

# Prevalence of carotid artery stenosis in neurologically asymptomatic patients undergoing coronary artery bypass grafting for coronary artery disease: Role of anesthesiologist in preoperative assessment and intraoperative management

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## ABSTRACT

**Objective(s):** This study aimed to determine the prevalence of carotid artery stenosis (CAS) due to atherosclerosis in neurologically asymptomatic patients undergoing coronary artery bypass grafting (CABG) for coronary artery disease (CAD). It contemplated a greater role for the cardiac anesthesiologist in the perioperative management of such patients with either previously undiagnosed carotid artery disease or towards re-assessment of severity of CAS. **Design:** Prospective, observational clinical study. **Setting:** Operation room of a cardiac surgery centre of a tertiary teaching hospital. **Participants:** A hundred adult patients with New York Heart Association (NYHA) classification I to III presenting electively for CABG. **Interventions:** All patients included in this study were subjected to ultrasonic examination by means of a carotid doppler scan to access for presence of CAS just prior to induction of general anesthesia. **Measurements and Main Results:** Based on parameters measured using carotid doppler, the presence of CAS was defined using standard criteria. The prevalence of CAS was found to be as high as 38% amongst the patients included in our study. The risk factors for CAS were identified to be advanced age, history of smoking, diabetes mellitus, dyslipidaemia and presence of a carotid bruit. **Conclusion:** This study points towards the relatively wide prevalence of carotid artery disease in neurologically asymptomatic patients undergoing CABG for CAD in the elective setting. It highlights the need to routinely incorporate carotid ultrasonography in the armamentarium of the cardiac anesthesiologist as standard of care for all patients presenting for CABG.

**Key words:** Carotid artery stenosis; Carotid Doppler; Coronary artery bypass grafting; Coronary artery disease; Neurological dysfunction; Role of anesthesiologist

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## INTRODUCTION

Neurological dysfunction after cardiopulmonary bypass (CPB) is a well-known and a potentially deleterious complication in patients undergoing coronary artery bypass grafting (CABG) with manifestations ranging from transient symptoms to evolved stroke. The overall incidence of stroke after CABG has been determined by previous studies to be in

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the range of 2.1–5.2% with a reported mortality of 0–38%.<sup>[1]</sup> The presence of an atheroma resulting in carotid artery stenosis (CAS) is a direct cause of cerebral ischemia during CPB with resultant postoperative neurological dysfunction contributing to a high incidence of morbidity and mortality. Detection of this impediment to adequate cerebral blood flow before CPB could allow clinicians to suitably alter the intraoperative management of these patients to reduce the occurrence of neurological deficits after CPB. Carotid ultrasound is a commonly available noninvasive modality that can be used preoperatively in the operation theater to detect the presence of CAS with relative ease and a high cost–benefit ratio. In the present prospective study, the authors delineate the importance of detecting CAS using carotid Doppler before induction of anesthesia in patients undergoing CABG. By utilizing this relatively simple and easy to perform bedside technique, patients at a high risk of cerebral ischemia are identified, thereby allowing for suitable adjustments in the conduct of anesthesia and CPB so as to avert adverse neurological sequel.

#### Aims and objectives

This study aimed to determine the prevalence of CAS due to atherosclerosis in neurologically asymptomatic patients undergoing CABG for coronary artery disease (CAD). The specific objectives were (a) determination of the presence of atheroma in the carotid arteries causing CAS, (b) evaluating the severity of stenosis by Doppler ultrasound, and (c) contemplating the possibility of a greater role for anaesthesiologists in the intraoperative management of these patients.

## MATERIALS AND METHODS

#### Study design: Prospective observational study

##### Setting

The study was undertaken in the operation theater of a cardiovascular sciences center of a large, tertiary teaching hospital which is an integral part of a national institute.

##### Patient population

After obtaining institutional ethical clearance and written informed consent from the participants, 100 consecutive adult patients with New York Heart Association (NYHA) classification I–III scheduled for elective CABG with CPB for CAD were evaluated ultrasonically for the presence of CAS.

#### Inclusion criteria

All neurologically asymptomatic patients with CAD in NYHA classification III and below scheduled for CABG with CPB were included in the study.

#### Exclusion criteria

Patients with previously known carotid artery disease, history of having undergone carotid artery endarterectomy or stroke or neurological symptoms attributable to CAS, hemodynamically unstable patients and patients who were unable to lie down supine for assessment, patients with arrhythmias or tricuspid valve disease, and those presenting for emergency CABG were excluded from the study.

#### Technique

A history of diabetes, dyslipidemia, smoking, hypertension and preexisting neurological dysfunction or stroke, and drug history was obtained preoperatively from the medical records of the patient. Echocardiography and coronary angiography were performed on all patients as part of the workup preceding surgery. On the day of surgery, all patients received their prescribed preoperative cardiac medication with the exception of angiotensin-converting enzyme inhibitors, angiotensin II antagonists, and diuretics. Premedication consisting of morphine in a dose of 0.1 mg/kg and intramuscular promethazine in a dose of 0.5 mg/kg was administered intramuscularly half an hour before shifting the patient inside the operating room (OR) for surgery. Before induction of anesthesia, all patients were examined clinically to detect the presence of a bruit or murmur over carotid vessels in the lateral aspect of neck bilaterally. The patients were then placed in a supine position on the operating table in the OR and subjected to an ultrasonic examination of the neck using a SonoSite M-Turbo machine (SonoSite Bothell, WA USA) with a linear 10–5 MHz probe to determine the presence of an atheroma or occlusion blood flow involving the carotid arteries bilaterally. Color Doppler was used to obtain the blood flow velocities in the common carotid, external and internal carotid arteries (ICAs). The parameters recorded were ICA peak systolic velocity, ICA – common carotid artery ratio (ICA), and ICA end diastolic velocity (ICA). The presence of plaque, calcification, and intimal thickening involving the carotid vessels was noted. A diagnosis of CAS made its severity graded as per the Society of Radiologists in Ultrasound criteria.<sup>[2]</sup> The

patients were accordingly classified into four groups as shown in Table 1.

All patients were monitored in the OR using electrocardiography, invasive arterial blood pressure, pulse oxymetry, temperature, end-tidal carbon dioxide, near infrared spectroscopy (NIRS), bispectral index, arterial blood gas analysis, and urine output charting throughout the conduct of the surgical procedure.

#### Data analysis

The prevalence of CAS (along with associated risk factors) in this select group of patients undergoing CABG was determined statistically from the data collected. Statistical analysis was performed using SPSS version 20 (IBM Corporation USA) software and significance was determined using the Pearson's Chi-square test. A  $P < 0.05$  was considered statistically significant.

## RESULTS

Among a total of 100 patients who were included in this study, 76 were male and 24 were female. Seven patients were 45 years or below, 32 were between 46 and 55 years, and 25 were older than 65 years. The mean age was  $59.27 \pm 9.18$  years. Thirty-one percent of the patients were smokers and 48% were nonsmokers. Fifty-two patients were hypertensive, 48 were normotensive, 40 had a history of diabetes, and 15 patients had left main (LM) CAD. Fourteen patients had mild left ventricular (LV) dysfunction whereas 11 patients had moderate and 4 had severe LV dysfunction. Seventy-one patients had normal LV function as determined by preoperative two-dimensional echocardiography. Twenty percent of the patients studied had a history of dyslipidemia. Six patients were found to have carotid bruit before induction of general anesthesia. The number of patients found to have carotid artery disease using preoperative Doppler examination was 38 (38%). Of these patients, 19 (50%) had bilateral disease and 19 (50%) had unilateral disease.

Sixty-two (62%) of the total number of patients studied were found to be normal whereas 38 (38%) were found to have  $>50\%$  CAS. Of these 38 patients with CAS, 28.0 (28%) patients had mild CAS, 8.0 (8%) had moderate CAS and 2.0 (2%) had severe CAS, 19 (19%) of the total number of patients with CAS had unilateral, and another 19 (19%) had bilateral CAS [Table 2].

Advanced age, history of smoking, diabetes, dyslipidemia, and the presence of a carotid bruit were determined to be

**Table 1: Classifications of patients with carotid stenosis**

Severity of stenosis	Characteristics
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

**Table 2: Distribution and severity of carotid artery stenosis**

Severity of stenosis	No disease	Unilateral disease	Bilateral disease	Total no. of cases
Normal				
No. of cases	62	0	0	62
Percentage	100.0	0.0	0.0	100.0
Mild				
No. of cases	0	16	12	28
Percentage	0.0	57.1	42.9	100.0
Moderate/severe				
No. of cases	0	3	7	10
Percentage	0.0	30.0	70.0	100.0
Total				
No. of cases	62	19	19	100
Percentage	62.0	19.0	19.0	100.0

risk factors for the development of CAS among patients included in this study [Table 3]. Age  $>65$  years was found to be an independent risk factor and was incrementally related with the degree of stenosis ( $P = 0.001$ ). Eighteen (47.4%) of the 88 patients with CAS were older than 65 years of age, 14 (36.8%) were in the age group of 56–65 years, 4 (10.5%) were in the 46–55 years age group, and 2 (5.3%) were  $<45$  years of age [Table 4].

Sex of the patient was not found to be associated with an increased risk of CAS in this study ( $P = 0.219$ ).

**Table 3: Risk factors for the development of carotid artery stenosis as determined in this study**

Risk factor	P value
Age	0.001
Smoking	<0.001
Diabetes	<0.001
Dyslipidaemia	<0.001
Carotid bruit	0.002
Gender	Insignificant
Hypertension	Insignificant
Left main coronary artery disease	Insignificant
Left ventricular function	Insignificant

Significance was determined by Pearsons Chi Square test

**Table 4: Age- wise distribution of carotid artery stenosis**

Age group	Degree of stenosis			Total
	Normal	Mild	Moderate/ severe	
<b>≤45</b>				
Number	5	1	1	7
Percentage	71.4	14.3	14.3	100.0
<b>46-55</b>				
Number	28	4	0	32
Percentage	87.5	12.5	0	100.0
<b>56-65</b>				
Number	22	10	4	36
Percentage	61.1	27.8	11.1	100.0
<b>&gt;65</b>				
Number	7	13	5	25
Percentage	28.0	52.0	20.0	100.0
<b>Total</b>				
Number	62	28	10	100
Percentage	62.0	28.0	10.0	100.0

Smoking was found to be an incremental risk factor for CAS ( $P < 0.001$ ). Of a total of 28 patients with mild CAS, 13 (46.4%) were smokers and 15 (53.6%) were nonsmokers while of the 10 patients with moderate to severe CAS, 7 (70%) were smokers and 3 were nonsmokers. Of the 62 patients who did not have carotid artery disease, only 11 (17.7%) were smokers and 51 (82.3%) were nonsmokers. Diabetes was found to be an independent risk factor for CAS ( $P = 0.001$ ) and incrementally correlated with the severity of disease ( $P = 0.003$ ). Twenty-three (60.5%) of the 38 patients with CAS were diabetic whereas only 17 (27.4%) of the 68 patients who did not have CAS had diabetes. Of a total of 28 patients with mild CAS <50% stenosis, 18 (64.3%) had diabetes while 10 (35.7%) did not and of the 10 patients with moderate/severe CAS, 5 (50%) each was diabetic and nondiabetic, respectively. Dyslipidemia was found

to be significantly associated with the presence of CAS and was found to an independent risk factor for CAS ( $P < 0.001$ ). Fifteen (39.5%) of the 38 patients with CAS had dyslipidemia as against 20 (20%) of the patients with normal carotid vessels. The degree of stenosis was significantly related to the presence of dyslipidemia ( $P = 0.000$ ). Of the 28 patients with mild CAS, 10 (35.7%) had dyslipidemia while of the 10 patients with moderate to severe CAS, 5 (50%) had dyslipidemia. The presence of a carotid bruit was significantly associated with CAS ( $P = 0.002$ ). Six (15.8%) of the 38 patients detected with CAS in this study were found to have a carotid bruit on clinical examination before induction of anesthesia. The overall prevalence of carotid bruit among who participated in the study was 6%. Carotid bruit was absent in all patients who did not have CAS and all patients with carotid bruit were diagnosed with moderate to severe stenosis.

Systemic hypertension was not found to be significantly independent risk factor for CAS in this study ( $P = 0.543$ ). Of the 38 patients with CAS, 20 (52.6%) were hypertensive and 18 (47.4%) were normotensive. Of the 62 normotensive patients, 32 (51.6%) had CAS whereas 30 (48.4%) did not have CAS. The presence of LM disease was also not found to be associated with CAS ( $P = 0.461$ ). Fifteen (15%) patients in this study had LM disease while 85% (85) did not have LM disease. The degree of CAS was not related with the severity of LV dysfunction ( $P = 0.743$ ).

## DISCUSSION

Previous studies that evaluated patients undergoing CABG with duplex ultrasound done preoperatively have reported a prevalence ranging from 6.1% to 66%.<sup>[1-7]</sup> In our study, the prevalence of CAS was found to be 38% which is consistent with that reported previously. Of these patients with CAS in our study, 28% had <50% degree of CAS, 8% had 50–69% stenosis, and 2% had >70% stenosis. None of the 100 patients studied had “near occlusion” or “total occlusion” of the carotid arteries. The prevalence of both unilateral or bilateral disease was 19%. Also, 57.16% of the patients with <50% CAS had unilateral disease and 4.29% had bilateral stenosis of the carotid arteries. In patients with >50% CAS, 30% had unilateral and 70% had bilateral CAS. The patients with severe CAS >70% had bilateral stenotic lesions affecting the carotid arteries. In a study comprising of 559 patients,



Wanamaker *et al.* determined an incidence of carotid artery disease (>50% stenosis) to be 36% with 18% unilateral moderate disease, 10% bilateral moderate and 8% severe disease.<sup>[8]</sup> Al-Fayez *et al.* reported that in their study comparing 102 patients, 86.3% had CAS while 16.6% had ≥50% stenosis of both carotids.<sup>[9]</sup> They found unilateral lesion >50% in 9.8% of the patients, bilateral lesions >50% in 6.8% of the patients and 2.9% with bilateral stenosis >80%. In another study, da Rosa and Portal found prevalence of CAS >50% to be 17.4% among 393 patients who underwent elective CABG. Of 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 ICA occlusion. About 67.1% (51) of the patients with a stenosis ≥50% were male.<sup>[10]</sup> Mahmoudi *et al.* performed carotid duplex ultrasound in 878 patients before isolated CABG and found that 13% had a carotid stenosis >75%. Significant predictors for CAS were age >69 and peripheral vascular disease.<sup>[5]</sup> D'Agostino stated that CAS >50% was seen in 20% with 8% of the patients having CAS >80% in their study with bilateral lesion >80% seen in 1.8% of the patients.<sup>[11]</sup> Durand *et al.* detected CAS >50% in 13.4% of patients, and Drohomirecka *et al.* found that CAS >50% in 18% of the patients studied with unilateral lesions in 12.9% and bilateral in 5.1%.<sup>[1,4]</sup> Rath *et al.* reported the prevalence of CAS as 84.5% whereas it was 61.6% in another study by Cirilo *et al.*<sup>[12,13]</sup> Shirani *et al.* reported the prevalence of CS >60% as 6.6% and 12.5% in patients who were 65 years and older. They found age >50 years, female gender, hypercholesterolemia, and diabetes mellitus to be independent risk factors for significant CAS.<sup>[14]</sup>

Age was found to be an incremental risk factor for CAS in our study with an increase in the number of patients with CAS with advancing age above 65 years (18%).

Faggioli *et al.* showed that the rate of significant CAS rose from 3.8% for patients younger than 60 years to 11.3% for patients above the age of 65 years.<sup>[15]</sup> Shirani *et al.* found age >50 years to be an independent risk factor for carotid stenosis with a prevalence of significant stenosis to be 7.9% for 50 years and over as compared to 1.3% for <50 years of age.<sup>[14]</sup> Berens *et al.* analyzed 1068 patients and found that 15.6% had carotid stenosis >50% with a 4% prevalence in those aged <60 that rose to 11% in patients >60 years and 15 and in those >70 years of age.<sup>[16]</sup> Several other studies showed advanced age to be an independent risk factor for stroke in

CABG.<sup>[4,8,11,17-19]</sup> The gender of the patient did not bear any correlation with CAS in our study as was also determined by Al-Fayez *et al.* and Siminelakis *et al.*<sup>[9,19]</sup> However, other studies found female gender to be a predictor of carotid stenosis. D'Agostino *et al.*, and Durand *et al.* identified female gender as a risk factor for significant carotid stenosis.<sup>[7,8,11,20,21]</sup> Smoking emerged as an independent risk factor in our study. This is in agreement with other studies that also found smoking to be a significant risk factor for development of CAS.<sup>[7,9,11,22]</sup> Diabetes was also found to be a significant predictor of CAS in our study as concluded in several other studies.<sup>[7,11,12]</sup> Dyslipidemia was identified as an independent risk factor for CAS in our study as was also reflected by Shirani *et al.* whereas Fagoli *et al.* did not identify dyslipidemia to be a significant risk factor in their study.<sup>[14,16]</sup> Carotid murmur was detected in 15.6% (6 patients) of the patients who has CAS in our study while da Rosa and Portal found it to be 35.5% (27 patients).<sup>[10]</sup>

In our study, hypertension was not determined a predictor for CAS. This is in contrast to previous studies that found that presence of hypertension was an independent risk factor of CAS.<sup>[7,9,11,20,21]</sup> Our study did not find an association of CAS with LM coronary artery (LMCA) disease as has also been reported by Kiernan and Taqueti. In contrast, Berens *et al.*<sup>[16]</sup> found that LMCA stenosis was an independent predictor of significant CAS as also other studies by Durand *et al.* and Sheiman and Bertrand.<sup>[1,7]</sup> Al-Fayez *et al.* reported the LMCA disease was an independent risk factor for CAS. In their study, 38% of the patients with significant LMCA disease were also found to have significant CAS while the overall incidence of LMCA disease in patients undergoing CABG was only 12.7%.<sup>[9]</sup> Salehiomran and Shirani showed that significant LMCA disease was seen in 12.1% and Rath *et al.* showed a prevalence of 12% in this respective studies.<sup>[12,20]</sup> Prior history of CVA/TIA has been reported as an independent risk factor in previous studies. Our study excluded patients with previous history of CVA/TIA to focus on neurologically asymptomatic patients undergoing CABG.<sup>[1,4,11]</sup> Prior stroke, peripheral vascular disease, and end-stage kidney disease have also been reported as risk factors in other studies.<sup>[8,18,19,23]</sup>

As per current recommendations delineated in the 2011 ACCF/AHA guideline for CABG surgery, in CABG patients with previous TIA or stroke and a significant

(50–99%) CAS, it is reasonable to consider carotid revascularization in conjunction with CABG. In such individuals, the sequence and timing (simultaneous or staged) of carotid intervention and CABG should be determined by the patient's relative magnitudes of cerebral and myocardial dysfunction (Class IIa, Level of Evidence: C). In patients scheduled to undergo CABG who have no history of TIA or stroke, carotid revascularization may be considered in the presence of bilateral severe (70–99%) carotid stenosis or a unilateral severe carotid stenosis with a contralateral occlusion<sup>[24]</sup> (Class IIb, Level of Evidence: C). However, there is still lack of clarity due to paucity of published randomized controlled trials regarding optimal management of patients with coexisting carotid artery disease and CAD. The different therapeutic approaches that are used include staged carotid endarterectomy and CABG, simultaneous carotid endarterectomy and CABG, or similar variations that use endovascular stenting as the primary carotid.<sup>[24,25]</sup>

#### Interventions undertaken in our study

Patients identified with significant impediment to carotid blood flow and thereby at a high risk for adverse neurological outcomes in this study were managed with higher pump flow maintaining mean arterial pressure in a higher target range of 70–90 mmHg with mild hypercarbia (PaCO<sub>2</sub> 40–45 mmHg) and induced hypothermia with temperature maintained between 30°C and 32°C during the bypass procedure. All patients were monitored using cerebral oxymetry (NIRS).<sup>[26-28]</sup> The regional cerebral oxygen saturation values were monitored and interventions made to normalize these in patients with significant carotid stenosis. Vasoactive drug infusions and cerebroprotective measures were, thus, so targeted to optimize cerebral perfusion and reduce the possibility of adverse neurological outcomes in these patients.

Of the 100 patients that were included in this study, one patient with critical CAS with 80% occlusion involving the right ICA was taken up for concomitant carotid endarterectomy and CABG in the same sitting. Patients were followed up in the postoperative period of 1 month after having undergone CABG and clinically assessed for the presence of neurological deficits including cognitive dysfunction, history suggestive of fresh TIA, and stroke. None of the patients participating in the study were found to manifest neurological dysfunction post-CABG during the follow-up period.

The authors recommend the use of color Doppler routinely in the preoperative assessment protocol in these patients before induction of anesthesia and the use of the described techniques to maintain adequate cerebral perfusion throughout the procedure.

#### Limitations

A limitation of this study is that carotid angiogram or cross-sectional computed tomographic imaging was not done to corroborate the findings of the color Doppler examination of the vessels of the neck. Risk stratification of the patient was also not carried out in the preoperative period. A selection bias could not be entirely ruled out as only those patients presenting to the OR were taken up in this study. Inter-observer bias was, however, excluded by means of the same operator performing the Doppler examinations in all patients.

#### CONCLUSION

This study points toward the relatively wide prevalence of carotid artery disease in neurologically asymptomatic patients undergoing CABG for CAD in the elective setting. It highlights the importance of subjecting these patients to evaluation by means of Doppler ultrasound of the carotid vessels in the OR immediately before induction of anesthesia and the subsequent customization of anesthetic technique as well as surgical approach. This would go a long way in ensuring the adequacy of cerebral perfusion with the aim of minimizing the possibility of devastating neurological sequel in the postoperative period. The authors recommend the incorporation of this commonly available and easy to use bedside technique of Doppler examination of the carotid vessels in routine intraoperative practice as the standard of care in all patients undergoing CABG for CAD.

However, larger multicenter studies are required to further establish the efficacy of this approach in reducing the incidence of neurological complications in this group of patients and demonstrating its impact on survival and reduction in morbidity and mortality. Nevertheless, the authors envisage a greater role for the cardiac anaesthesiologist in the perioperative management of such patients with either previously undiagnosed carotid artery disease or toward reassessment of severity of CAS.

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#### Conflicts of interest

There are no conflicts of interest.

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