ORIGINAL ARTICLE

CAROTID DISEASE IN DIABETIC PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING

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Objective: To compare the severity of carotid artery disease in diabetic and non-diabetic patients undergoing coronary artery bypass grafting. **Methods:** From January to June 2008, 379 patients undergoing elective coronary artery bypass surgery were preoperatively evaluated for the presence of carotid stenoses by duplex scanning. Patients were divided into two groups, Group I, 156 (41.2%) diabetic patients and Group II, 223 (58.8%) non-diabetic patients. **Results:** There were 314 (82.8%) males and 65 (17.2%) females with a mean age of 57.2±9.1 years. In diabetic group there were 125 (80.1%) males and 31 (19.9%) females with a mean age of 56.3±8.9 years. Left main stem stenosis was present in 59 (37.8%) diabetics and 45 (20.2%) non-diabetics (p<0.0001). Diffuse disease in left anterior descending (LAD) artery was observed in more diabetic patients 72 (46.2%) as compared to non-diabetics 83 (37.2%) (p<0.295). Single tight stenosis in LAD was observed in more non-diabetics. Significant carotid artery stenosis was observed in 50 (13.2%) patients. Carotid artery stenosis was observed in 30 (19.2%) diabetics as compared to 20 (9%) non-diabetics (p<0.004). Analysis of percentage stenosis of carotid artery disease in the study population revealed that >70% stenosis was present in 20 (5.3%) with 13 (8.3%) diabetics and 7 (3.1%) non-diabetics (p<0.025). Stenosis of 50–70% was observed in 30 (7.9%) of which 17 (10.9%) were diabetics and 13 (5.8%) were non-diabetics. **Conclusion:** Presence of diabetes mellitus is associated with diffuse coronary artery disease and significant carotid artery disease in patients undergoing coronary artery bypass grafting.

Keywords: Atherosclerosis, Coronary artery disease, Carotid artery disease, Coronary artery bypass grafting, Diabetes Mellitus

INTRODUCTION

Diabetes Mellitus is a major risk factor for cardiovascular morbidity and mortality.[1,2] The risk of developing coronary, cerebro-vascular and peripheral arterial disease is increased four fold in patients with diabetes mellitus.[1,2] Diabetics have a greater *de novo* disease progression compared to non-diabetic patients.[1,3,4]

Diabetes is a major risk factor of stroke. Diabetes increases the risk of stroke three fold.[4–6] In patients with coronary artery disease (CAD) the prevalence of carotid stenosis is 30–70%.[7,8] For those undergoing coronary artery bypass grafting (CABG) the prevalence of >50% narrowing of at least one internal carotid artery is thought to be around 20%, and >70% stenosis is found in 2–21% of cases.[9,10–15]

Stroke and other ischemic neurological events are one of the most important side effects of cardiac surgery with a reported mortality of 21–27% after CABG.[10]

Coronary disease is included in a multi-focal atherosclerotic disease with a significant rate of concomitant atherosclerotic cerebro-vascular disease which contributes to the risk of postoperative stroke after CABG.[10] Patients with severe CAD such as left main stem (LMS) or three vessel disease comprise a heterogeneous population with a wide spectrum of disease severity; for optimum peri-operative management, they should be screened for carotid artery disease before bypass surgery.[16]

In Pakistan studies have been done on diagnostic accuracy of carotid duplex scanning.[17,18] But none have so far reported the severity of carotid disease in diabetics so this study has been designed to compare the severity of carotid artery disease in diabetic and non-diabetic patients undergoing CABG.

MATERIAL AND METHODS

From January to June 2008, 379 patients undergoing elective coronary artery bypass surgery were preoperatively evaluated for the presence of carotid stenoses by duplex scanning. Patients were divided into two groups, Group I, 156 (41.2%) diabetic patients and Group II, 223 (58.8%) Non-diabetic patients.

A detailed history was taken to evaluate risk factors including sex, age, hypertension, diabetes mellitus, hyperlipidemia, smoking, familial history of CAD, and previous cerebrovascular accidents including transient ischemic attack or stroke. Hypertension was defined as present if a subject took medication for hypertension or if the subject's blood pressure was >140 mm Hg systolic or >90 mm Hg diastolic for ≥2 repeated measurements. Diabetes mellitus was defined as a serum glycosylated haemoglobin concentration of >5.8%, if the repeated

fasting plasma glucose exceeded 126 mg/dL, or if the patients took medication for diabetes. Hyperlipidemia was defined as taking lipid-lowering medications, a fasting serum total cholesterol concentration of >200 mg/dL, low density lipoprotein cholesterol concentration of >140 mg/dL, high density lipoprotein cholesterol concentration of <40 mg/dL, or triglyceride concentration of >150 mg/dL. A familial history of CAD was defined as a history of CAD in any first-degree relatives <60 years of age. A transient ischemic attack (TIA) was referred when there was brief neurologic dysfunction that persisted, for less than 24 hours; if symptoms persisted more than 24 hours then it was categorized as a stroke.

Coronary angiography was performed to evaluate the severity of CAD. The diameter stenosis was calculated by quantitative coronary angiography with an automated coronary analysis system. Stenoses were evaluated and classified as significant if the mean luminal narrowing was 50% or greater by using a validated quantitative coronary angiographic algorithm (Cardiovascular Angiography Analysis System, CAAS II; Pie Medical Imaging, Maastricht, the Netherlands). CAD was defined as a lumen diameter stenosis of >50% in ≥1 major coronary artery. The number of diseased vessels was reported as: 1-vessel disease (i.e., patients with disease in 1 vessel), 2-vessel disease (i.e., patients with disease in 2 vessels without left main trunk disease), 3-vessel disease (i.e., patients with disease in 3 vessels without left main trunk disease). LMS with 3-vessel disease (i.e., patients with disease in 3 vessels with left main trunk disease). Left main stenosis was regarded as disease of the left anterior descending coronary artery (LAD) and the left circumflex coronary artery (LCX). A 'diffuse disease' was defined by the presence of significant stenosis in ≥2 segments of a vessel.

Atherosclerosis of carotid artery was analysed by duplex ultrasound scanning in the all enrolled patients. A commercially available machine (Vivid 7, GE Healthcare, Milwaukee, USA) with a 10-MHz linear array transducer was used. Imaging was performed while subjects were lying in a supine position with the head turned away from the side being scanned and the neck extended. Transverse and longitudinal scans were obtained on the common carotid artery, the carotid bifurcation, and the internal and external carotid artery by B-mode and colour Doppler ultrasound. Area stenosis (percent) was measured as: [1-(the area of residual lumen/the area of the normal vessels)] X100 by B-mode ultrasound. Doppler spectral analysis can determine the peak systolic velocity (PSV) by sampling at the area of turbulence. The PSV was measured only when the turbulence was found. To measure blood flow velocity on longitudinal scans, a 5–7 mm sample was set in the carotid artery and displayed as linearly as possible. Special care was taken to maintain the incident angle between the carotid artery and the beam at 30–60°. We defined echo-graphic carotid artery stenosis as the carotid atherosclerosis with area stenosis of >50% or PSV of >200 cm/s on the common carotid artery, the carotid bifurcation, and the internal carotid artery.

All the data were analyzed by SPSS-14. Categorical variables were expressed as frequencies and percentages and continuous variables as Mean±SD. Cardiovascular risk factors, coronary and carotid artery disease were compared between diabetic and non-diabetic groups by applying Chi-Square test and *p*-values were calculated, $p<0.05$ was taken as significant.

RESULTS

There were 314 (82.8%) males and 65 (17.2%) females with a mean age of 57.2±9.1 years. In diabetic group there were 125 (80.1%) males and 31 (19.9%) females with a mean age of 56.3±8.9 years. Male to female ratio was similar in the two groups. Hypertension was marginally more in diabetic group 83 (53.2%) as compared to non-diabetic group 103 (46.2%) ($p<0.107$). Smoking was observed more in the non-diabetic group 93 (41.7%) than diabetics 46 (29.5%) ($p<0.015$). Dyslipidemia was present in 33 (21.2%) diabetics and 26 (11.7%) non-diabetics ($p<0.012$). Family history of ischemic heart disease was present in almost similar proportions in the two groups with a non-significant association. History of cerebro-vascular events revealed that transient ischemic attacks occurred in 16 (10.3%) diabetics and 10 (4.5%) non-diabetics. History of cerebro-vascular accidents with delayed recovery was also more frequent in diabetics 8 (5.1%) as compared to non-diabetics 7 (3.1%) ($p<0.002$). None of the patients had residual neurological deficit (Table-1).

Table-1: Epidemiological characteristics

Characteristics	Diabetic Group (n=156)	Non-diabetic Group (n=223)	Total (n=379)	*p*
Age mean years	56.3±8.9	58.2±9.3	57.2±9.1	<0.524
Male Female	125 (80.1%) 31 (19.9%)	189 (84.8%) 34 (15.2%)	314 (82.8%) 65 (17.2%)	<0.24
Hypertension	83 (53.2%)	103 (46.2%)	186 (49.1%)	<0.107
Smoking	46 (29.5%)	93 (41.7%)	139 (36.7%)	<0.015
Dyslipidemia	33 (21.2%)	26 (11.7%)	59 (15.6%)	<0.012
F/H of IHD	60 (38.5%)	72 (32.3%)	132 (34.8%)	<0.214
History of CVA TIAs CVAs	24 (15.4%) 16 (10.3%) 8 (5.1%)	17 (7.6%) 10 (4.5%) 7 (3.1%)	41 (10.8%) 26 (6.9%) 15 (3.9%)	<0.002

CVAs= Cerebrovascular accidents; F/H= Family history; IHD= Ischemic heart disease; TIAs= Transient ischemic attacks

Left main stem stenosis was present in 59 (37.8%) diabetics and 45 (20.2%) non-diabetics ($p<0.0001$). Diffuse disease in left anterior descending (LAD) artery was observed in more diabetic patients 72 (46.2%) as compared to non-diabetics 83 (37.2%)

(p<0.295). While single tight stenosis in LAD was observed in 64 (41%) diabetics and 83 (37.2%) non-diabetics. Circumflex stenosis was observed in 88 (56.4%) diabetics and 105 (47%) non-diabetics (p<0.18). Disease pattern in right coronary artery (RCA) was similar in diabetics and non-diabetics. Ramus Intermedius had tight stenosis in 22 (14.1%) diabetics as compared to 23 (10.3%) non-diabetics (p<0.05).

Table-2: Diseased coronary arteries in two groups

Characteristics	Diabetic Group (n=156)	Non-diabetic Group (n=223)	Total (n=379)	*p*
LMS	59 (37.8%)	45 (20.2%)	104 (27.4%)	<0.0001
LAD				
>50% stenosis	84 (53.8%)	140 (62.8%)	224 (59.1%)	
Diffuse disease	72 (46.2%)	83 (37.2%)	155 (40.9%)	<0.295
LCX				
>50% stenosis	88 (56.4%)	105 (47.1%)	193 (50.9%)	
Diffuse disease	38 (23.1%)	58 (26%)	94 (24.8%)	<0.18
RCA				
>50% stenosis	82 (52.6%)	119 (53.4%)	201 (53%)	
Diffuse disease	50 (32.1%)	60 (26.9%)	110 (29%)	<0.404
RI				
>50% stenosis	22 (14.1%)	23 (10.3%)	45 (11.9%)	
Diffuse disease	0	3 (1.3%)	3 (0.8%)	<0.05

LMS= left main stem; LAD= Left anterior descending; LCX= Left circumflex; RCA= Right coronary artery; RI= Ramus Intermedius

Number of diseased vessels per patient is shown in Figure-1. Three vessel coronary artery disease (TVCAD) occurred in 194 (51.2%) patients, of whom 71 (45.5%) were diabetic and 123 (55.2%) were non-diabetic. LMS with TVCAD was next common occurrence with 100 (26.4%) patients. In this subgroup there was a preponderance of diabetic patients as 56 (35.9%) diabetics had LMS with TVCAD as compared to 44 (19.7%) non-diabetic patients. Isolated LMS disease was also more frequently observed in diabetics as compared to non-diabetics (p<0.007).

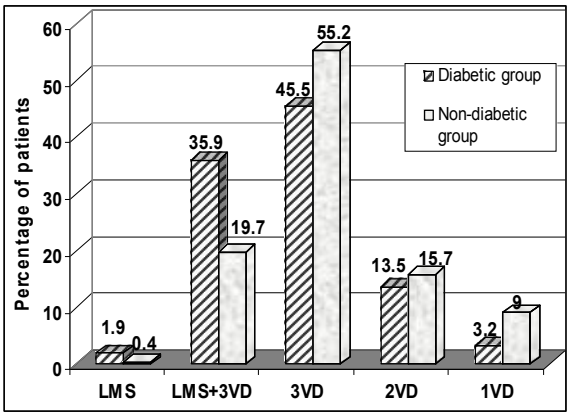

Figure-1: Distribution of coronary artery disease by diseased vessel (p<0.007)

Significant carotid artery stenosis was observed in 50 (13.2%) patients. Carotid artery stenosis was observed in 30 (19.2%) diabetics as compared to 20 (9%) non-diabetics (p<0.004). Analysis of percentage stenosis of carotid artery disease in the study population revealed that >70% stenosis was present in 20 (5.3%) with 13 (8.3%) diabetics and 7 (3.1%) non-diabetics (p<0.025). Stenosis of 50–70% was observed in 30 (7.9%) of which 17 (10.9%) were diabetics and 13 (5.8%) were non-diabetics. Majority of patients 174 (46.4%) patients had normal carotids followed by 153 (40.4%) patients having <50% stenosis of carotid artery with more non-diabetics (Table-3).

Table-3: Comparison of carotid artery disease in the two groups

Carotid stenosis	Diabetic Group (n=156)	Non-diabetic Group (n=223)	Total (n=379)	*p*
Normal carotids	64 (41%)	112 (50.2%)	176 (64.4%)	
<50% stenosis	62 (39.7%)	91 (40.8%)	153 (40.4%)	<0.025
50-70% stenosis	17 (10.9%)	13 (5.8%)	30 (7.9%)	
>70% stenosis	13 (8.3%)	7 (3.1%)	20 (5.3%)	
Significant carotid disease	30 (19.2%)	20 (9%)	50 (13.2%)	<0.004

Table-4: Comparison of percent stenosis in carotid arteries in the two groups

Characteristics	Diabetic Group (n=156)	Non-diabetic Group (n=223)	Total (n=379)	*p*
RCCA				
50–70% stenosis	10 (6.4%)	6 (2.7%)	16 (4.2%)	
>70% stenosis	0	2 (0.9%)	2 (0.5%)	<0.149
RICA				
50–70% stenosis	5 (3.2%)	2 (0.9%)	7 (1.8%)	
>70% stenosis	7(4.5%)	4 (1.8%)	11 (2.9%)	<0.09
LCCA				
50–70% stenosis	9 (5.8%)	5 (2.2%)	14 (3.5%)	
>70% stenosis	2 (1.3%)	3 (1.3%)	5 (1.3%)	<0.291
LICA				
50–70% stenosis	5 (3.2%)	3 (1.3%)	8 (2.1%)	
>70% stenosis	8 (5.1%)	1 (0.4%)	9 (2.4%)	<0.016
Right carotid artery				
50–70% stenosis	15 (9.6%)	8 (3.6%)	23 (6.1%)	
>70% stenosis	7 (4.5%)	6 (2.7%)	13 (3.4%)	<0.094
Left carotid artery				
50–70% stenosis	14 (8.9%)	8 (3.6%)	22 (5.8%)	
>70% stenosis	10 (2.6%)	4 (1.8%)	14 (3.6%)	<0.037

RCCA=Right Common carotid artery, RICA=Right internal carotid artery, LCCA=Left Common carotid artery, LICA=Left internal carotid artery

Table-4 shows significant stenosis in individual carotid arteries. More than 70% right carotid artery stenosis was observed in 13 (3.4%) patients, 7 (4.5%) in diabetic group and 6 (2.7%) in non-diabetic group. Fifty to seventy percent stenosis was observed in 23 (6.1%) patients, 15 (9.6%) in diabetic group and 8 (3.6%) in non-diabetic group. Right common carotid artery (RCCA) and right internal carotid artery (RICA) had more stenoses in diabetics compared to non-diabetics. More than 70% left carotid artery stenosis was observed in 14 (3.7%) patients, 10 (6.4%) in diabetic group and 4 (1.8%) in non-diabetic group (p<0.037). Fifty to seventy percent stenosis in left carotid artery was observed in 22 (5.8%) patients, 14 (8.9%) diabetics and 8 (3.6%) non-diabetics, similarly, left common carotid artery (LCCA) and left internal carotid artery (LICA) were more frequently diseased in diabetics as compared to non-diabetics.

DISCUSSION

Diabetes Mellitus increases four fold the risk of developing coronary, cerebro-vascular and peripheral arterial disease. There is also increased atherosclerotic disease progression in diabetes. In patients with coronary artery disease there is 30–70% prevalence of carotid artery disease. In patients planned for CABG the prevalence of significant carotid artery stenosis is around 20%. The significance of carotid artery disease in CABG patients is the high postoperative stroke mortality. This reason merits screening of CAD patients for carotid disease prior to undergoing CABG.

In the current study >50% stenosis in a carotid artery was observed in 10.9% diabetics as compared to 5.8% non-diabetics. While >70% stenosis in any carotid artery was observed in 8.3% diabetics and 3.1% non-diabetics ($p<0.025$). Our results are in accordance with the previous studies. Carotid artery disease has been reported in 2–21% patients undergoing CABG.[11–15,19]

Birincioglu *et al*[13] reported frequency of carotid disease in patients of elective CABG. Birincioglu *et al*[13] observed <60% stenosis in 46.2% patients, 60–70% stenosis in 7.1% and 80–99% stenosis in 4.6% and total occlusion in 1.2%. In diabetic patients <60% stenosis was observed in 18.5%, 60–79% stenosis in 12.5% and 80–99% stenosis in 19.35%. Birincioglu *et al*[13] observed a linear association between carotid disease and coronary disease. Previous cerebral, ischemic events, hypertension, smoking, advanced age and female sex was identified as high risk factors for carotid artery stenosis. We also studied the association of diabetes mellitus with carotid disease in patients undergoing CABG and observed a statistically significant association on comparison of carotid disease in diabetics and non-diabetics. In our study diabetic patients had history of previous cerebro-vascular events in 15.4% patients as compared to 7.6% non-diabetic patients.

Mitsuhashi *et al*[19] reported relationship between carotid atherosclerosis measured as carotid intima media thickness (IMT) and CAD in 40 type 2 diabetic patients and 40 controls. Carotid IMT was greater in diabetic patients than in control subjects. IMT was significantly greater in the CABG group than the Non-CABG group. Most diabetic patients with CAD had multivessel disease and diffuse stenosis of the coronary arteries and some of them suffered asymptomatic myocardial infarction. In our study we also observed multivessel and diffuse disease more frequently in diabetic patients as compared to non-diabetics. Carotid artery disease was similarly more prevalent in our diabetic patients as compared to non-diabetics. All of our patients were planned for elective CABG. In our study patients were known cases of coronary artery disease so we did not measure IMT of our study population. We agree with Paraskevas *et al*[20] and Komorovsky *et al*[21] that IMT is a useful predictor of future cardiovascular events and is routinely measured for assessment of risk of coronary artery disease in previously healthy individuals with diabetes mellitus.[20,21]

Chen *et al*[15] reported 153 Chinese patients with documented CAD undergoing Carotid Doppler examination for carotid disease. Carotid stenosis of ≥50% of one or more extracranial cerebral arteries was found in 21%. Diabetes mellitus, hypertension, a history of transient ischemic attacks or stroke and PVD were significantly associated with extracranial carotid and vertebral artery disease. Our results are similar to this study. In our study pattern of CAD is different from reported by Chen *et al*[15] as we had majority of patients having 3 vessel disease with a significant association while Chen *et al*[15] reported similar number of patients having one-vessel, two vessel and three vessel disease in their study.

Tanimoto *et al*[14] reported carotid stenosis in 19.6%. There were 29.1% diabetics, Age, hypertension, diabetes mellitus, past history of myocardial infarction, previous CABG and the extent of CAD were associated with echographic carotid stenosis. Angiographic CAD was present in 68.5%. In our study all patients had coronary artery disease and were planned for CABG.

In a study of 271 patients conducted in Iran Tarzamni *et al*[11] have reported a very low prevalence of significant carotid artery disease. Carotid disease was observed in 1.8% patients among them critical stenosis was observed in 1.1% patients. Tarzamni *et al*[11] have reported 28% diabetic patients in their study. We have studied specifically diabetic population for carotid stenosis and compared it with a non-diabetic group. In our population we observed a higher prevalence of carotid disease probably due to more severe and diffuse coronary artery disease in our population as compared to Irani population studied by Trazamni *et al*.[11]

Paulose *et al*[12] reported a prevalence of carotid disease of 18% in diabetic patients. Carotid artery disease was six fold in patients above the age of 55 and five fold in patients with more than 15 years of diabetes duration. In our study 68.9% patients were >50–70 years of age however similar number of patients were present in both groups with a non-significant association. Paulose *et al*[12] studied carotid circulation of type 2 diabetic patients who were not known cases of coronary artery disease so they observed a majority of patients suffering from nephropathy in their study.

CONCLUSION

Presence of diabetes mellitus is associated with diffuse coronary artery disease and significant carotid artery disease in patients undergoing coronary artery bypass grafting.

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