Evaluation of Asymptomatic Carotid Artery Stenosis Prior to Coronary Artery Bypass Grafting - A Prospective Observational Study in North Indian Population

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Abstract

**Background:** Carotid artery stenosis (CAS) is an established risk factor for peri-operative neurological complications in patients following coronary artery bypass grafting (CABG). However, routine pre-surgical screening for CAS is still a matter of debate. This study was conducted to study the prevalence of asymptomatic carotid artery disease in patients undergoing CABG and to determine the predictors of significant carotid stenosis in them. **Methods:** In this prospective observational study, 112 patients, who were planned for CABG, were enrolled, and their demographic details, risk factor profile, and coronary angiogram parameters were analyzed. **Results:** Carotid stenosis was observed in 75.0% of the study population with 11.6% having unilateral and 63.4% having bilateral carotid stenosis. A total of 56.2% of the patients had mild, 14.3% had moderate, and 4.5% had severe carotid stenosis. The presence of significant carotid stenosis showed a correlation with chronic stable angina (P = 0.009), significant left main (LM) disease (P = 0.001), chronic total occlusion (P = 0.043), and coronary vessel calcification (P = 0.004). Multivariate analysis of all the predictor variables in a regression model showed that significant LM disease (Odds ratio (OR):6.5, P = 0.002) and coronary artery calcification (OR: 4.3, P = 0.024) were the only independent predictors of significant CAS in the study population. **Conclusion:** The presence of significant carotid vessel stenosis in patients undergoing CABG in the Indian population has a stronger association with the chronicity of the coronary artery disease rather than the coronary atheroma load (as determined by the modified Gensini score). The presence of significant LM disease and coronary artery calcification may be useful in detecting high-risk patients for significant CAS during the pre-surgical workup.

**Keywords:** Atherosclerosis, carotid artery stenosis, coronary artery bypass grafting, coronary artery calcification, coronary artery disease, left main disease, stroke

**Introduction**

In the past century, India has witnessed a sudden rise in cardiovascular diseases as a major contributor to mortality.[1] As compared to the people of European descent, cardiovascular diseases impact the Indian population much earlier, thereby, affecting their working years. The data from western countries reported 23% cardiovascular disease-related deaths before the age of 70 years whereas it is as high as 52% in many parts of India.[2,3]

Atherosclerosis is a generalized process involving whole-body vasculature. In patients presenting with advanced coronary artery disease (CAD), who are planned for coronary artery bypass grafting (CABG), carotid arteries may also be affected by atherosclerosis. Several studies have shown that the extent of CAD might determine the incidence of carotid artery stenosis (CAS). CABG is the treatment of choice in patients presenting with a high atherosclerotic burden in the coronary arteries.[4] However, cerebrovascular accidents following CABG are a major source of morbidity as well as mortality. Though the exact pathophysiology of adverse neurological outcomes post-CABG is still unknown, the reported risk factors include CAS, hypotension, arrhythmias, aortic atherosclerotic disease, and transient prothrombotic state.[5] The global data on post-operative stroke in patients undergoing CABG predict an average risk of 0.4–6% with a relatively higher risk in the elderly age group and a reported mortality of 0–38%.[6,7] Furthermore, the incidence of stroke following surgery is 2.9% in asymptomatic unilateral carotid stenosis which increases up to 6.7% in bilateral stenosis.[8]

So, here in this study, we have analyzed the prevalence of significant CAS in the Indian patients planned for CABG who were otherwise asymptomatic for carotid artery disease. Also, we have attempted to determine certain patient-related factors that might be linked to the incidence of CAS in these patients.
risk factors and other laboratory parameters that can be used as accurate predictors of significant CAS in these patients.

**Materials and Methods**

This study was a prospective, observational study conducted at a tertiary center in North India over 18 months from July 2019 to December 2020. The study enrolled 112 patients from a single center (Advanced Cardiac Center, Postgraduate Institute of Medical Education and Research) who were planned for CABG in view of severe coronary atherosclerosis and had no previous history suggestive of carotid disease. Written and informed consent was obtained from all the participants of the study. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and has been approved by the Institute Ethics Committee (NK/5776/MD/462 – 27.11.19).

Detailed history regarding the patient’s demography including the patient’s age, sex, area of residence, race and ethnicity, medical history, and history regarding the symptoms and progression over the years was taken. The daily physical activity level of the patients was determined with the help of the ‘International Physical Activity Questionnaire (IPAQ)—short form’ which divided the participants into three categories of low (sedentary), moderate, and high (heavy) physical activity. Carotid auscultation was performed in all the patients to record the presence of any audible carotid bruit. Echocardiography was performed in all the patients using an EPIQ 7 C ultrasound system (Philips Healthcare™, Andover, MA, United States) by an experienced cardiologist according to standard guidelines and modified Simpson’s method was used to assess the left ventricular systolic function.

**Assessment of coronary angiography and modified Gensini score**

Coronary angiogram was obtained either through the radial or femoral route, and then, interpreted by a single experienced observer. The interpreter was blinded to the history and carotid artery Doppler findings of the patient. Based upon the interpretation, the modified Gensini score was calculated.

Other parameters like the presence of significant left main (LM) disease (>50% stenosis), chronic total occlusions (CTO), coronary artery calcification, and any evidence of collateral circulation were also noted.

**Carotid artery Doppler ultrasound**

Carotid artery Doppler ultrasound was performed by a single experienced radiologist using B-mode images (Philips iU22; Philips Medical Systems™, Bothell, WA, United States) with a high-resolution transducer of 5–12 dB. The patients were advised not to have alcohol or nicotine 12 h before examination and recommended to consume only clear liquids. The findings of the carotid artery Doppler ultrasound were documented as the degree of stenosis (%), peak systolic velocity (cm/s), and degree of plaque (%). According to these parameters, the patients were stratified into no, mild, moderate, and severe stenosis [Table 1].

Both moderate and severe stenoses were considered as significant CAS.

**Statistical analysis**

All the data were analyzed using IBM SPSS version 26.0. Continuous and categorical variables were represented as mean ± standard deviation and as frequency (percentage), respectively. The Chi-square test and Fisher’s exact test were used to compare the categorical variables while Student’s t-test or Wilcoxon’s–Mann–Whitney test was used for comparison of continuous variables. A multivariate regression analysis model was used to determine the independent predictors of outcome among all the parameters that showed significant correlation individually. Statistical significance was considered for P value < 0.05.

**Results**

Among the total 112 enrolled patients, 86 (76.8%) patients were males. A majority (65.2%) of the participants presented as unstable angina/non-ST-elevation myocardial infarction followed by ST-elevation myocardial infarction (27.7%) and chronic stable angina (6.2%). The baseline demographic, risk factors of the patients, characteristics of coronary angiograms, and carotid Doppler are depicted in Table 2. Carotid bruit was noted in 10.7% of the patients. LM disease was present in 23.2% of the patients and CTO was reported in 29.5% of the patients. The mean ejection fraction of the population was 38.39 ± 11.51% and left ventricular systolic dysfunction (ejection fraction <45%) was noted in 71.4% of the patients. The mean of the modified Gensini score was 139.86 ± 83.34 and the median (Interquartile range (IQR)) of the modified Gensini score was 126 (72.75–188.25). CAS was observed in 75% (n = 84) of the patients of which 84.5% (71/84) had bilateral stenosis. Significant stenosis (moderate and severe) was seen in 25% (21/84) of the patients with CAS and 18.8% (21/112) of the total population.

The comparison of the risk factors and CAD characteristics in the patients with significant CAS is shown in Table 3. The incidence of diabetes mellitus, hypertension, smoking, dyslipidemia, and family history of CAD was found to be similar in the groups with and without CAS. More number of patients with chronic stable angina had significant CAS (19.04% vs. 3.2%, P = 0.009). Carotid bruit was seen in 57.1% of the patients with significant CAS. LM disease was higher in patients with significant CAS (52.3% vs. 16.4%, P < 0.001). Coronary artery calcification was seen more in patients with significant CAS (42.8% vs. 13.1%, P = 0.004). Modified Gensini score was similar in patients with and without significant CAS (164.52 ± 105.41 vs. 134.16 ± 76.95, P = 0.288).

Multivariate analysis of the predictor variables (P < 0.1) in a regression model showed that significant LM disease (OR: 6.5, P = 0.002) and coronary vessel calcification (OR: 4.3, P = 0.024) were the only independent predictors of the significant carotid stenosis in the study population [Table 4].
**Table 1: Grading of the severity of stenosis**

| Severity of CAS   | Degree of Stenosis (%) | PSV (cm/s) | Degree of Plaque (%) |
|-------------------|-------------------------|------------|----------------------|
| No stenosis       | Normal                  | <125       | None                 |
| Mild stenosis     | <50%                    | <125       | <50%                 |
| Moderate stenosis | 50-69%                  | 125-230    | >=50%                |
| Severe stenosis   | 70-99%                  | >230       | >=50%                |
| Near-total occlusion | High, low, or undetectable |           | Visible              |
| Total occlusion   | Undetectable            |            | Visible with no detectable lumen |

**Table 2: Baseline details and findings on coronary angiography and carotid Doppler ultrasound of the study patients**

| Characteristics                                      | n (%)     |
|------------------------------------------------------|-----------|
| Risk Factors                                         |           |
| Diabetes mellitus                                    | 43 (38.4%)|
| Hypertension                                         | 59 (52.7%)|
| Smoking history                                      | 39 (35.3%)|
| Alcohol intake history                               | 50 (44.6%)|
| Family history of coronary artery disease            | 15 (13.4%)|
| Dyslipidemia                                         | 81 (72.3%)|
| Physical Activity—International Physical Activity    |           |
| Questionnaires (IPAQ)—short form                    |           |
| Low (Sedentary)                                      | 40 (35.7%)|
| Moderate                                             | 72 (64.3%)|
| High (heavy)                                         | 0 (0.0%)  |
| Coronary/Carotid Parameters                          |           |
| Significant left main disease                        | 26 (23.2%)|
| Triple vessel disease                                | 105 (93.8%)|
| Chronic total occlusion                              | 33 (29.5%)|
| Coronary calcification                               | 21 (18.8%)|
| Carotid artery stenosis severity (n=84)              |           |
| Mild                                                  | 63 (75.0%)|
| Moderate                                              | 16 (19.0%)|
| Severe                                                | 5 (6.0%)  |
| Significant carotid stenosis (n=84)                  | 21 (25.0%)|
| Significant carotid stenosis (n=112)                 | 21 (18.8%)|

Data are presented as mean±SD, or n (%)

**DISCUSSION**

Stroke, after CABG, is an unwarranted and devastating complication that adds to morbidity as well as mortality pertaining to the surgical procedure. CAS has been identified as a significant risk factor of this neurological complication. Atheroma in the carotid vessels increases the risk of stroke by embolization from an ulcerated plaque or due to distal hypoperfusion in the vessels with critical stenosis. The existing guidelines recommend routine screening for carotid stenosis in patients with a history of transient ischemic attack/stroke/carotid disease/peripheral vascular disease, however, there is a lack of guidelines which recommend such screening for carotid stenosis in asymptomatic patients with no such history. Also, the existing guidelines have been formulated using data collected from patients in western countries, and hence, may not be relevant to the Indian population. Hence, this study has been conducted to evaluate the prevalence of significant CAS in patients undergoing CABG in North India.

In this study, significant CAS was reported in 18.8% of the patients undergoing CABG. Furthermore, the presence of significant LM disease and coronary artery calcification was found to be the independent predictors of significant CAS. Carotid stenosis was observed in 75% of the patients of whom 56.2% had mild, 14.3% had moderate, and 4.5% had severe stenosis. A numerically higher percentage of significant carotid stenosis (18.8%) was reported in our study as compared to the studies by Taneja et al. (10.0%) and Masabni et al. (13.5%), however, similar results were reported by Drohomirecka et al. (18%). Carotid bruit was heard in 57.1% of the patients with significant CAS which was significantly higher than reported in a previous study by Rosa et al. (35.1%).

In our study, univariate analysis revealed a significant association of the presence of significant CAS with chronic stable angina, presence of significant LM disease, CTO, and coronary artery calcification. However, the multivariate analysis showed significant LM disease and coronary artery calcification as independent predictors of significant CAS, which was in agreement with the previous studies by Berens et al., Durand et al., and Sheiman et al.. On the contrary, various previous studies have also shown hypertension, female gender, diabetes, and dyslipidemia as independent predictors of significant CAS. Furthermore, the modified Gensini score is a surrogate marker of the atherosclerotic burden of coronary arteries. However, in our study, this score could not differentiate between the patients with and without significant CAS as compared to a previous study by Avcı et al. where they found a significant correlation between the modified Gensini score and significant CAS.

Thus, it can be implicated from the study that the presence of significant CAS in patients undergoing CABG in the Indian population has a stronger association with the chronicity of CAD (higher proportion in chronic stable angina than acute coronary syndrome, significant LM disease, CTO, and coronary artery calcification) rather than the coronary atheroma load (as determined by the modified Gensini score). The possible explanation for such an observation may be the faster progression of atherosclerosis in the coronary vessels as compared to the rest of the central and peripheral vessels.
vasculature in the Indian population. This observation may also be attributed to the differential caliber of the coronary and the carotid vessels (significant stenosis of the LM has an association with significant stenosis of the carotid vessels and both have comparable vessel diameters—LM [4.5 ± 0.5 mm], internal carotid artery [4.66 ± 0.78 mm], and common carotid artery [6.10 ± 0.80 mm]).[23,29] Furthermore, as the presence of the significant LM disease and coronary artery calcification are independent predictors of significant carotid stenosis, they should be utilized as indicators to detect those patients who may have an asymptomatic significant carotid disease, and hence, require evaluation before CABG to prevent post-operative neurological complications.

**Study limitations**

There are several limitations in our study which include a small sample size leading to various biases; quantitative coronary angiography was not used which may have improved the efficacy of the study. The neurological complications following CABG were not analyzed in our study. Also, therapeutic options (carotid endarterectomy during CABG) for the significant carotid disease were not analyzed. Further, larger studies on heterogeneous patient populations are required in the future to validate our findings.

**Conclusion**

As it can be observed from the study that significant LM disease and coronary artery calcification are the independent predictors of significant CAS in patients undergoing CABG, patients with these features on conventional coronary angiography should be screened for carotid disease before CABG.

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**Conflicts of interest**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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