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Original Article

Severity of Coronary Artery Disease in Patients with or without Diabetic Retinopathy

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Abstract

Background: To determine the frequency of diabetic retinopathy in type 2 diabetic patients undergoing angiographic evaluation and compare the severity (Mean vessel score and mean Gensini score) of coronary artery disease in patients with or without diabetic retinopathy.

Methods: In this cross sectional study, 300 diabetic patients, with suspected coronary artery disease undergoing coronary angiography, were included. All the patients were assessed for the presence or absence of diabetic retinopathy and severity of coronary artery disease.

Results: One hundred and three out of 300 patients (34.3%) had diabetic retinopathy. In patients with diabetic retinopathy, the mean vessel score was 2.62 + 0.60 as compared to 1.90 + 1.03 in non retinopathy group (p=0.000). Gensini score was also found to be significantly higher in diabetic retinopathy group (103 + 37.17 versus 38.5508 + 22.205) (p=0.000).

Conclusions: Severity scores (Vessel and Gensini scores) of coronary artery disease were significantly higher in patient with diabetic retinopathy as compared to those without diabetic retinopathy.

Key Words: Coronary artery disease,Vessel score, Gensini score,Diabetic retinopathy

Introduction

Coronary artery disease (CAD) has become one of the most important health problems worldwide. Diabetes mellitus (DM) due to its atherogenic potential is among the major risk factors of CAD. In type-2 diabetics, the presence of retinopathy signifies an increased CHD risk.Ischemic heart disease is among 10 leading causes of death worldwide. [1] In 2011 alone, CAD resulted in 7 million deaths worldwide. [2] Someone suffers a coronary event every 26 seconds, and someone dies from one every minute in the United States. [3] One in four subjects aged more than 40 years may have underlying coronary heart disease in Pakistan. [4]

CAD is a devastating disease precisely because an otherwise healthy person in the prime of life may die or become disabled without warning. CAD in a young person can have devastating consequences to the patient and to the family. A recently published study with a retrospective design concluded that Myocardial Infarction is found in 32.7% of young patients admitted to the Emergency Department with CP and elevated serum cardiac Troponin-I concentration. [5] People of Indo-Asian origin have one of the highest susceptibilities to CAD in the world as well as rising incidence of premature coronary artery disease and it is therefore not surprising that CAD is now the leading cause of death in the Indo-Pakistan subcontinent. [6-8] The management of CAD has always been a challenge for treating physicians. There is a need for making prompt diagnosis and deliver appropriate therapy expeditiously. [9]

Diabetes Mellitus is a heterogeneous primary disorder of carbohydrate metabolism with absolute insulin deficiency (Type 1) or relative insulin deficiency (type 2), resistance or both leading to hyperglycemia. [10] The number of patients with type 2 diabetes is increasing rapidly in both developed and developing countries around the world. It is projected that by 2025 there will be 380 million people with type 2 diabetes and 418 million people with impaired glucose tolerance. [11] The South Asian region shares a major proportion of this worldwide burden of diabetes. The prevalence of diabetes ranges from 0.9% in Bangladesh to 21.2% in India. [12]

DM due to its micro and macro-vascular complications is an important risk factor for CAD.[13] In individuals with type-2 diabetes, the presence of retinopathy signifies an increased CHD risk, independent of glycaemic levels,symptomatology, [16] other cardiovascular risk factors and is also associated with an increased risk of mortality and cardiovascular events.[14-18]

Demerdash EF et al. reported that evidence of coronary artery stenosis was present in 80% of the proliferative diabetic retinopathy group and in 70% of the nonproliferative diabetic retinopathy group but was not present in nonretinopathic diabetic group. [19] In another study, the frequency of diabetic retinopathy was 44.9% and comparison of coronary angiography

data showed that the patients with diabetic retinopathy had significantly higher vessel (2.3 ± 0.9 versus 1.3 ± 1.1, P< 0.001) and severity (63.7 ± 41.0 versus 22.6 ± 14.9, P< 0.001) score than patients with no evidence of diabetic retinopathy. [20]

Pakistan is one of the top 10 countries in the world with the highest prevalence (7-11%) of diabetes.[21] Lack of awareness of diabetes symptoms and complications, myths about treatment of diabetes and associated economical burden are the major determinants of delay in the health seeking behavior, poor glycaemic controls and increased incidence of complications associated with diabetes mellitus. [22,23] This, in turn predicts higher cardiovascular complications rate and more severe CAD in Pakistani diabetic population. [21-27] Coronary artery disease may accompany atypical or no symptoms in diabetic patients especially in males and those with diabetic retinopathy causing a rise in morbidity and mortality. Therefore, making the diagnosis of CAD in patients with DM has critical importance. Meanwhile, a fundus examination is a simple, noninvasive and routinely employed technique used in the follow-up of diabetic patients. [28,29]

Patients and Methods

This cross sectional study was performed in Catheterization department, Rawalpindi institute of Cardiology, Rawalpindi., from August 2015 to January 2016. In this study Type-2 diabetic patients (BSF .126 mg/dl or BSR >200 mg/dl or taking treatment for diabetes) (n=300), were included. All these patients were under evaluation for coronary angiography. Patients having diabetes mellitus of less 1 year, uncontrolled hypertension (Systolic blood pressure >180 mmHg and/or diastolic blood pressure >100mmHg), previous coronary bypass surgery or percutaneous coronary intervention (history or documents of procedure or scar mark),diabetic nephropathy (serum creatinine levels > 1.5 mg/dl) and with known non-diabetic retinal changes, were excluded. The fundi of all patients were categorized on bedside examination with an ophthalmoscope by two cardiologists. Later, coronary angiographies of these patients were performed and interpreted by two experienced consultant cardiologists to determine the vessel score and Gensini score. The mean and standard deviation were calculated for continuous variables like age, duration of diabetes, Vessel score and Gensini score. The normality of data was assessed using Shapiro-Wilk test and normal distribution curve. Significance of the difference between two groups for continuous variables was assessed with the Mann-Whitney U test. A probability value of <0.005 was considered significant. Data was stratified for the variables i.e. duration of diabetes less than 5 years or more than 5 years to address the effect of modifiers. The mean vessel and Gensini scores for known diabetics for less than 5 years were compared to those who were known diabetics for more than 5 years in the subgroups of patients with diabetic retinopathy and without retinopathy separately.

According to the Gensini score, the narrowing of the lumen of the coronary arteries is graded as follows: 1 point, ≤25%; 2 points, 26-50%; 4 points, 51-75%; 8 points, 76-90%; 16 points, 91-99% and 32 points for total occlusion (Figure 1). In addition, this primary score is multiplied by a factor that takes into account the importance of the coronary containing the lesion (5 for left main coronary artery, 2.5 for the proximal portion of the left anterior descending artery or proximal left circumflex artery and 1.5 for mid region, 1 for the distal left anterior descending artery and 1 for the mid-distal region of the left circumflex artery or right coronary artery). The sum of the total score obtained will give Gensini score.

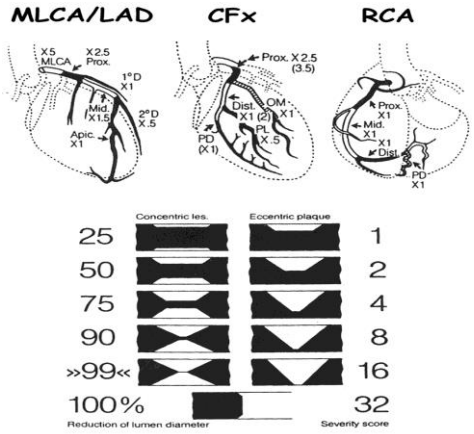

Figure 1: Gensini score

Results

Out of the 300 diabetic patients included in the study, 34.3% were found to have developed diabetic retinopathy. Mean age of the patients was 54.18 ± 8.75 years (range 35 – 70 years). No statistically significant difference was found between the mean ages of the patients with diabetic retinopathy when compared to those without diabetic retinopathy (55.57 ± 9.05 vs 53.45 ± 8.52; p = 0.072). Majority (77.7%) of the patients included in the study were males(Table 1). The mean

duration of diabetes was 9.53 ± 5.49 years. The mean duration of diabetes was significantly higher in the diabetic retinopathy group as compared to the non-retinopathy group (12.09 ± 5.11 vs 8.19 ± 5.22; p = 0.000). Majority (74%) were taking oral hypoglycemic agents for diabetes control, while 78 (26%) patients were using insulin. There were 4% patients in the age range of 35 – 40 years, 32% patients in the age range of 41 – 50 years, 36.7% patients in the age range of 51 – 60 years and 27.3% patients in the age range of 61 – 70 years. The mean vessel score was significantly higher in patients who had developed diabetic retinopathy at presentation (2.62 ± 0.60 versus 1.90 ± 1.03, p=0.000) as compared to DR negative group. Similarly, Gensini score was also found to be significantly higher in DR positive group compared to DR negative group (103 ± 37.17 vs 38.5508 ± 22.205, p=0.000). Weakly positive correlation was observed between age and mean vessel score (R = 0.116; p = 0.045) and mean Gensini score (R = 0.256; p = 0.000) whereas, there was no statistically significant difference between the mean age of the two groups. On the other hand, there was moderate positive correlation between duration of diabetes and vessel score (R = 0.319; p = 0.000) while, strongly positive correlation was observed between duration of diabetes and Gensini score (R = 0.477; p = 0.000). Further stratification of data revealed that 92 (30.7%) of patients were known diabetic for ≤ 5 years (Group I) and 208 (69.3%) were known diabetics for more than 5 years (Group II). In the Group I, the mean age was 49.33 ± 7.81; only 10.9% were having diabetic retinopathy. Among the patients in Group II, mean age was 56.33 ± 8.28; and 44.7% were DR positive. The mean vessel and Gensini scores were significantly higher in patients with diabetic retinopathy as compared to those without retinopathy in both the subgroups (Table 2). On studying the diabetic retinopathy subgroup, we found that there was no statistically significant difference in the mean vessel (2.60 ± 0.52 vs 2.61 ± 0.61; p = 0.746) and Gensini (87.10 ± 14.31 vs 105.12 ± 38.77; p = 0.242) scores of patients who were known diabetics for less than 5 years as compared to those who were known diabetics for more than 5 years (Table 2). Analysis of data of the patients without diabetic retinopathy showed that there was no statistically significant difference between mean vessel scores (1.73 ± 1.17 vs 2.03 ± 0.91; p = 0.103) of those who were known diabetics for less than 5 years compared to those who were known diabetics for more than 5 years. On the other hand, the Gensini scores (30.29 ± 19.49 vs 44.68 ± 22.46; p = 0.000) were significantly higher for those who were known diabetics for more than 5 years.

Table 1. Mean age, duration of diabetes, gender distribution, vessel score and Gensini scores of patients with diabetic retinopathy compared to those without diabetic retinopathy (n = 300)

Characteristics	DR +	DR -	p value
Mean age (years)	55.57 ± 9.05	53.45 ± 8.52	0.072
Duration of Diabetes	12.09 ± 5.11	8.19 ± 5.22	0.000
Gender			
Male (n=233)	38.6%	61.4%	0.003
Female (n=67)	19.4%	80.6%	
Vessel score	2.62 ± 0.60	1.90 ± 1.03	0.000
Gensini Score	103 ± 37.17	38.55 ± 22.20	0.000

Table 2: Comparison of mean vessel and Gensini scores of patients with or without retinopathy divided into subgroups according to the duration of diabetes (≤ 5 years or > 5 years).

Characteristics	Duration of Diabetes ≤ 5 years (n = 92)		p-value
	DR + (n = 10)	DR – (n = 82)	
Mean Age	45.40 ± 6.65	49.80 ± 7.85	0.047
Vessel score	2.60 ± 0.52	1.73 ± 1.17	0.030
Gensini Score	87.10 ± 14.31	30.29 ± 19.49	0.000
	Duration of Diabetes > 5 years (n = 208)		
	DR + (n = 93)	DR – (n = 115)	
Mean Age	56.67 ± 8.59	56.05 ± 8.04	0.680
Vessel Score	2.61 ± 0.61	2.03 ± 0.91	0.000
Gensini Score	105.12 ± 38.77	44.68 ± 22.46	0.000

Discussion

Both diabetic retinopathy and coronary artery disease are known complications of diabetes mellitus. Retinopathy in diabetics is a predictor of ischemic heart disease independent of other risk factors. Different frequencies of retinopathy have been reported by different studies among diabetic populations.[14,20] The prevalence of diabetic retinopathy in Pakistani population ranges from 12 to 54% as shown by more recent studies.[30,31] Not only there is increasing incidence of coronary artery disease among

the peoples of Indian subcontinent, but also they succumb to heart attacks 5-10 years earlier as compared to the Western populations.[20,32,33]

Present study shows that the mean vessel score and Gensini score increases with the increasing age. The mean duration of diabetes mellitus in our study was 9.5317 ± 5.4 years. Furthermore, mean duration of diabetes was 8.18 ± 5.22 in DR negative patients whereas it was 12.12 ± 5.07 in DR positive patients. In individuals with type 2 diabetes, the presence of retinopathy signifies an increased CHD risk, independent of known risk factors. [34] A five-year follow-up of the Milan Study on Atherosclerosis and Diabetes (MiSAD) showed DR is an independent predictor of cardiac events.[35] Yoon, et al described the relation of DR with coronary ischemia determined by thallium myocardial perfusion scintigraphy. [36] In another study, scores of coronary calcification determined by electron beam computed tomography were found to be closely related to the extent of diabetes complications including DR. [37] Rong J et.al, showed that the prevalence of coronary atherosclerosis, is significantly higher in the patients with T2DM with DR compared with those without DR. [38]

In present study, the mean vessel score was found to be significantly higher in diabetic retinopathy group (2.62 ± 0.60) as compared to 1.90 ± 1.03 in non retinopathy group. Similarly, Gensini score was also found to be significantly higher in diabetic retinopathy group (103 ± 37.17 versus 38.55 ± 22.20). In the previous study by Norgaz, et al, it was shown that the patients with diabetic retinopathy had significantly higher vessel (2.3 ± 0.9 versus 1.3 ± 1.1, P< 0.001) and severity (63.7 ± 41.0 versus 22.6 ± 14.9, P< 0.001) score than patients with no evidence of diabetic retinopathy. In the results of both the studies, it can be seen that vessel score and Gensini scores were higher for the patients with retinopathy patients as compared to non diabetic retinopathy group. [20] The mean vessel score (1.83 ± 1.14 versus 2.29 ± 0.83, p=0.000) and mean Gensini scores (36.47 ± 25.96 versus 71.70 ± 43.05, p=0.000) were significantly higher in Group II compared to Group I.

Conclusion

1.The frequency of diabetic retinopathy was found to be high and increased with the increasing number of years of diabetes.

2. Higher vessel and Gensini scores were found in patients with diabetic retinopathy as compared to those who did not develop diabetic retinopathy.

3. Funduscopy should be assessed as a screening and risk stratification tool in the assessment of coronary artery disease.

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