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Original Research Article

Prevalence of carotid artery stenosis and perioperative stroke in neurologically asymptomatic patients undergoing off pump coronary artery bypass grafting in a tertiary care hospital: An observational study

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ABSTRACT

Background: The study aimed to determine the prevalence of carotid artery stenosis, it's severity and relation with peri-operative stroke in neurologically asymptomatic patients undergoing CABG for coronary artery disease (CAD) in a tertiary care hospital. It also evaluates the relationship of hemodynamic alterations with the prevalence of stroke. It is a cross sectional study with prospective observations.
Materials and Methods: 97 neurologically asymptomatic patients with CAD in NYHA classification I, II and III scheduled for Off Pump CABG in our cardiac surgery operation theatre. Colour doppler ultrasound was performed in all patients prior to induction to determine the presence of carotid artery stenosis. Based on parameters measured in ultrasound, CAS was classified as per the Society of Radiologists criteria. Prevalence of carotid artery stenosis was assessed.
Results: The prevalence of carotid artery stenosis in our study population was 40.2%. The risk factors associated with CAS in our study were BMI >25kg/m2, smoking, left main coronary artery involvement, left ventricular systolic dysfunction (EF<50%). However, risk of CAS was also increased in hypertensive patients and those of age more than 55 years.
Conclusions: This study suggested relatively wide prevalence (40.2%) of carotid artery disease in neurologically asymptomatic patients undergoing CABG for coronary artery disease in the elective setting. It demonstrated the importance of subjecting these patients to evaluation by doppler ultrasound of the carotid vessels in the operating room immediately before induction of anaesthesia and the subsequent planning of anaesthetic management as well as surgical approach.

1. Introduction

Neurological dysfunction is a deleterious complication in patients posted for coronary artery bypass grafting (CABG) with manifestations ranging from transient symptoms to advanced stroke.[1] The presence of carotid artery stenosis (CAS) in patients coming for CABG increases the risk of ischemic stroke during and after surgery leading to reduced quality of life, increased morbidity and mortality.

The global incidence of stroke following CABG has been observed by previous literatures to be in the range of 2.1–5.2% with a mortality of 0–38%.[1] The etiology of ischaemic events in these patients with CAS may be multifactorial. Previous studies highlighted the significance of impaired cerebral auto-regulation distal to CAS as a primary etiology. The shedding of debris from carotid or aortic atherosclerotic plaques, embolization of intracardiac clots, decrease in perfusion pressure to < 60 mm Hg, inflammatory and neurohumoral derangements in the

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perioperative period are the causes of stroke.

The development of approaches to decrease the incidence of postoperative neurologic events has been affected by the lack of a clear understanding of the pathophysiology of such outcomes. Various strategies have been used historically to reduce the occurrence of perioperative stroke. This includes early treatment of arrhythmias, preventing manipulation and cannulation of the aorta, use of membrane oxygenators and arterial filters, avoiding hyperglycemia, maintaining good brain oxygenation. Owing partly to the assumption that adverse neurologic events were specifically related to the use of extracorporeal cardiopulmonary bypass, methods were evolved for performing CABG without the use of cardiopulmonary bypass (i.e., off-pump surgery). Although off-pump CABG can escape the adverse events of extracorporeal circulation, the impact of CAS on neurological events in patients posted for off-pump CABG has not been well documented in previous studies. We therefore decided to conduct a study to analyse the outcome of off-pump CABG in patients with unprotected CAS.

Carotid ultrasound is a easily available non-invasive device that can be used preoperatively to detect the presence of CAS.[1] In this study, carotid disease was assessed in patients with the help of ultrasound after induction of anaesthesia.

The aim of this study was to determine the prevalence of carotid artery stenosis and perioperative stroke in neurologically asymptomatic patients undergoing CABG for coronary artery disease (CAD) in our hospital.

The primary objectives of this study were:

1. To analyse the presence of any atherosclerotic lesion leading to carotid artery stenosis, it's prevalence and severity by Doppler ultrasound.
2. To evaluate the prevalence of ischaemic events in patients undergoing off pump CABG.

Secondary objectives were:

1. Correlation of possible risk factors like age, gender, type-2 diabetes, hypertension, dyslipidemia, smoking history, coronary artery involvement, LV dysfunction with carotid artery stenosis in our study population.
2. To set up a greater role of anaesthesiologists in the perioperative management of patients with CAS posted for off-pump CABG.

2. Materials and Methods

This study was a cross sectional study with prospective observations in the Department of Cardiac Anaesthesiology, Apollo Gleneagles Hospital, Kolkata from December 2016 to June 2018 (18 months).

Sample size calculation**:** As per the study by Taneja et al.[1] the prevalence of carotid artery stenosis was 38%. Hence, proportion of patients with CAS was taken as 38% i.e. p= 0.38.

Using the formula for sample size calculation and keeping loss of information at 26% (Power was 74%), sample size was estimated to be 96.54 ~ 97.

A total of 97 patients who satisfied the inclusion criteria were selected for this study after proper consent and ethical clearance.

All neurologically asymptomatic patients with CAD in NYHA classification I, II and III undergoing Off Pump CABG were included in the study.

2.1. Exclusion criteria

1. Patients with past history of carotid artery disease.
2. History of carotid artery endarterectomy in the past.
3. History of
4. Hemodynamically unstable patients.
5. Patients with arrhythmias or any cardiac valvular abnormalities.
6. Patients posted for emergency CABG.

Detailed medical history of the patients, baseline blood investigations and echocardiography were noted and coronary angiography were performed in the preoperative period.

After adequate pre oxygenation with 100% oxygen, induction was done with injection propofol (1-2 mg/kg) and fentanyl (2-3 mcg/kg). Neuromuscular blockade was achieved by Injection rocuronium (1.2mg/kg) prior to intubation. Urinary catheterisation was done and Transoesophagial Echocardiography probe was inserted. Anaesthesia was maintained with sevoflurane, oxygen, air and fentanyl infusion. Examination of the neck was done in supine position by a senior anaesthesiologist who had previous training in regional anaesthesia. Vivid-iQ^{TM} (GE, Chicago, Illinois, USA) ultrasound machine with a linear 5-10 MHz probe was used to determine the presence of atheromatous plaque or blood flow obstruction involving the carotid arteries. Colour doppler was used to detect flow velocities in the common carotid, external and internal carotid arteries (CCA, ECA & ICA). The parameters recorded were ICA peak systolic velocity (PSV), ratio of ICA & CCA peak systolic velocity and ICA end diastolic velocity. The presence of plaque, calcification, and intimal thickening involving the carotid vessels were noted. CAS was diagnosed and it's severity was graded as per the Society of Radiologists criteria as shown below.[2]

Monitoring was done using pulse oximetry, electrocardiography, invasive arterial blood pressure, end-tidal carbon dioxide, temperature and urine output charting. Central venous and pulmonary arterial catheter were placed via right Internal Jugular Vein under ultrasound guidance.

Severity of Stenosis	Characteristic
Normal	
	No carotid stenosis with ICA PSV <125 cm/s
	No plaque
	ICA/CCA <2
	ICA EDV <40 cm/s
Mild	
	<50% carotid stenosis
	ICA PSV <125 cm/s
	Plaque estimate <50%
	ICA/CCA ratio <2
	ICA EDV <40 cm/s
Moderate	
	50-69% carotid stenosis
	ICA PSV 125-230 cm/s
	Plaque estimate 50% or greater
	ICA/CCA ratio 2-4
	ICA EDV 40-100 cm/s
Severe	
	70% or greater carotid stenosis
	ICA PSV >230 cm/s
	Plaque estimate 50% or greater
	ICA/CCA ratio >4
	ICA EDV >100 cm/s

[ICA: Internal carotid artery, CCA: Common carotid artery ratio, PSV: Peak systolic velocity, EDV: End diastolic velocity]

Mean arterial pressure (60-80 mm Hg) was maintained with administration of fluid, vasopressors, maintaining heart rate and sinus rhythm. Nor-adrenaline infusion was started at the rate of 0.01-0.1 mcg/kg/minute when there was reduction of blood pressure more than 20 mmHg from the baseline & titrated to response. Pulmonary arterial pressure was maintained by adjusting nitrate infusion.

Temperature was maintained between 35.5-36.5 degrees celsius with warm fluids, low fresh gas flow, warming blankets and heat exchangers.

One of the goals in the perioperative management was cerebral protection by ensuring normotension, normocapnia, normothermia and euglycemia. Continuous invasive blood pressure monitoring was done throughout the conduct of the surgical procedure. Mean arterial pressure was documented as follows: Baseline (pre induction), pre-heparinization, post-heparinization, during grafting and post-protamine. Additionally, any variations in MAP more than 20mm Hg from baseline was considered as a significant event and was recorded. Normocapnia was maintained with serial ABG monitoring and adjustment of ventilator settings. $EtCO_2$ was titrated to 25-35mm Hg. Serial blood glucose monitoring was done at appropriate intervals. Target blood glucose was maintained between 120-180 mg/dl. For blood glucose levels above ≥ 180 mg/dl, an insulin infusion (1U/ml) was started. Normothermia (temperature between 35.5-36.5 degrees Celsius) was ensured as mentioned above. Postoperatively, patients were shifted to ICU on mechanical ventilation. Neurological examination was performed after extubation. Patients were followed up for one week in the postoperative period and clinically assessed for the presence of any ischaemic events including cognitive dysfunction, history suggestive of new TIA and stroke. A neurologist consultation was done when any suspicion of a neurologic symptom noticed and CT scan brain (plain) was performed. The study was concerned only with hemispheric strokes or transient ischemic attacks (TIAs).

Statistical Analysis was done with help of Epi Info ™ 7.2.2.2

Epi Info is a trademark of the Centers for Disease Control and Prevention (CDC).

Descriptive statistical analysis was carried out to calculate the means with corresponding standard deviations (s.d). Test of proportion was used to find the Standard Normal Deviate (Z) to compare the difference proportions. Chi-square (X^2) test was performed to find the associations between the variables. Corrected Chi-square (X^2) test was done to demonstrate the relation between the variables when one of the cell frequencies was less than zero. Z-test (Standard Normal Deviate) was used to identify the significant difference between two proportions. T-test was done to compare the means. Odds Ratio (OR) with 95% confidence interval (CI) was calculated to find the risk factors.

$p \leq 0.05$ was taken to be statistically significant and confidence intervals were set at 95%.

3. Results

Out of the 97 patients included in our study, 79 were male and 18 were female. Nineteen patients were aged 54 years or below, 44 patients were between 55 and 64 years and 34 patients were aged more than 65 years. The mean age (mean ± s.d.) of the patients was 61.32 ± 7.50 years with a range of 46 – 77 years and the median age was 61 years. Around seventy percent (63.9%) of the patients were smokers and the rest were non-smokers. Forty-four patients had a history of diabetes, 86 patients were hypertensive and 88 patients had a history of dyslipidemia. Around seventy percent had an ejection fraction of more than 50%, while the rest had below 50%. Forty-one patients had normal left ventricular systolic function as determined by preoperative echocardiography. Left main coronary artery was involved in 39 patients. Double vessel disease was present in 77 patients whereas 20 patients had involvement of multiple vessels. In the postoperative period only one patient had a single episode of transient ischemic attack.

About forty percent of the patients undergoing CABG had carotid artery stenosis which was lower than patients without carotid artery stenosis which was statistically significant ($Z=2.77$; $p<0.0001$). The prevalence of carotid

artery stenosis in our study was 40.2%. No patient had severe CAS.

There was significant association between severity of carotid artery stenosis and distribution among patients who were included in our study (p=<0.0001). Mild cases were prevalent significantly in higher proportion among the unilateral cases and moderate cases were prevalent significantly in higher proportion among the bilateral cases. (Table 1)

In our study risk factors associated with carotid artery stenosis were BMI >25kg/m2 (Table 4), smoking, left main coronary artery involvement and left ventricular systolic dysfunction (EF<50%).(Table 2) However, risk of CAS was also increased in hypertensive patients and those of age more than 55 years. Most of the patients (80.5%) were aged ≥ 55 years which was significantly higher than other age groups (Z=8.62; p<0.0001). This reflects that coronary artery disease is more prevalent among patients of older age group. However, age was not an independent risk factor of developing carotid artery stenosis in patients undergoing off pump CABG.

The proportion of males (81.4%) was significantly higher than that of females undergoing CABG (18.6%) (Z= 8.88; p<0.001). The above statement reflects that more male patients underwent CABG in comparison to female patients in our institution during the study period. Although the mean age of males was higher than that of females, t-test showed that there was no significant difference in mean age of males and females (t_{95}=0.82; p=0.27). There was no significant association between gender and carotid artery stenosis amongst patients who were included in our study (p=0.68). However, proportion of carotid artery stenosis was higher among the female patients (20.5%) as compared to male (17.2%) but it was not statistically significant (Z=0.59; p=0.41). The risk of carotid artery stenosis was 1.23 times more among the female patients as compared to the male patients but the risk was not significant [OR-1.28(0.44, 3.48); p=0.6].

There was significant association between habit of smoking and carotid artery stenosis (p=0.02) as shown in table no. 5. The risk of carotid artery stenosis was 2.70 times more among the smokers which was statistically significant [OR-2.70(1.09,6.70); p=0.02].

Around forty-five percent (45.2%) of the patients undergoing CABG had Type 2 Diabetes Mellitus (T2DM) but it was not significant statistically (Z=1.30; p=0.17). Even though proportion of carotid artery stenosis was higher among diabetic patients (48.7%) as compared to non-diabetic (43.1%), it was not significant (Z=0.79; p=0.66). The risk of carotid artery stenosis was 1.25 times more among diabetic patients as compared to non-diabetic but the risk was not significant statistically [OR-1.25(0.55, 2.83); p=0.58].

In our study, 88.7% of the patients undergoing off pump CABG had hypertension (HTN) which was significant statistically (Z=10.94; p<0.0001). However, there was no significant association between HTN and carotid artery stenosis (p=0.35). Although, the risk of carotid artery stenosis was 1.92 times more among the patients with HTN [OR-1.92(0.47, 7.74); p=0.35].

In our study population 90.7% of the patients had dyslipidemia which was significant statistically (Z=11.51; p<0.0001). Chi-square (X^2) test showed that there was no significant relation between dyslipidemia and carotid artery stenosis (p=0.32).

The mean left ventricular ejection fraction (LVEF) (mean ± s.d.) of the patients in our study population was 52.73% with range 42 – 60% and the median was 53%. The risk of CAS was 24.10 times higher among the patients with LVEF between 40-50% as compared to the patients with more than 50% which was significant statistically [OR-24.10(7.20, 80.69); p<0.001]. There was significant association between LV systolic dysfunction and carotid artery stenosis in the patients (p<0.001).

Left main coronary artery (LMCA) was involved in 87.2% of the patients who had carotid artery stenosis. The risk of carotid artery stenosis was 72.08 times more among the patients with LMCA involvement which was significant statistically [OR-72.08(19.40, 267.75); p<0.001].

In our study population, 79.4% of the patients who underwent CABG had double coronary vessel involvement (DVD) which was significantly higher than patients with multiple coronary vessel (MVD) involvement (20.6%) (Z=8.31; p<0.0001). However, Fisher Exact test showed that all patients with MVD involvement had CAS which was significant statistically (p<0.00001).

None of the patients had intraoperative change in Mean arterial pressure of >20 mmHg from baseline value throughout the conduct of anaesthesia. A single episode of neurological event (TIA) occurred only in one patient (1.03%) on the 1^{st} postoperative day. There were no episodes of stroke within 24 hours of surgery in our study population.

4. Discussion

Several literatures have revealed that presence of carotid artery stenosis (CAS) in subjects undergoing cardiopulmonary bypass increases the chance of adverse neurological events.[3–7] Previous studies that evaluated patients undergoing CABG with ultrasound have reported a prevalence of CAS varying from 6.1% to 66%.[8–12] In our study, the prevalence of CAS was found to be 40.2% which is consistent with previous studies. Mild disease was significantly higher among the unilateral cases while moderate cases were significantly higher in prevalence among the bilateral cases. Similarly, in a study comprising of 559 patients, Wanamaker et al.[13] shown a prevalence of

Table 1: Showing severity and distribution of carotid artery stenosis

Carotid artery stenosis severity	Distribution of Carotid Artery Stenosis			Total
	No disease	Unilateral	Bilateral	
Normal	58	0	0	58
Row %	100.0	0.0	0.0	100.0
Col %	100.0	0.0	0.0	59.8
Mild	0	20	13	33
Row %	0.0	60.6	39.4	100.0
Col %	0.0	100.0	68.4	34.0
Moderate	0	0	6	6
Row %	0.0	0.0	100.0	100.0
Col %	0.0	0.0	31.6	6.2
Total	58	20	19	97
Row %	59.8	20.6	19.6	100.0
Col %	100.0	100.0	100.0	100.0

P value < 0.0001

Table 2: Showing risk factors for the development of carotid artery stenosis as determined by this study

Risk Factor	P value
Age>=55 Years	<0.0001
Smoking	0.02
BMI>25.0 KG/M2	< 0.001
Diabetes	0.58
Dyslipidemia	0.32
Gender	0.68
Hypertension	0.35
Left Main Coronary Artery Disease	<0.001
Left Ventricular Function<50%	<0.001

Table 3: Showing association between BMI and Carotid artery stenosis in the patients

BMI (kg/m2)	With Carotid artery stenosis (n=39)	Without Carotid artery stenosis (n=58)	Total
>25	39	24	63
Row %	61.9	38.1	100.0
Col %	100.0	41.4	64.9
≤25	0	34	34
Row %	0.0	100.0	100.0
Col %	0.0	58.6	35.1
Total	39	58	97
Row %	40.2	59.8	100.0
Col %	100.0	100.0	100.0

Table 4: Showing association between habit of smoking and Carotid artery stenosis in the patients

Habit of smoking	With Carotid artery stenosis (n=39)	Without Carotid artery stenosis (n=58)	Total
Present	30	32	62
Row %	48.4	51.6	100.0
Col %	76.9	55.2	63.9
Absent	9	26	35
Row %	25.7	74.3	100.0
Col %	23.1	44.8	36.1
Total	39	58	97
Row %	40.2	59.8	100.0
Col %	100.0	100.0	100.0

P value 0.02

Table 5: Showing association of Left ventricular systolic dysfunction with carotid artery stenosis in the patients

Left ventricular systolic dysfunction	With Carotid artery stenosis (n=18)	Without Carotid artery stenosis (n=48)	Total
Moderate	8	0	8
Row %	100.0	0.0	100.0
Col %	20.5	0.0	8.2
Mild	24	24	48
Row %	50.0	50.0	100.0
Col %	61.5	41.4	49.5
Normal	7	34	41
Row %	17.1	82.9	100.0
Col %	17.9	58.6	42.3
Total	39	58	97
Row %	40.2	59.8	100.0
Col %	100.0	100.0	100.0

P value < 0.001

carotid artery disease (>50% stenosis) to be 36% with 18% having unilateral moderate disease, 10% bilateral moderate and 8% having severe disease. In another study, da Rosa et al.[14] demonstrated the prevalence of CAS >50% to be 17.4% among 393 patients who underwent elective CABG. Among these, 12.0% (47) had a stenosis between 50% and 69%, 7.1% (28) had a stenosis between 70% and 99%, and 0.3% (1) had an occlusion of ICA. In a study by Taneja et al.[1] age more than 65 years was found to be an independent risk factor for significant CAS. Faggioli et al.[15] showed that the rate of significant CAS rose from 3.8% for patients younger than 60 years to 11.3% for patients aged more than 65 years. In our current observation, coronary artery disease was mostly prevalent among the patients of age ≥55 years. However, there was no significant correlation between carotid artery stenosis severity and age of the patients who underwent off pump CABG (p=0.89).

No significant association was observed between gender and carotid artery stenosis (p=0.68). The age distribution of females showed a comparatively younger group had higher prevalence of CAS. Similarly, the gender of the patient did not bear any relation with CAS in a study by Siminelakis et al.[16] However, female patients coming for CABG are at greater risk for major adverse events than male patients because of the comorbidities that are associated with the old age at which women present for coronary surgery and not because of gender. On the contrary D'Agostino et al.[5] and Durand et al.[9] identified female gender as a risk factor for significant carotid stenosis. In our observation, there was no significant association between age and gender of the patients (p=0.48). Smoking emerged as an independent determinant of carotid artery stenosis in our study. This is in agreement with other literatures that also showed smoking to be a significant risk factor for the development of CAS.[5,10] Hypertension was not described to be a significant predictor of carotid artery stenosis in our observation. On the contrary, several other studies showed HTN as an independent determinant.[5,10,17] Dyslipidemia was identified as an independent risk factor for CAS in the study by Taneja et al.[1] whereas Faggioli et al.[15] did not demonstrate dyslipidemia to be a significant predictor. [20] In our observation, dyslipidemic patient was not found to be a determinant of CAS. Diabetes was not a risk factor of CAS in our observation. This is in contrast to previous literatures that demonstrated diabetes as an independent predictor.[5,10]

Mean body mass index (BMI) > 25 kg/m2 was found to be significantly associated with CAS in our study population. On the contrary, the study by Cheng et al.[18] found the BMI of patients with CAS significantly lower (25.0 +/- 2.7 kg/m2) than that of the patients without CAS (25 +/- 3.1 kg/m2). In our current observation, most of the patients who underwent off pump CABG had an ejection fraction (EF) of >50% (70.1%) which was significant statistically. However, the risk of carotid artery stenosis was 24.10 times more in patients with LVEF between 40-50% as compared to the patients with LVEF>50%. In our study, carotid artery stenosis and LMCA involvement were found to be significantly associated (p<0.001). Similarly, Berens et al.[19] found that LMCA stenosis was an independent predictor of significant CAS. Similar findings were also observed in other studies by Durand et al.[9] and Sheiman et al.[10] On the contrary, the study by Taneja et al.[1] did not find a correlation of CAS with LMCA disease. Stroke is a detrimental complication of coronary artery bypass grafting (CABG) with an incidence of 1.2%.[20] The majority of these ischaemic events occur in the first post operative day and are associated with a mortality rate of ~ 25%. In a survey of 2,108 patients for CABG by Roach and colleagues[7] 6.1% incidence of serious adverse neurologic events were described. Three percent of these patients had perioperative transient ischaemic episodes, whereas a further 3.1% had prolonged unconsciousness, seizures or encephalopathy. Advanced age and duration of CPB were the major predictors for adverse neurologic events. In another large prospective study, Newman and colleagues[21] observed that 3.2% of their study population

had neurologic consequences after isolated CABG. With the advent of off-pump CABG, there exists a possibility to reduce the incidence of adverse neurologic events. Off-pump coronary artery bypass doesnot require aortic cannulation and cross-clamping and hence avoid injury to the aorta and dislodgement of any atheroma. It also eliminates the formation of micro emboli from the bypass circuit, hence reducing the chance of thromboembolism. Most literatures have shown better neurologic outcomes in off-pump coronary surgery when compared with on-pump techniques,[22–25] while some have not.[26–28] Other studies showed a significant reduction in neurocognitive impairment in off-pump patients in small randomized controlled trials [24,25].

In our observation, 1.03% of the population with CAS were found to manifest transient ischaemic attack on postoperative day one during the follow up period. CT scan brain (plain) was done & neurologist opinion was sought.

Our study highlighted towards the vast prevalence (40.2%) of carotid artery stenosis in neurologically asymptomatic patients coming for elective off-pump CABG. This study emphasized the importance of evaluation of carotid stenosis by doppler ultrasound in the theatre and the subsequent modification of intraoperative anaesthetic management by ensuring normotension, normocapnia, normothermia and euglycemia. This would secure the adequacy of cerebral perfusion and minimize the chance of adverse neurological events in the postoperative period. Our study established a greater function for the anaesthesiologist in the perioperative management of these patients with either previously undiagnosed carotid artery disease or toward reassessment of severity of CAS.

Long term management of patients with carotid artery stenosis is based on medical therapy mainly. Carotid endarterectomy or carotid artery stenting is considered in symptomatic moderate and asymptomatic severe stenosis. In our study no patients had severe stenosis. Patients with mild and moderate CAS were followed up later as an outpatient basis and conservative management was approached in the form of lifestyle modification and pharmacological intervention.

5. Source of Funding

None.

6. Conflict of Interest

None.

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