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Original Research

Carotid Angiographic Profile in Patients with Coronary ArteryDisease

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ABSTRACT:

Background: This study was conducted with an aim of assessing the angiographic incidence of carotid artery stenosis (CAS) in patients undergoing coronary angiography for the diagnosis of coronary artery disease (CAD). **Methods:** This single centre study included 50 patients with stable CAD or acute coronary syndromes, undergoing coronary angiography for diagnostic or therapeutic indications, who gave consent for concomitant carotid digital subtraction angiography (DSA). Significant CAD was defined as ≥ 50% diameter stenosis in at least one major coronary artery or its first order branches, and was categorized as single vessel disease (SVD), double vessel disease (DVD), or triple vessel disease (TVD) according to number of vessels involved. Significant CAS was defined as a diameter stenosis of ≥50% in the common carotid artery, the carotid bifurcation, or the internal carotid artery. For statistical analysis, patients were divided into two groups i.e. patients without or with CAS. Patient characteristics in these groups were then analysed and compared to each other. **Results:** the coronary and carotid angiographic profile of the study population. Although 58.8% females had normal coronary angio-gram compared to only 25.5% in males, we did not find any statistically significant difference between the coronary angiographic profile of males and females (p = 0.173). Among 12 patients (22%) who had CAS, 7 (72%) had bilateral CAS while 5 patients (31%) had unilateral CAS. Again, there was no significant difference between males and females visa vis carotid angiographic profile (p = 0.462). All 12 patients with CAS had TVD on coronary angiography and none of the patients with normal coronary angiography, SVD or DVD had associated significant CAS (p ≤ 0.0001). In other words, 33.21% patients with significant CAD and 84.5% patients with TVD had associated significant CAS. **Conclusion:** It was found that CIMT is an independent predictor and is strongly associated with ISR. Hence, the non-invasive nature and ease of estimation are positive correlates to recommend measurement of CIMT in routine clinical practice in both pre- and post-PCI patients.

Keywords: Carotid artery stenosis, Carotid angiography, Coronary Artery Disease.

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INTRODUCTION

Myocardial infarctionis the leading cause of long-term mortality in stroke surviving patients, although stroke is the leading cause of disability in the world.[1,2] Athero-sclerosis is a systemic disease, with multifocal involvement not being an infrequent finding.[3] Coronary and carotid arteries are the most frequent sites of atherosclerotic involvement. The association between carotid artery stenosis (CAS) and CAD has been widely reported in literature.[4-6] In the western countries, approximately 8% to 14% of patients undergoing myocardial revascularization for CAD have significant CAS. Conversely, 28% of patients undergoing carotid endarterectomy for CAS have signifi-cant CAD.[7,8] The data from Asian countries is somewhat different, with some studies showing that more than 50% of patients with CAD have associated significant CAS and vice versa.[9,10] Additionally, the distribution and severity of carotid atherosclerosis, as well as cardiovascular risk factor profile has been shown to demonstrate racial differences.[11] The presence of concomitant CAS in patients with CAD not only increases their overall cardiovascular risk but also has a significant impact on the choice of management strategy. This study was conducted with an aim of assessing the angiographic incidence of hitherto undiagnosed CAS in patients undergoing coronary angiography for the diagnosis of CAD.

The magnitude of problem imposed by "left main disease" (LMD), though well established in men, has not been explored in women. Moreover the strategy of stent deployment (provisional side branch stenting

strategy or two stent strategy) in the interventions of LMCA depends on the pattern of CAD. Hence, a study about angiographic prevalence and pattern of CAD especially LMD in women will definitely open up new avenues for the better understanding of the strategy for percutaneous coronary intervention.

It is well established that the prevalence of CAD is lesser in women compared to men.[12,13] Among women who routinely undergo CAG prior to radiofrequency ablation, the angiographically determined prevalence of "single vessel disease" (SVD), "double vessel disease" (DVD) and "triple vessel disease" (TVD) are 2.5%, 1.3% and 0% respectively.[12] CAD in women less than 45years of age does not differ from other patients.[14] Significant CAD is seen in 55% of women with more than two risk factors.[14] Study done by Dave et al among Indian women undergoing coronary angiography showed greater proportion of TVD (39.6%) than DVD (12.9%) or SVD (15.8%).

Myocardial revascularization has been shown to confer significant benefits in terms of symptom control and improved prognosis. However, the long-term success of revascularization by balloon angioplasty technique has been limited by restenosis.[15-17] To overcome this problem, stents were introduced, which have improved the results of percutaneous coronary revascularization but also introduced in-stent restenosis (ISR).[18]

METHODS

The study was approved by institutional ethics committee. Informed consent from all the patients was obtained in local language prior to study. Smoking was defined as if the patient smoked >1 cigarette per day regularly for more than 6 months or had quit smoking for less than 2 years. Diabetes Mellitus was diagnosed on the basis of fasting plasma glu- cose of ≥ 126 mg/dL or Hemoglobin A_1C greater than 6.5%or symptoms of diabetes plus random blood glucose concentration ≥ 200 mg/dL or pa-tient on anti-diabetic medications. Hypertension was considered to be present if the patient was taking any anti-hypertensive drugs at the time of presentation or if blood pressure recorded was ≥ 140mmHg systolic and/or ≥ 90mmHg diastolic, on at least two separate occasions. Dyslipidemia was defined as total cholesterol ≥ 200 mg/dL, or LDL cholesterol ≥130 mg/dL, or triglycerides ≥ 150 mg/dL, or HDL cholesterol ≤40 mg/dL or any combination of these criteria. Complete physical examination in- cluding cardiovascular examination was then performed. Base line inves-tigations including electrocardiogram (ECG), chest X ray, complete blood count, kidney function tests, liver function tests, serum electrolytes, and coagulation profile were obtained. Echocardiography for the evaluation of regional wall motion abnormalities, left and right ventricular functions, and associated structural heart disease was also done in all the cases.

Coronary angiography was performed via trans-radial or trans-femoral approach using the standard Judkins technique in our cardiac cath- eterization laboratory (Axiom Artis, Seimens, Germany). For complete visualisation of the left coronary artery system at least four different projections were used.

Inclusion criteria include patients of age ≥18 years with ISR (with at least 50% diameter stenosis in-stent or in-segmenton at least two orthogonal projections) as cases. Asymptomatic patients of age ≥18 years who had underwent PCI with stent placement and symptoms free at least 6 months prior to the study were included as controls. Exclusion criteria include patients with age group <18 years, with angiographic evidence of acute/subacute stent thrombosis and with duration of hospital stay <24 h.

STUDY POPULATION

We included 50 consecutive patients with stable CAD or acute coronary syndromes, undergoing coronary angiography for diagnostic or therapeutic indications, who fulfilled the eligibility criteria as described below.

INCLUSION CRITERIA

(i) Patients with chronic stable angina who had an indication for diag- nostic coronary angiography according to ACC/AHA guidelines.[13]

(ii) Patients with acute coronary syndromes [Unstable angina (UA), Non ST elevation myocardial infarction (NSTEMI) or ST elevation myocardial infarction (STEMI)], who were undergoing coronary angiography for diagnostic or therapeutic purpose.

(iii) Patients who gave consent for the study.

(iv) Exclusion criteria

(v) Patients who did not have an indication for invasive coronary angi-ography.

(vi) Patients with history of allergy to contrast agents.

(vii) Patients with documented history of cerebrovascular disease (CVD)

(viii) i.e. stroke or transient ischemic attack (TIA).

(ix) Patients with serious comorbidities like chronic renal failure (eGFR< 30 ml/min), sepsis, or malignancies and pregnant ladies.

(x) Patients who refused to give consent for the study.

RESULTS

The mean age of study group was 59.71 ± 10.01 years with a range of 40 to 71 years. Out of 70 patients studied 43 (61.4%) were males and 27 (38.5%) were females; with male to female ratio of 1.9:1. Overall STEMI and stable angina were the most common modes of presentation (33%) each, followed by NSTEMI (23%) and UA (16%).In males STEMI was the most common indication for coronary angiography (37.4%), while in females stable angina was the major indication (36.6%). Among patients with STEMI, 55% had anterior wall myocardial infarction (AWMI) and 48% had inferior wall myocardial infarction (IWMI). The risk factor profile of study population is depicted in Table 1.

Table 1: Risk factor profile of the study group

Risk Factor	Male N=43	%	Female N=27	%	Total N=70	%	P value
Hypertension	30	69.7	17	44.4	47	67.1	0.98
Diabetes Mellitus	13	30.2	15	55.5	28	40.0	0.009
Dyslipidemia	12	27.9	8	29.6	20	28.5	0.88
Smoking	23	53.4	6	22.2	29	41.4	0.009

Table 2 describes the coronary and carotid angiographic profile of the study population. Although 58.8% females had normal coronary angiogram compared to only 25.5% in males, we did not find any statistically significant difference between the coronary angiographic profile of males and females ($p = 0.173$). Among 12 patients (22%) who had CAS, 7 (72%) had bilateral CAS while 5 patients (31%) had unilateral CAS. Again, there was no significant difference between males and females vis a vis carotid angiographic profile ($p = 0.462$). All 12 patients with CAS had TVD on coronary angiography and none of the patients with normal coronary angiography, SVD or DVD had associated significant CAS ($p \leq 0.0001$). In other words, 33.21% patients with significant CAD and 84.5% patients with TVD had associated significant CAS.

Table 2: Coronary and carotid angiographic profile of the study group

Angiographic Profile		Male N=43	%	Female N=27	%	Total N=70	%	P value
Coronary Angiogram	Normal	11	25.5	12	44.4	23	32.8	
	SVD	11	25.5	5	18.5	16	22.8	0.173
	DVD	8	18.6	2	7.4	10	14.2	
	TVD	11	25.5	5	18.5	16	22.8	
Carotid Angiogram	CAS present	9	20.9	4	14.8	13	18.5	0.462
	CAS absent	26	60.4	16	59.2	42	60.0	

We compared the demographic characteristics and the risk factor sta- tus of the two groups i.e. patients without CAS (group I) and patients with CAS (group II). The results are shown in Table 3. Although we did not find any statistically significant differences between the two groups in terms of their demographic or risk factor profile, it is pertinent to mention that patients with CAS were more likely to be older than those without CAS ($p = 0.069$). Additionally, 81% of patients with CAS were males and all of them were hypertensive. Smoking and diabetic status was equally distributed between the two groups.

Table 3: Demographic and risk factor profile of patients with and without CAS

Variable		CAS Group 1 (Absent)	CAS Group 2 (Present)	Total N (70)	Total %	P value
Age (years)	40 - 49	14	2	16	22.8	
	50 - 59	12	0	12	17.1	0.069
	60 - 69	18	11	29	41.4	
	≥ 70	6	7	13	18.5	
Gender	Male	30	13	43	61.4	0.462
	Female	20	7	27	38.5	
Hypertension	Absent	12	0	12	17.1	0.099
	Present	33	14	45	64.2	
Diabetes	Absent	24	8	32	45.7	0.882
	Present	21	8	29	41.4	
Dyslipidemia	Absent	33	13	46	65.7	0.531
	Present	17	7	24	34.2	
Smoking	Absent	25	10	35	50.0	1.000
	Present	25	10	35	50.0	

DISCUSSION

To the best of our knowledge, this is the first Indian study evaluating the carotid angiographic profile in patients with suspected or proven CAD. Although patients with atherosclerotic vascular disease come to clinical attention due to symptoms related to one vascular territory, given its multifocal nature, concomitant subclinical involvement of other vascular beds is not an uncommon observation.[19] CAD and CVD are the most fearsome complications of atherosclerosis, presenting dramatically as acute myocardial infarction or stroke in more than 50% of previously asymptomatic patients. The association between carotid artery disease and CAD is well

documented.[20-22] In fact just increased carotid intimal medial thickness (CIMT), even without carotid stenosis, has been established as a surrogate marker of subclinical atherosclerosis and is independently associated with adverse cardiovascular outcomes. In the western countries, approximately 8% to 14% of patients undergoing myocardial revascularization for CAD have significant CAS, and 28% of patients undergoing carotid endarterectomy for CAS have significant CAD.[23,24] The data from Asian countries is somewhat different, with studies showing that more than 50% of patients with CAD have associated significant CAS and vice versa.[25,26] In most of these studies carotid ultrasound/Doppler was used to identify and quantify CAS. Compared with selective intra-arterial DSA, color duplex sonography has an overall sensitivity of 91% to 95% and a specificity of 86% to 97% for diagnosing CAS, and therefore, false positive or negative results may be present in the data reported in these studies. DSA has also been demonstrated to be more accurate than other non-invasive methods such as computerized tomographic angiography (CTA) and magnetic resonance angiography (MRA) in detecting CAS.[27,28] Our study demonstrated that 20% of patients undergoing coronary angiography, and one third of patients with angiographically documented CAD, have associated significant CAS on DSA. Thus, prevalence of CAS in Indian patients with CAD seems to be intermediate between Western and other Asian countries. The presence of coexistent carotid artery disease in patients with CAD has an adverse impact on their short term and long term prognosis. Hence, knowledge of associated CAS aids in refining the cardiovascular risk stratification of these patients, and strongly calls for more aggressive management strategies. Another interesting fact vis a vis cerebrovascular disease is that in contrast to CAD where non-critical rupture prone plaques are responsible for majority of the serious clinical events, severity of stenosis plays a dominant role in dictating the clinical course of patients with CAS. Furthermore, presence of concomitant CAS dramatically increases the risk of periprocedural stroke in patients undergoing coronary revascularization. Coronary artery bypass grafting (CABG) in patients without carotid atherosclerosis carries an approximate 1% to 2% risk of perioperative stroke, but in the presence of untreated major carotid stenosis, this risk rises exponentially to about 14%. It is also clear that the risk of perioperative stroke highly correlates with-the degree of CAS. Hence early diagnosis of concomitant carotid steno- sis may have a direct bearing on the choice of revascularisation strategy. Some patients may benefit from synchronous coronary and carotid operations. Optionally, patients at high risk with advanced but stable CAD may require prior intervention in the carotid arteries followed by coronary intervention. A few authors have also reported simultaneousstenting of the carotid artery and coronary arteries in patients with high operative risk.

Higher mean BMI was found in ISR patients and it was statistically associated with restenosis. But it was not an independent predictor after multivariate regression analysis and this was consistent with the previous findings.[29-31] Blood pressure (both systolic and diastolic), pulse rate, and blood glucose level were not associated with restenosis, which was homogeneous with the findings of Bourassa et al.[32] Lower mean eGFR was associated with restenosis in study patients, and this was equivalent to the study of Matsuo et al.[33] as chronic kidney disease creates an inflammatory milieu, which increases the incidence of restenosis and repeat revascularizations.

Although hypercholesterolemia has been an established risk factor for atherosclerosis, lipid profile of patients in this study showed that no other component except higher mean LDL cholesterol level has association with restenosis.

When the effects of individual drugs, such as antiplatelet, statins, ACE inhibitor, ARB, calcium channel blockers, and beta-blockers were analyzed on restenosis, except for nitrates, clopidogrel, and metaprolol, none of them provided a statistically significant clinical benefit. Similar findings of higher usage of nitrates in ISR patients were seen in previous studies, which may be due to the ischemia. Metaprolol and clopidogrel intake was negatively associated with restenosis. But there was no link between restenosis and anti-platelet therapy in other studies. The poor drug compliance was statistically associated with restenosis in the study patients, which was reported in previous studies too.

CONCLUSION

It was found that CIMT is an independent predictor and is strongly associated with ISR. Hence, the non-invasive nature and ease of estimation are positive correlates to recommend measurement of CIMT in routine clinical practice in both pre- and post-PCI patients. Given the grave consequences that the patients with this deadly combination face, this strategy may allow superior risk stratification and better planning in terms of choice and sequence of revascularization strategy in these patients.

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