October 2011

Frequency of silent myocardial ischaemia in diabetics: a single centre study

Adil Sheikh
Aga Khan University

Syed Shah Faisal
Aga Khan University

Abdul Jabbar
Aga Khan University

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Adil Sheikh, Syed Shah Faisal, Abdul Jabbar
Department of Medicine, Aga Khan University, Karachi.

Abstract

Objective: To find the frequency of silent myocardial ischaemia in diabetics as compared to non-diabetics.

Methods: This was a cross sectional study conducted between November 2008 and March 2010. Two hundred subjects were recruited by convenience sampling after informed cnosent. All were subjected to an exercise stress test. Electro-cardiographic changes were noted for silent Ischaemia Descriptive Statistics were applied for significance.

Result: Of the 200 subjects included in the study, 31 had diabetes and 1`69 were non-diabetics. The mean age was 46±10 years. Twenty eight subjects tested positive for silent ischaemia, of whom six were diabetics(19%) and 22 were non-diabetics(13%).Hypertension and obesity were found more frequently in diabetics (48% Vs 27%) p=0.019 and (35% Vs 18%) p=0.027 respectively.

Despite the greater proportion of diabetics having asymptomatic myocardial ischaemia as compared to non-diabetics statistical significance(p = 0.397) was not observed.

Conclusion: There was no significant difference in the frequency of silent ischaemia amongst the two groups.

Keywords: Exercise test, Ischaemia, Diabetes Mellitus, Hypertension, Obesity (JPMA 61:1037; 2011).

Introduction

Diabetes Mellitus is a well established risk factor for coronary heart disease. Sudden cardiac death or acute coronary events are twice as common in diabetics compared to non- diabetics.[1] Cardiovascular complications are a major cause of mortality , accounting for 65% to 85% deaths in the diabetic population.[2] The cardiovascular prognosis is worse in diabetics compared to non diabetics with cardiovascular disease - so much so that diabetes has been labeled as a 'coronary heart disease equivalent.'[3] Not only is coronary heart disease more extensive in diabetics but it also has an atypical presentation with myocardial ischaemia not manifesting with pain in a significant proportion of cases.[4]

Silent myocardial ischaemia has always been a poorly understood clinical entity. The cause of silent ischaemia has often been attributed to autonomic neuropathy arising in diabetes mellitus.[5] It has been postulated that a combination of abnormalities in the sympathetic and parasympathetic pathways may be responsible.[6] However paradoxical findings of presence of silent myocardial infarction in diabetics without neuropathy and presentation of angina in diabetics have also been made.[4,7] The reported prevalence of silent myocardial ischaemia in diabetic patients, as observed in many clinical studies has been found to be ranging between 20%-50% and has been higher than non diabetics. However in retrospect some authors do not report any significant difference in the finding of silent ischaemia when diabetic patients were compared to non-diabetic subjects.[4,5,8,9]

It has been reported that silent myocardial ischaemia (SMI) is not different from symptomatic Coronary Artery Disease with respect to the ischaemic insult and acute coronary events or sudden cardiac death later on.[1,7] Objectively SMI has been labeled as a predictor of severe coronary heart disease[10] with 40-90% patients having SMI showing evidence of coronary artery stenosis on

angiography.[3] Evidence suggests that individuals having co-morbidity with type 2 diabetes present in association with other coronary risk factors and are more likely to have silent myocardial ischaemia.[3,11,12] Therefore in patients having type 2 diabetes mellitus and a coronary risk factor profile an aggressive diagnostic and therapeutic approach is warranted[13] since they are known to develop accelerated coronary artery disease. The importance of coronary risk factors in developing coronary artery disease has been highlighted by De Luca et al.[11] who observed that episodes of silent myocardial ischaemia increased in both diabetic and non-diabetic subjects if two or more coronary risk factors were present.

Literature regarding the finding of silent myocardial ischaemia in Asian diabetic patients has been scarce. Differing prevalence of SMI in previous studies has been explained by different characteristics of study population in each setting.[4] This study was conducted in a single centre, describing and comparing the frequency of Silent Myocardial Ischaemia in diabetics and non-diabetics going through a screening Exercise Stress Test. Our primary objective was to compare frequency of silent myocardial ischaemia in diabetics and non-diabetics.

Patients and Methods

In this cross sectional study, two Hundred patients were prospectively recruited in the Cardiopulmonary Department of Aga Khan University Hospital (AKUH) for health screening to assess their functional capacity by exercise stress test. AKUH is a tertiary care hospital which caters to wide variety of patient population in the urban metropolis of Karachi, the largest city and commercial hub of the country.

This study was conducted between the period spanning from November 2008 to March 2010, with data collection being completed by January 2010. Convenience sampling was applied and sampling size was calculated using Sample Size Determination in Health Studies software provided by the World Health Organization. Using an anticipated population proportion of 15%[14] for silent myocardial ischaemia, with an absolute precision of 5% with 95% confidence interval, the sample size calculated was 196.

To be included in the study, respondents had to be physically fit for exercise with a normal resting (baseline) ECG with no prior history of coronary heart disease. Informed consent was obtained before inclusion in the study.

Exclusion criteria applied were to subjects with a positive history of coronary heart disease, with symptoms of angina, subjects taking digoxin or beta blockers, subjects with a permanent pacemaker and those who were physically disabled or unable to take a stress test. Subjects with resting systolic blood pressure values greater than 200mm Hg and abnormal baseline ECG changes like ST-segment depression, right or left bundle branch block were also excluded.

After taking formal consent - patients' weight, height, pulse, respiratory rate and blood pressure were measured. Laboratory investigations for haemoglobin and lipid profile (HDL, LDL and total cholesterol) were estimated. Urine analysis was done for proteinuria. Twelve (12) lead resting ECG (baseline) was also done in all subjects and assessed for any abnormal changes.

Prior to exercise testing, each recruited patient underwent a structured history and medical record review to document co-morbidities and relevant past medical history. A questionnaire was used for documentation of major coronary risk factors including history of hypertension, dyslipidaemia, previous myocardial infarction or acute coronary events, any coronary interventional procedures (revascularization or angioplasty), diabetes mellitus-including duration of disease and mode of treatment used, obesity, family history of coronary heart disease and smoking habits.

Hypertension was defined according to the Joint National Committee Guidelines,[15] as a systolic blood pressure of 140 mmHg or higher, a diastolic blood pressure of 90 mmHg or more, or the use of antihypertensive medication.In respondents who were diabetic, hypertension was defined as a systolic blood pressure greater than 130 mm of Hg and diastolic pressure above 80 mm of Hg. Hyperlipidaemia was defined as a total cholesterol level of 200 mg/dl (5.18 mmol /l) or higher or the use of lipid-lowering drugs. Diabetes was defined by blood glucose levels either a fasting blood glucose >126mg/dl or random glucose >200mg/dl.

Electrocardiogram changes were assessed among respondents undergoing an exercise stress test (E.S.T) to look out for ischaemic changes in otherwise asymptomatic subjects without any prior evidence of coronary heart disease. The E.S.T was done on a Precor® treadmill after demonstration to all subjects. Bruce protocol was used. At the end of each stage blood pressure and ECG tracings were recorded. ECG was also taken at peak of exercise and immediately after the end of exercise. Exercise endpoints are summarized in Table-1.

During recovery ECG and blood pressure was monitored three times; two minutes , five minutes and ten minutes after completion of EST. Maximal ST - segment change at 80 milliseconds after the J-point was assessed on ECG tracings. Horizontal or downsloping ST -segment depression of at least 1mm or up sloping of 1.5mm or more was considered a positive test result for silent myocardial ischaemia. The electrocardiographic criteria for silent

myocardial ischaemia has been extensively used in other patient cohorts undergoing an E.S.T.[16]

The data set was stored and data entries were verified against the primary data, confidentiality of record was ensured by keeping the data on a single desktop computer system.

SPSS version 17.0 was used to analyze the data. Descriptive statistics, chi-square and students T-test was used for statistical calculations. Statistical significance was considered with a p-value ≤ 0.05.

Results

The two hundred respondents comprised of one-hundred and seventy (170) males and thirty (30) females. Sample age ranged from 30 years to 76 years with a mean age of 46 ±10 years.

Thirty one out of two hundred subjects (16%) were diabetic and one hundred and sixty nine (84%) were non-diabetic. The diabetic group comprised of twenty-three (23) males and eight (8) females.

Coronary risk factor profile for the 200 subjects in the study is summarized in Table 2.

When these risk factors were compared in diabetic and non-diabetic groups only hypertension and obesity were found more frequently in diabetics (48% Vs 27%) p=0.019 and (35% Vs 18%) p=0.027 respectively. The frequency of other risk factors in both the groups showed no major bias-69(34%) respondents had a history of smoking, 94(47%) had a family history of coronary artery disease. Lipid profile revealed total cholesterol ranging from108mg/dl to 318mg/dl (mean 196±28).

Total time consumed by subjects during EST ranged from two minutes to eighteen (18) minutes. METS was from 2 to 19. Among 200 subjects 42 (21%) achieved 100% maximum predicted heart rate and 31 (16%) achieved < 85% of maximum predicted heart rate and 127 (63%) achieved between 85 to 99%. Blood pressure response of exercise was normal in 166 (83%) and hypertensive in 34 (17%).

Table-1: Exercise endpoints.

Physical exhaustion
Severe angina
Sustained ventricular tachycardia
Exertional hypotension
Supraventricular arrhythmias
Exertional hypertension (systolic ≥ 250mmhg)

Table-2: Coronary risk factor profile for study sample.

Hypertensive	98(49%)
Dyslipidaemia	61(30%)
Positive Family History for CAD	94 (47%)
Obesity(BMI ≥ 30 kg/m2)	41(20%)
Smoking habit	69(34%)

Table-3: Results for EST in study subjects.

Negative for exercise induced reversible myocardial ischaemia	150 (75%)
Positive for asymptomatic exercise induced reversible myocardial ischaemia	28 (14%)
Positive for symptomatic exercise induced reversible myocardial ischaemia	7 (3.5%)
Test was inconclusive (due to reasons in table 2.2)	15 (7.5%)

Results are categorized and summarized in Table-3.

The twenty-eight subjects who had silent myocardial ischaemia comprised of 6(19%) diabetic patients and 22(13%) non-diabetic patients.. Despite the greater proportion of diabetics having asymptomatic myocardial ischaemia as compared to non-diabetics, the result which was not statistically significant. (p = 0.397).

Discussion

Diabetes mellitus is a well known risk factor for coronary heart disease. Diabetics have been observed to have more extensive coronary heart disease[17,18] and it is generally believed that myocardial ischaemia is often asymptomatic.[9,19-21] The reported frequency of silent myocardial ischaemia in diabetics is variable with some studies reporting it as the same in non-diabetics.[5,9,22,23] Our study results are in line with findings of Caraccilo,[5] Chipkin et al[22] and Airaksinen et al,[8] with no significant difference in silent myocardial ischaemia in diabetics and non diabetics (19% vs 13%). Amongst reasons for asymptomatic myocardial ischaemia other than autonomic neuropathy are mechanisms, such as the intensity of the stimulus, differences in pain threshold, a defective anginal warning system and ischaemic damage to nerve endings.[4]

There is divided opinion regarding the screening of diabetic patients for heart disease and silent ischaemia. Presently non invasive screening methods are recommended for the group of diabetic patients who have a significant coronary risk factor profile i.e having two or more risk factors.[11] Non invasive screening methods include Exercise Stress Test, stress Myocardial Perfusion Imaging ,Cardiac Computed tomography and dobutamine stress echocardiography and all have helped to various degrees in early detection of heart disease- which is vital for favourable outcomes and prevention of acute cardiac events. Despite their diagnostic value screening methods add to direct and indirect health care costs for the patient and understandably there have been calls to improve screening strategy-by limiting screening for silent ischaemia in diabetic patients with high coronary artery disease risk.[3,24]

An exercise stress test was used for screening of

subjects for silent myocardial ischaemia in the presented study, since it is a safe, inexpensive and non invasive screening test.[25-28] Along with the mentioned attributes, the real advantage of using the exercise tolerance test lies in its high negative predictive value.[7,25] Even though false positive results in exercise testing for silent ischaemia have been reported, the chances of a false positive result in asymptomatic population with coronary risk factors is low.[10] Moreover it has been shown that the positive predictive value of EST, in screening silent ischaemia increases if two or more cardiac risk factors are present.[25] Thereby justifying our use of exercise tolerance test as a screening tool since it is seldom negative in patients with silent myocardial ischaemia.

The clinical significance of silent myocardial ischaemia is similar to that of symptomatic cardiac ischaemia. Prospective studies have shown that patients with silent myocardial ischaemia have an increased risk of acute coronary events,[29] even though the extent of ischaemia is similar to that in symptomatic ischaemic heart disease. Patients with silent ischaemia are given less cardioprotective treatment and revascularization due to the latent presentation.[30] The American Diabetes Association has recommended that diabetic patients along with two or more coronary risk factors must be screened for silent myocardial ischaemia for diagnosing early cardiovascular disease.[31,32] As our results suggest no significant difference in frequency of silent myocardial ischaemia between diabetics and non-diabetics (19% vs 13%) despite of higher prevalence of hypertension and obesity in the diabetic group-again this creates an argument for those questioning the need and criteria for screening recommendations.

It has been shown that silent myocardial ischaemia is a strong predictor for coronary heart disease in patients with an unfavourable risk factor profile.[7,10] 49% of our total study sample had hypertension. Amongst the diabetic group of 31 subjects 48% had hypertension compared with 27% of hypertensive patients in the non-diabetic group. Also 35% of the diabetics were obese compared to 18% in the non diabetic group. Other coronary risk factors such as Dyslipidaemia , smoking and a family history of coronary artery disease were present in both groups and were not responsible for the higher incidence of SMI seen. De Luca et al[33] showed that incidence of silent ischaemia increases with poor blood glucose control however in our sample none of the diabetics had evidence of proteinuria and diabetic retinopathy -indicating that our sample comprised of a low risk group of type 2 diabetics. The higher frequency of silent ischaemia seen in the diabetic group (19%) could have been explained by the higher proportion of diabetics having coronary risk factors but statistical significance (p=0.397) could not be established. More work needs to be done on the subject preferably with a more sensitive screening test such as stress myocardial imaging for some definitive answers.

In our study female patients showed very low incidence of silent ischaemia (2 out of 28) this may be because most of the female subjects included in the study were below 45 years of age. In this period women are naturally protected against atherosclerotic coronary artery disease as shown by Barret. et al.[34]

Conclusion

With the results of our cross sectional study we found that the frequency of silent myocardial ischaemia was not significantly different in diabetics as compared to non-diabetic subjects in this cohort-despite the greater prevalence of hypertension in the diabetic group. However more studies from this region are required as many attributes of diabetes complications are different from that reported from Western countries, due to different population characteristics.

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