Comparison of Severity of Coronary Artery Disease in Diabetic and Non-Diabetic Subjects using Gensini Score in Indian Subjects

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Abstract

Background: Diabetes mellitus is usually associated with higher risk of microvascular and macrovascular complication especially Coronary Artery Disease (CAD). The Study was aimed to study the severity of CAD in diabetic and nondiabetic population who has undergone coronary angiography using Gensini scoring.

Methodology: 233 subjects admitted for coronary angiography were studied. All subjects were subjected to full medical history and physical examination; echocardiography, measurement of glycated hemoglobin (HbA1c), detection of urine microalbumin and coronary angiography was carried on. Severity of CAD was assessed by using Gensini score.

Results: Out of 233 subjects, 140 were diabetics (60.1%). Among diabetics 95% had abnormal Gensini score, which is statistically significant (p=0.004>0.01), among nondiabetic subjects 84% had abnormal Gensini score (suggests CAD), with odd’s ratio 3.6 (CI 1.4 to 9.3). There was good correlation between diabetes duration and Gensini score with r=0.626 (p=0.0001). Mean age in diabetics is 60 years and in nondiabetics is 58 years. Multiple regression analysis of diabetes duration, smoke pack years, hypertension, Ankle Brachial Index (ABI), Left Ventricular ejection fraction, glycated hemoglobin, Total Cholesterol/High density cholesterol (TC/HDL), Non-HDL cholesterol, urine microalbumin, BMI (Body Mass Index) and Waist Hip ratio with Gensini score; showed significant positive impact on Gensini score by Diabetes duration (beta=0.455), Urine microalbumin (beta=0.207), TC/HDL (beta=0.173) and significant negative impact on Gensini score by ABI (beta=-0.388), LVEF (beta= -0.102).

Conclusion: Severity of CAD as assessed by Gensini Score was higher in subjects with diabetes when compared to nondiabetic Indian subjects.

Keywords: Diabetes; Coronary artery disease; Gensini score

Introduction

The association between Type 2 Diabetes Mellitus and a higher incidence of coronary artery disease is well known [1]. A positive association has been reported between the duration of diabetes and the risk of developing CAD (coronary artery disease) [2]. Studies of small sample size have shown an association between the metabolic control and duration of diabetes and the severity of coronary artery disease in subjects with diabetes [3]. An independent association between fatal coronary artery disease and increasing duration of DM (Diabetes mellitus) has been shown in men [4]. There is evidence to show that the duration of diabetes is associated with greater risk of Acute coronary syndromes [5]. The UKPDS3 demonstrated that intensive glucose control, by keeping the HbA1c <7% (glycated hemoglobin) helped to reduce microvascular complications; the reduction in risk of MI was of borderline significance. Other studies suggest that coronary artery disease and HbA1c are predictors of cardiovascular mortality [6-8]. Individuals with diabetes-associated nephropathy typically have long periods of excessive albuminuria with gradual reductions in creatinine clearance as they approach end stage. There is a graded increase in risk for cardiovascular and total mortality with incremental increases in urine albumin:creatinine ratio among high-risk individuals with hypertension and diabetes [9-11].

Extensive review of literature revealed that there are no studies which have compared the severity of coronary artery disease in diabetic and nondiabetic subjects using Gensini scoring among Indian population.

Subjects and Methods

The subjects were approached individually and explained about the objectives of study in their preferred language. A written consent was taken from the subjects who were willing to participate in study. Ethics committee approval was obtained from the institutional Ethics Committee of KMC (Kasturba Medical College), Mangalore (affiliated to Manipal University), India prior to the commencement of study.

The present cross-sectional study was conducted between December 2011 and December 2012, 233 subjects admitted to the department of cardiology, KMC Mangalore, for elective coronary angiography were enrolled in the study. Information pertaining to study variables were collected using semi-structured proforma, which included age, sex, presenting complaints, family and past history of angina or ischemic heart disease, duration of diabetes, duration of HTN (hypertension), duration of smoking, duration of alcohol consumption and subjects were divided into diabetic and non-diabetes. All the subjects were recruited from KMC, Mangalore.

Blood and urine investigations like HbA1c, TC/HDL (ratio of total...
cholsterol and high density cholesterol) and urine microalbumin were done in KMC hospital lab, Mangalore.

BMI (Body Mass Index)

Patient's weight was recorded, in kilograms, to the nearest whole number. Their height was recorded, in meters. BMI was then calculated as Weight (in kgs)/Height^2 (in mt).

W: H (Waist Hip ratio)

Waist circumference was calculated as described. Hip circumference was calculated at the level of greater trochanter of the femur and the most prominent part of the gluteal region using a non-stretchable measuring tape. Waist – hip ratio was then calculated by waist circumference / hip circumference.

All subjects LVEF (Left Ventricular Ejection Fraction %) calculated using echocardiography by cardiologist.

ABI (Ankle Brachial Index) was calculated by conventional methods using both palpatory and auscultatory techniques. Ankle systolic blood pressure was calculated by tying the standard cuff to the calf muscle and palpating the posterior tibial artery. The ratio was then calculated by dividing Ankle SBP by brachial SBP On the basis of this ratio.

Urine spot sample was sent K.M.C. Hospital lab, where quantitative estimation of urine albumin was done by an autoanalyser. On the basis of urine albumin excretion, patients were graded as: 0-20 mg/L: Normal and >20 mg/L: Microalbuminuria (abnormal).

Coronary angiogram

The diagnostic procedure was performed using Seldenger's technique, all images were recorded digitally. Assessment of the severity of coronary artery disease was done using Gensini score [12]. Gensini score grades narrowing of the lumen of the coronary artery and scores it with numerical values with the following method; score 1 for 1–25% narrowing, 2 for 26–50% narrowing, 4 for 51–75%, 8 for 76–90%, 16 for 91–99%, and 32 for a completely occluded artery. This score is then multiplied by a factor that represents the importance of the lesion's location in the coronary artery system. For the location scores, 5 points were given for the left main lesion; 2.5 for the proximal left anterior descending (LAD) or left circumflex (LCX) artery; 1.5 for the mid segment LAD and LCX; 1 for the distal segment of LAD and LCX, first diagonal branch, first obtuse marginal branch, right coronary artery, posterior descending artery, and intermediate artery; and 0.5 for the second diagonal and second obtuse marginal branches. Gensini score is highly significant as the sum of the scores for all three coronary arteries to evaluate the entire extent of coronary artery disease.

The statistical methods

Comparison of numerical variables between the study groups was done using Student t test for independent samples. For comparing categorical data, Chi square (x2) test was performed. Correlation between various variables was done using Karl Pearson correlation. p values less than 0.05 was considered statistically significant. Multiple regression analysis was done to remove confounding factor. All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA).

Results

A total of 233 subjects were enrolled in the study. The Mean age of subjects was 58 years with nearly 2/3rd of them in age group of 50 to 70 years, they included 168 male and 65 female. Out of 233 subjects 140 were diabetics.

In the study hypertension was present in 118 (50.6%) subjects, family history of diabetes was present in 177 (76%) and 129 (55.4%) subjects were smokers. The average Gensini score of our studied population was 53.83. Around 21 subjects (9%) had Gensini score of Zero (Normal Gensini score means No coronary artery disease).

When diabetic and nondiabetic subjects are compared, more number of diabetic subjects (95%, 133 subjects) had abnormal Gensini scores. Among nondiabetic subjects 84% (78 subjects) had abnormal Gensini score (suggests CAD), as shown in Table 1. Mean age in diabetics is 60 years and in nondiabetics is 58 years. Diabetic subjects had risk of developing CAD 3.6 times more than non-diabetics. Strength of association of DM and CAD is very strong as odds ratio is 3.654 (with confidence interval of 1.428 to 9.351), p value for above comparison is 0.004, which is highly significant.

As shown in Table 2, when Diabetes duration compared with Gensini scores, as the duration of diabetes increases the number of subjects with abnormal Gensini scores increases; 88% (37 subjects) with DM duration of 1 to 5 years had abnormal Gensini score, whereas 100% (66 subjects) with DM duration of 11 to 30 years had abnormal Gensini score. Majority of subjects with abnormal Gensini score were having DM duration of 11 to 20 years. P value for above is 0.007, which is highly significant.

Among the subjects with urine microalbumin >20 around 99% (105 subjects) had abnormal Gensini score (suggests CAD) and among the subjects with urine microalbumin <20 around 83% (106 subjects) had abnormal Gensini score, which is shown in Table 3. The probability of developing CAD in subjects with high microalbumin levels is very strong as odds ratio is 21 (confidence interval of 2.748 to 157.485), the above association is statistically significant (p=0.000).

| GENSINI score | No. of subjects (percentage) | TOTAL |
|---------------|-------------------------------|-------|
| Abnormal      | Normal                        |       |
| Diabetics     | 133 (95%)                     | 7 (5%) | 140               |
| Nondiabetics  | 78 (84%)                      | 15 (16%) | 93           |
| Total         | 211 (85%)                     | 12 (5%) | 233 (100%)       |

Table 1: Comparison of Diabetics and Nondiabetics with Gensini score.

| DM Duration In years | GENSINI score | No. of subjects (percentage) | TOTAL |
|----------------------|---------------|-------------------------------|-------|
|                      | Abnormal      | Normal                        |       |
| 1 – 5                | 37 (88%)      | 5 (12%)                       | 42    |
| 6 – 10               | 30 (94%)      | 2 (6%)                        | 32    |
| 11 – 20              | 41 (100%)     | 0 (0%)                        | 41    |
| 21 – 30              | 25 (100%)     | 0 (0%)                        | 25    |
| TOTAL                | 133 (85%)     | 7 (5%)                        | 140 (100%) |

Table 2: Comparison of DM Duration with Gensini score.

| Urine Microalbumin (microgram/min) | GENSINI score | No. of subjects (percentage) | TOTAL |
|-----------------------------------|---------------|-------------------------------|-------|
|                                   | Abnormal      | Normal                        |       |
| >20                               | 105 (99%)     | 1 (1%)                        | 106   |
| <20                               | 106 (83%)     | 21 (17%)                      | 127   |
| Total                             | 211 (85%)     | 12 (5%)                       | 233 (100%) |

Table 3: Comparison of Urine microalbumin with Gensini score.
As shown in Table 4, when the relationship between Gensini score and all variables was assessed with Karl Pearson coefficient, we observed in our study that DM duration (r=+0.626), urine microalbumin (r=+0.510), Smoke pack years (r=+0.317), TC/HDL (r=+0.266) and HbA1c (r=+0.212) have strong positive correlation with Gensini score. ABI (r=−0.525) and LVEF% (r=−0.278) have strong negative correlation with Gensini score.

It is also observed in the study, age (r=+0.161), HTN duration (r=+0.161) non-HDL cholesterol (r=+0.124) and W:H (r=+0.115) have positive correlation with Gensini score.

The correlation of age, DM duration, HTN duration, smoke pack years, alcohol years, ABI, LVEF%, HbA1c, TC/HDL, and urine microalbumin with Gensini score are statistically significant.

As showed in Table 5, when multivariate analysis (Regression) with ANOVA was done for predictors (constant) like DM duration, HTN duration, BMI, W:H (Waist Hip ratio), ABI, LVEF%, HbA1c, TC/HDL, Non-HDL cholesterol, creatinine and urine microalbumin with dependent variable Gensini score it is found that correlation standardized coefficient (beta) of DM duration is +0.455, urine microalbumin is +0.207, TC/HDL is +0.173, ABI is -0.388, creatinine is -0.115 and LVEF% is -0.102; p values for all the beta values is less than 0.05.

The impression from the above is Gensini score increases with increasing DM duration, urine microalbumin levels and TC/HDL; Gensini score increases with decreasing ABI and LVEF% values. The impressions from multivariate analysis are CAD has high positive correlation with DM duration and urine microalbumin and strength of association between them is strong. Also CAD has high negative correlation with ABI and LVEF% with strong strength of association.

**Discussion**

The results showed that there is a statistically significant positive correlation between duration of diabetes and Gensini scores (P value 0.007). My finding was confirmed by data published in year 2010 in a study by GuoLixin et al. [13], where Spearman's correlation analysis was performed with Gensini score as dependent variable and all risk factors as independent variables. This analysis showed that Gensini score was positively correlated with duration of diabetes mellitus.

In our study, we found statistically significant higher severity of CAD in subjects with microalbuminuria (P<0.001). This matched with the study of Deveci et al. [14] who studied the relationship between microalbuminuria and the presence and extent of coronary atherosclerosis in four hundred and two subjects and found a positive correlation between microalbuminuria and extent of CAD both in the diabetic and nondiabetic subjects and concluded that Microalbuminuria is an independent predictor for the presence (P<0.001) and severity of CAD (P<0.001, β=0.563). Also our result goes hand in hand with the data published by Defilippis et al. [15] in 2010 who conducted the MESA study (Multi Ethnic Study of Atherosclerosis).

GuoLixin et al. [13] also concluded that there was a positive correlation between severity of CAD and microalbuminuria and that this association was significant in the subgroup of subjects with type 2 diabetes (P=0.045) and in those without diabetes (P=0.023).

Our study results showed positive correlation of Gensini score with TC/HDL, with Karl Pearson correlation coefficient of 0.266, p<0.001.

Multiple regression analysis showed positive correlation of Gensini with Diabetes duration, urine microalbumin and TC/HDL (coefficient beta of 0.455, 0.207 and 0.173 respectively).

**Table 4:** Karl Pearson correlation of different variables of subjects with Gensini score.

| Variable                  | Karl Pearson correlation r value | p    |
|---------------------------|---------------------------------|------|
| AGE                       | -0.161(*)                       | .014 Sig |
| DM duration               | 0.626(**)                       | .000 Sig |
| HTN duration              | -0.161(*)                       | .014 Sig |
| Smoking pack-yrs          | 0.317(**)                       | .000 Sig |
| Alcohol yrs               | -0.12 .081                      | .861 |
| BMI (Body Mass Index)     | 0.062 .349                     |      |
| Waisthip                  | 0.115 .079                     |      |
| ABI (Ankle Brachial Index)| -0.525(**)                      | .000 Sig |
| LVEF % (Left ventricular Ejection Fraction) | -0.278(**) | .000 Sig |
| HbA1C                     | 0.212(**)                       | .001 Sig |
| TC/HDL                    | 0.266(**)                       | .000 Sig |
| Non HDL cholesterol (Total cholesterol minus HDL) | 0.124 | 0.58 |
| CREATININE                | 0.063 .342                     |      |
| URINE MICROALBUMIN        | 0.510(**)                       | .000 Sig |

*Correlation is significant at the 0.05 level (2-tailed).
**Correlation is significant at the 0.01 level (2-tailed).

| Coefficients* | Model | Coefficient | Std Error | t | Sig |
|---------------|-------|-------------|-----------|---|-----|
| (Constant)    |       | 143.827     | 182.871   | 0.78 | .439 |
| BMI           | -0.388 | 0.115       | -3.36     | 0.001 | .000 |
| DM duration   | 0.161  | 0.007       | 2.39      | 0.024 | .018 |
| HTN duration  | 0.214  | 0.007       | 2.66      | 0.008 | .009 |
| Smoking pack  | 0.124  | 0.007       | 1.82      | 0.068 | .000 |
| Alcohol yrs   | 0.062  | 0.007       | 0.86      | 0.392 | .000 |
| BMI            | 0.115  | 0.007       | 1.57      | 0.116 | .000 |

**Table 5:** Multiple regression analysis of all variables in subjects.
**Limitations of our Study**

A detail of treatment of diabetes and hypertension was not collected in detail.

Details of content, amount and type of alcohol was not collected.

In the future, there is a need for study with larger sample size to confirm the results obtained.

**Conclusion**

Severity of CAD as assessed by Gensini Score was higher in subjects with diabetes when compared to nondiabetic Indian subjects.

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