Coronary Angiographic Findings in Diabetic Patients Versus non-Diabetics with Coronary Heart Disease

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ABSTRACT

Background :Atherosclerosis is the most frequent underlying cause of ischemic heart disease and a major cause of death all over the world. This study was carried out to analyze and compare the angiographic findings in patients with diabetes mellitus versus non diabetics with coronary heart disease , and to correlate these findings with some risk factors for coronary heart disease.

Methods: A total of 100 patients were studied, 50 with diabetes mellitus, and 50 non diabetics. This study was carried out at Al-Sadr teaching hospital in Basrah, Southern Iraq during the period April 2009- September 2009. All patients were known to have coronary heart disease. Risk factors for coronary heart disease were studied and coronary angiography was performed to define coronary lesions for all patients, and were classified into those who had single , two , three or four vessels disease, according to the number of critical coronary vessels involed. Angiography was considered as normal when the test did not identify any obstruction of any major epicardial artery.

Results: Diabetic patients had more multi-vessels involvement coronary heart disease than non diabetics. Right coronary artery, left main stem artery, left circumflex artery involvement and left ventricular systolic dysfunction were seen more in diabetics than non diabetic patients.

Conclusions: This study showed that diabetic patients had more critical multi-vessels involvement than non diabetic. Diabetic patients had also worse coronary angiographic findings independent on the presence or absence of other risk factors
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Al – Kindy Col Med J 2013; Vol. 9 No. 1 P:23

Introduction

Coronary heart disease (CHD) due to atherosclerosis is a major cause of death all over the world and is the most common form of heart disease [1, 2]. Its incidence is increasing among different societies and by 2020 it is estimated that it will be the major cause of death in all regions of the world [2]. Until recently, atherosclerosis was thought as a degenerative slowly progressive disease predominantly affecting the elderly, however, laboratory and pathological data support the idea that inflammation has a role in both initiation and progression of atherosclerosis and anti inflammatory agents may have a role in the prevention of cardiovascular disease [3, 4]. Despite that CHD increases with age and that the age is the most important risk factor, but CHD in general tend to be multifactorial and directly related to the prevalence of multiple cardiovascular risk factors .The Framingham heart study[5] particularly played a vital role in defining the contribution of risk factors to CHD occurrence in the general population .The major risk factors extensively studied at Framingham heart study included cigarettes smoking, hypertension, high serum cholesterol and various cholesterol fractions, low level of high density lipoprotein (HDL) cholesterol and diabetes mellitus, advancing age was also included as risk factor in the Framingham chart because of increased absolute risk with aging. Factors other than listed as major risk factors, which have been studied at Framingham or elsewhere ,are obesity, physical inactivity, family history of premature CHD, hypertriglyceridemia, small low density lipoprotein(LDL) particles, increased lipoprotein a , increased serum homocystine, stress, dietary habit and abnormalities in several coagulation factors that increase the likelihood for developing CHD [6]. Coronary artery disease with normal or patent coronary circulation by angiography has been documented .The overall prevalence rate of ischemic heart disease with normal angiogram is low and various mechanism have been hypothesized including coronary spasm, coagulation disorders, and embolizations[7]. Although there are more promising modalities for evaluation of coronary lesions ,like intravascular ultrasonography or electron beam or ultrafast CT-scan for detection of coronary calcification, coronary angiography remain the 'gold standard' for identifying the

presence or absence of stenosis due to coronary artery disease and provide the most reliable anatomical information for determining the appropriateness of medical therapy, percutaneous coronary intervention, or coronary artery bypass graft in patients with ischemic heart disease. [8]

Epidemiological data from the Framingham study demonstrated a two –to four fold increase in atherosclerotic disease in diabetic patients and the risk of death from cardiovascular disease is much higher for patients with diabetes compared to patients without diabetes[9] and diabetic patients who have had myocardial infarction have a higher mortality rate in the acute phase of myocardial infarction and in long term follow up even when they treated with fibrinolytic regimen.[10]In diabetic patients plaque erosion appear to occur with higher frequency. Close control of blood sugar improves micro vascular complications, but has little effect on CHD events. [11]

Methods

A total of 100 patients were studied, 50 with diabetes mellitus, 31 males and 19 females with an age ranged from 40-70 years (mean age 59.2 years) and 50 non diabetics, 35 males and 15 females with an age ranged from 40-70 years (mean age 57.9 years). Patients were referred to the cardiology department in Al-Sadr teaching hospital for diagnostic angiography between April 2009 and September 2009. Written informed consent was obtained from all patients before the study. All patients were known to have CHD confirmed by typical history of disease, electrocardiography (ECG), and positive exercise ECG test for majority of the patients. Echocardiographies were done for all patients to asses left ventricular function (LV) function. All 50 Patients with diabetes mellitus were already on insulin or oral antidiabetic agents. The non diabetics were considered as a control group, they were all tested for fasting plasma sugar (FPS). FPS was considered as normal if it was less than 7 mmol/l.

Preliminary evaluation of all patients included the clinical characteristics of the patients' age, sex, systemic hypertension which was considered to be present if the patient was already diagnosed with hypertension and on treatment, current smoking which was considered present if the patient has smoked everyday within the previous month .[12] Family history of premature CHD which was defined as any first degree relative of patients who had documented CHD under age of 55 years in males and under 65 years in females[13] . The degree of obesity was expressed as body mass index (BMI) according to Quetelets formula. [14]

Lipid profile was not tested because it was not available at the time of this study.

Coronary angiography was performed to define coronary lesions in the department of invasive cardiology. Coronary angiography was performed by the Seldengers technique and visually analyzed by a cardiologist. The degree of luminal narrowing was recorded in percentage of prestenotic diameter. Critical CHD was considered when there was at least 70% reduction in the diameter of a major epicardial coronary artery as right coronary artery (RCA), left circumflex artery (LCx), left anterior descending artery (LAD) or at least reduction 40% in the diameter of left main stem artery (LMS). Angiography was considered as normal when the test did not identify any obstruction of any major epicardial artery. The numbers of critical coronary vessels involved were recorded; accordingly the patients were classified into those who had single, two, three or four vessels disease.

Data were coded and fed on computer. Analysis was done on SPSS. For the determination of statistical significance among different variables, a descriptive statistics like mean together with analytic statistics like chi squared test, have been done when appropriate. A p-value less than 0.05 were considered significant.

Results

Almost 50% of patients in both groups were at the age between 60-70, however no statistical significant differences were found between all age groups and between male and female diabetic and non diabetic patients. P= 0.78, 0.288 respectively.

A Single vessel involvement was significantly more in non diabetics as compared to diabetic patients. P= 0.001, while there were no statistically significant differences in two vessel involvement in both groups. P= 0.001.

Three and four vessels involvements were more seen in diabetic than non diabetic patients. Statistically these differences were significant.
P= 0.001. Table 1

As regard to the site of critical coronary artery involvement, it was found that RCA, LCx and LMS were involved more in diabetic as compared to non diabetic patients. The differences were statistically significant. P= 0.001, 0.001 and 0.001 respectively.

Although LAD involvement was more in diabetic than non diabetic patients, but the differences were statistically not significant. P=0.488.

Normal angiographies were more in non diabetic than diabetic patients. Statistically these differences were significant. P= 0.001. Table 2.

Left ventricular systolic dysfunction was more in diabetic than non diabetic patients. The differences were statistically significant between the two groups. P= 0.001.

There were no statistically significant differences in critical angiographic findings between diabetic and non diabetic hypertensive. P= 0.063. Table 3.

There were no significant differences between the effect of smoking, sex, family history of CHD, BMI and critical angiographic findings in both groups. P= 0.062, 0.183, 0.160, 0.046, and 0.855 respectively.

Table 4, 5, 5, 7, and 8 respectively.

Table 1 Number of vessels involved in studied patients.

Extent of coronary artery disease	Diabetic	Non Diabetic	Total	P-value
	No. (%)	No. (%)		
Normal angiography	1 (2%)	5 (10%)	6 (6%)	0.001
Single vessel disease	8 (16%)	24 (48%)	32 (32%)	0.001
Two vessels disease	10 (20%)	11 (22%)	21 (21%)	NS
Three vessels disease	26 (52%)	8 (16%)	34 (34%)	0.001
Four vessels disease	5 (10%)	2 (4%)	7 (7%)	0.001
Total	50 (100%)	50 (100%)	50 (100%)	

Table 2 Coronary artery involvement in studied patients.

Coronary artery*	Diabetic	Non Diabetic	P-value
	No.(%)	No. (%)	
LMS	14 (28%)	2 (4%)	0.001
LCX	37 (74%)	17 (34%)	0.001
RCA	37 (74%)	21 (42%)	0.001
LAD	39 (78%)	36 (72%)	NS

**More than one coronary artery involvement could be present*

Table 3 Angiographic findings in diabetic and non diabetic hypertensive.

Angiographic Results	Diabetic+HT No.=31	Non diabetic+HT No.=28	Total
Normal angiography No. (%)	1 (3%)	5 (18%)	6 (10%)
Abnormal angiography(one vessel involved or more) No. (%)	30 (97%)	23 (82%)	53 (90%)
Total (%)	31 (100%)	28 (100%)	59 (100%)
P= 0.063			

Table 4 Correlation of smoking and, normal critical vessel involvement.

Angiographic Results	Diabetic+ current smoking No.=8	Non diabetic+ current smoking No.=14	Total
Normal angiography No. (%)	0 (0%)	2 (14%)	2 (9%)
Abnormal angiography (one vessel involved or more) No. (%)	8 (100%)	12 (86%)	20 (91%)
Total (%)	8 (100%)	14 (100%)	22 (100%)
P= 0.062			

Table 5 Correlation of male sex, normal and critical vessel involvement.

Angiographic results	Diabetic males No.=31	Non diabetic males No.=36	Total
Normal angiography No. (%)	0 (0%)	2 (6%)	2 (3%)
Abnormal angiography (one vessel involved or more) No. (%)	31 (100%)	34 (94%)	65 (97%)
Total (%)	31 (100%)	36 (100%)	67 (100%)
P = 0.183			

Table 6 Correlation of female sex, normal and critical vessel involvement.

Angiographic results	Diabetic females No.=19	Non diabetic females No.=14	Total
Normal angiography No. (%)	1 (4%)	3 (21%)	4 (12%)
Abnormal angiography (one vessel involved or more) No. (%)	18 (96%)	11 (79%)	29 (88%)
Total (%)	19 (100%)	14 (100%)	33 (100%)

P= 0.160

Table 7 Correlation of family history of CHD, normal and critical vessel involvement.

Angiographic Results	Diabetic+ family history of CHD No.=5	Non diabetic+ family history of CHD No.=10	Total
Normal angiography No. (%)	0 (0%)	1 (10%)	1 (7%)
Abnormal angiography one vessel involved or more) No. (%)	5 (100%)	9 (90%)	14 (93%)
Total (%)	5 (100%)	10 (100%)	15 (100%)

P= 0.046

Table 8 Correlation of BMI, normal and critical vessel involvement.

Angiographic Results	Diabetic+ BMI>25 No.=31	Non diabetic+ BMI>25 No.=40	Total
Normal Angiography No. (%)	1 (3%)	1 (3%)	2 (3%)
Abnormal Angiography (one vessel involved or more) No. (%)	30 (97%)	39 (97%)	69 (97%)
Total (%)	31 (100%)	40 (100%)	71 (100%)

P= 0.855

Discussion

Diabetes mellitus is considered as one of the modifiable risk factor for IHD.

There are many mechanisms that explain the higher incidence of stenosis and occlusion rate in diabetic patients .These mechanisms include:

1) Haemostatic abnormalities; that predispose them for increased risk of vascular thrombosis. Platelets aggregation is increased with enhanced synthesis of thromboxane A2 [(15)], and platelet activation (platelet factor 4 and B-thromboglobulin) can be elevated [(16)].

2) A relative hypercoagulopathy state may be present in diabetic patients. Procoagulant factors include fibrinogen, factor VII, and von willebrand factor may be increased in diabetic patients while the synthesis of prostacyclin is reduced [(17)]. Fibrinolysis may be attenuated because of increased in plasminogen activator inhibitor type 1 and

lower level of urokinase –type plasminogen activator [18].

3) Functional abnormalities of the vascular endothelium; vascular endothelial dysfunction which may further enhance the tendency to vasospasm and coronary thrombosis as hyperglycemia causes endothelial dysfunction by decreasing the production of endothelium-derived relaxing factor [19], increasing oxidative stress by vascular protein glycation [20] , and free radicals formation [21] , and decreased prostacyclin production[22]. Moreover, lipoprotein abnormalities [23] may impair endothelin-dependent relaxation [24] and greater growth factor stimulation occurs in diabetics [25]. These factors are likely to produce a prothrombotic state in patient with diabetes mellitus, and may account for more aggressive coronary artery lesion. All these mechanisms, the prothrombotic state, imbalance of fibrinolytic systems and endothelial dysfunction may contribute and explain the problem of coronary stenosis with poor angiographic outcome in patients with diabetes mellitus.

In this study diabetics were slightly older than non diabetics, with a mean age of 59.2, and no differences were found between all age groups and between males and females diabetics and non diabetics .These results were consistent with other study [26], who showed that diabetic patients were slightly older than non diabetic and no differences were found between their males and females patients.

IHD with normal angiography in this study may be explained by causes other than obstructive lesions of coronary arteries, like coronary spasm which is probably the main cause or other rare causes like spontaneous lyses of the thrombus, short duration of disease or lesions overlooked on coronary angiography [27]. Normal angiography were more in non diabetics than diabetic patients this result was consistent with other studies [28, 29], who found that 13% of their IHD patients have normal angiography.

Normal angiographic findings in non diabetics could be explained by that non diabetics are lacking the mechanisms which predispose them to high incidence of stenosis and occlusion rate and hence more vessel involvement.

There were no statistically significant differences between diabetic and non diabetic patients in correlation between critical vessels involvement and some risk factors for IHD as hypertension, smoking, sex, family history of IHD and BMI. These results were not consistent with other study. [30] This disagreement between current study and study can be explained by a small sample size used in this study.

Multi vessel disease 3 and four vessels were seen more in diabetics than non diabetic's patients. These results were consistent with so many other studies. [31, 32, 33-35] This again could be explained by mechanisms which predispose diabetics more to stenosis and occlusion than non diabetics.

In this study Left main stem , LCx and RCA involvement were significantly higher in diabetics .These results were consistent with other studies.[34-37] This higher involvement in diabetics could be due to factors other than smoking, hypertension and obesity since all these risk factors did not show any effect regarding critical vessel involvement, between diabetics and non diabetics.

Left ventricular systolic dysfunction was more in diabetic than non diabetic's patients which was similar to other studies. [36, 38] This could be explained by multi vessel involvement in diabetics, therefore causing more hypokinesia or akinesia and hence LV systolic dysfunction.

Unfortunately, lipid profile was not studied in this study to show the effect of lipoprotein abnormalities in coronary artery disease by mechanisms impairing endothelin-dependent relaxation[24], greater growth factor stimulation[25] and hence prothrombotic state.

In conclusions this study showed that diabetic patients had more critical multi-vessel involvement than non diabetics and had worse coronary angiographic findings independent on the presence or absence of risk factors.

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