.7%) patients had 1 graft during CABG, of which 1 (5.3%) patient developed stroke post-operatively, while 60 (11.6%) patients had 2 grafts, of which none of them developed stroke, 246 (47.7%) patients had 3 grafts of which 10 (4.1%) patients developed stroke post operatively and 166 (32.2%) had 4 grafts of which 2 (1.2%) patients developed stroke post operatively and 25 (4.8%) patients had 5 grafts of which none of them developed stroke post operatively. The 44 (8.5%) patients did not have arterial grafts of which 3 (6.8%) patients developed stroke post-operatively, while 416 (80.6%) had 1 arterial graft of which 10 (23.1%) patients developed stroke post operatively, 52 (10.1%) had 2 arterial grafts of which none of them developed stroke, 3 (0.6%) patients had 3 arterial grafts of which none of them

developed stroke and 1 (0.2%) patient had 4 arterial grafts who did not develop stroke post operatively.

Lee et al investigated the connection between cerebral atherosclerosis and stroke after coronary artery bypass grafting (CABG).[3] Cerebral atherosclerosis was found to be strongly linked to the occurrence of post-CABG stroke, serving as both an independent risk factor and the cause of a large number of strokes. Hedberg et al found that stroke is associated with elderly age, deranged renal functions, atherosclerosis of the ascending aorta, and prolonged CPB time in the early post-operative period, while arrhythmias, LCOS post-operatively, and pre-operative MI are associated with stroke in the late post-operative period.[4] Their findings support OPCAB as a strategy to further minimize stroke after CABG, particularly in high-risk patients.

Early stroke mortality mostly manifests itself in the acute period, but delayed stroke survival remained reduced even in the long term. In a multicenter population-based research, Rocha et al evaluated the long-term clinical results of total arterial revascularization (TAR) with non-TAR (CABG with at least 1 arterial and 1 saphenous vein graft).[11] They concluded that complete arterial revascularization was linked to a lower risk of major adverse cardiac and cerebrovascular events, mortality, and myocardial infarction over time, and that it may be the surgery of choice for patients with a reasonable life expectancy who require CABG. Bucerius et al concluded that identifying stroke predictors is critical for understanding the deadly condition's etiology and devising preventive measures.[12] Selnes et al observed that cerebro vascular disease and peripheral vascular disease are associated with stroke post CABG.[13]

The 478 (92.6%) patients underwent left internal mammary artery usage for grafting of which 13 (2.7%) patients developed stroke post operatively and 38 (7.4%) patients underwent bilateral internal mammary artery usage for grafting of which none of them developed stroke post operatively. None of the patients had post-operative MI and 13 (2.5%) patients developed stroke post operatively. The 506 (98.1%) patients did not have CCF pre operatively of which 11 (2.2%) patients developed stroke post operatively while 10 (1.9%) had CCF pre op of which 2 (20%) patients developed stroke post operatively. One percentages patient had prior cardiac surgery of which none of them developed stroke while 511 (99%) did not have prior cardiac surgery of which 13 (2.5%) patients developed stroke post operatively. Four (0.8%) patients underwent CABG as urgent procedure of which 2 (50%) patients developed stroke post operatively while 512 (99.2%) patients had CABG as elective procedure of which 11 (2.1%) patients developed stroke post operatively. The 480 (93%) patients did not develop low cardiac output syndrome post operatively of which 7 (1.5%) patients developed stroke post operatively while 36 (7%) patients developed low cardiac output syndrome post operatively of which 6 (16.7%) patients developed stroke post operatively. Out of 516 patients, 503 (97.5%) did not develop stroke while 13 (2.5%) patients developed stroke in the post-operative period.

Stamou et al found that stroke following CABG is linked to a significant rate of short-term morbidity and death.[7] Preoperative and postoperative clinical variables can indicate increased stroke risk. Domanski et al examined demographic and clinical factors related with perioperative and late stroke in diabetic patients having multivessel CABG.[8] The future revascularization evaluation in patients with diabetes mellitus: optimal management of multivessel disease (FREEDOM) found that when compared to percutaneous intervention, FREEDOM patients had improved survival free of mortality, myocardial infarction, or stroke, as well as enhanced overall survival. However, the risk of stroke was higher after CABG than after percutaneous intervention.

Huang et al found that individuals with significant stenosis in both the carotid and coronary arteries are more likely to have an ischemic cerebral stroke, but other important variables that contribute to ischemic cerebral stroke should not be overlooked.[9] Retrospective analysis of surgical outcomes and follow-up findings was performed. They concluded that individuals with significant stenosis in both the carotid and coronary arteries are more likely to have an ischemic cerebral stroke.

Limitations

This is a single center study, as the number of patients who developed CVE was less, risk factor analysis could not be effectively done hence a larger sample size is required.

CONCLUSION

The incidence of CVE after CABG is 2.52%. All the patients who developed stroke had multiple risk factors. High LDL, low LVEF, deranged renal functions, PVD, arrhythmia pre op, anti-coagulation pre op, on pump surgery, Cardioplegia usage, CCF pre op, urgent surgery, LCOS post operatively are risk factors for post-operative stroke.

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Recommendations

Pre-operative CT chest/intra operative epi aortic echo to rule out diseased ascending aorta for planning of conduits for bypass grafting. Maintaining higher MAP

peri-operatively in patient with carotid artery disease. Reduce the number of venous grafts/ aorta manipulation in patients withdiseased aorta.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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