SILENT ISCHEMIA IN TYPE I DIABETIC PATIENTS: A STUDY OF EKG CHANGES

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Abstract

INTRODUCTION: Ischemic Heart Diseases (IHD) is the major cause of mortality and morbidity worldwide. Diabetes Mellitus (DM) is known as one of the main risk factors of IHD. Silent ischemia is seen in diabetic patients more that in others. Identification of these cases is of great value in clinical practice. In this study, ECG changes and their relationship with clinical symptoms of ischemia were evaluated in diabetes type II patients.

METHODS: In a cross-sectional study at Isfahan Endocrinology and Metabolism Research Center on diabetes type II patients (2004), 500 consecutive records out of nearly 5000 active records were selected via a simple sampling method. 12-lead resting ECG was taken from all patients. Minnesota codes were used to study ECG changes. Patients with electrocardiograms suggestive of ischemia or MI but no chest pain were considered as having silent ischemia.

RESULTS: A total of 500 subjects (44.4% men and 55.6% women) were studied. EKG changes favoring MI, probable MI, and ischemia were seen in 2%, 12.4%, and 13.6% of patients. Silent ischemia had a prevalence of 85.6%. Of this number, 6.3% had suffered definitive MI based on EKG changes.

DISCUSSION: Silent ischemia is very common in diabetic patients. Alertness to silent ischemia, especially in the elderly can greatly contribute to early detection of CVD and adoption of timely therapeutic measures in these patients. However, as this study was merely based on resting-state EKG changes, the findings may be questionable. Hence, further studies using more accurate ischemia detection methods are warranted.

Introduction

Mortality due to cardiovascular diseases (CVD) constitutes a major health problem the world over. The number of CVD-related deaths is on the rise in Iran.[1] Diabetes mellitus is an important CVD risk factor.

Diabetic patients stand a 4-6 times higher risk of myocardial infarction (MI).[2] Various mechanisms have been proposed for the increased rate of CVD in diabetic patients: atherosclerosis is more prevalent in diabetics than in non-diabetics.[3] Diabetes increases the risk of thrombosis, reduces fibrinolysis and boosts the inflammatory response.[4]

Protein glycosylation alters vascular wall physiology, leading to increased risk.[5] Diabetic patients are at risk of asymptomatic atherosclerosis. Clinically asymptomatic MI and stroke are more common in diabetics.[6]

The Cardiovascular Health Study (CHS) found that silent ischemia is the main cause of the higher prevalence of cardiovascular diseases in elderly diabetics.[7] The higher prevalence in diabetics of CVD risk factors, i.e. lipid disorders, obesity, hypertension, proteinuria, and hyperglycemia contribute to CVD complications in these patients.[8] The large MONICA study demonstrated that 20-30% of Q-wave MI cases had no clinical symptoms.[9] The same study shoed that impaired glucose tolerance is accompanied by abnormal ECG changes suggestive of silent MI.[9,10]

Asymptomatic pathologies constitute a major risk for the development of full-blown cardiovascular diseases. Hence, diagnosis of asymptomatic CVD can serve as a good predictive factor in diabetic patients. Various methods have been used to study ischemia in asymptomatic patients. Examining resting state ECG by use of Minnesota codes is one important such method. The Minnesota coding system was first developed to estimate the prevalence of cardiovascular diseases and is presently used more than other coding systems in epidemiological studies.[11]

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In this study, ECG changes and their relationship with clinical symptoms of ischemia were evaluated in diabetes type II patients.

Materials and methods

This cross-sectional study was conducted in 2004 at Isfahan Endocrinology and Metabolism Research Center on diabetes type II patients. Five-hundred consecutive records out of nearly 5000 active records at the center were selected in reverse order. Simple sampling method was used. All patients with diabetes type II were previously known cases of the disease according to ADA criteria. The selected patients were studied based on time of referring to the center. Complete patient information, as well as physical examination data, blood pressure, blood glucose, HbA1c, serum lipids, 24-hour urine protein, ophthalmologic exam report (presence or otherwise of retinopathy) are available in the patients' records. 12-lead resting ECG was taken from all patients. Minnesota codes were used to study and group ECG changes. Minnesota codes used in this study are presented in table 1. The patients were thus divided into four groups: group A: patients with normal ECG, group B: patients with ECG changes favoring MI, group C: patients with ECG changes favoring probable MI, group D: patients with ECG changes favoring ischemia.

The electrocardiograms were examined by a trained technician with relevant background. Faulty electrocardiograms were excluded and the rest were interpreted by a cardiologist. Blood pressure was measured twice in sitting position and resting state using a standard mercury sphygmomanometer. Patients with systolic blood pressure higher than 130 mmHg or diastolic blood pressure higher than 80 mmHg were considered as hypertensive. HbA1c was measured via chromatography. Total cholesterol, TG and HDL were measured with the enzymatic method and LDL was calculated using the Friedwald formula. Blood samples were taken after a 12-hour fasting period. All laboratory tests were conducted at the Endocrinology and Metabolism Research Center.

Total cholesterol levels higher than 200 mg/dl, LDL levels higher than 100 mg/dl, HDL levels below 40 mg/dl, and TG levels greater than 150 mg/dl were considered as abnormal. The presence of more than 300 mg albumin in 24-hour urine was defined as albuminuria.

Subjects who smoked at least one cigarette a day for three consecutive months were considered as smokers. All of the patients were examined by physicians at Isfahan Endocrinology and Metabolism Center. Patients responding negatively to the question: "have you ever experienced chest pain?" were considered as asymptomatic and those with a positive response were considered symptomatic. Patients with electrocardiograms suggestive of ischemia or MI (groups B, C, D) but no chest pain were considered as having silent ischemia. The prevalence of silent ischemia in these patients and its relationship with CVD risk factors were studied. All statistical analyses were performed with SPSS at Isfahan Endocrinology and Metabolism Research Center. T-test and chi-square test were used to assess the differences between the groups in respect of ECG changes and the presence or otherwise of chest pain. Multiple regression analysis was used to evaluate the relationship between silent ischemia and major CVD risk factors.

Results

A total of 500 subjects (44.4% men and 55.6% women) were studied. The subjects had a mean age of 49.59 years (18-80 years) (table 2). Hypertension, lipid disorders, cigarette smoking, retinopathy and proteinuria were seen in 45.8%, 61.8%, 6.3%, 76.4%, and 14.3% of the sample under study. 71.4% of patients had normal electrocardiograms, i.e. showing no changes suggestive of ischemia or MI. EKG changes favoring MI, probable MI, and ischemia were seen in 2%, 12.4%, and 13.6% of patients. 85.6% of patients with EKG changes had no chest pain (table 3), i.e. silent ischemia had a prevalence of 85.6%. Of this number, 6.3% had suffered definitive MI based on EKG changes.

TABLE 1. Age distribution in the population under study

Age	Frequency (%)
<40	18.8%
41-50	38.1%
51-60	26.2%
61-70	14.4%
>70	2.5%

TABLE 2. Prevalence of chest pain according to EKG changes

		EKG				
		Total	(D) Ischemia	(C) Probable MI	(B) MI	(A) Normal
Chest pain	No	13.5%	4.5%	32.7%	34.6%	85.3%
	Yes	2.6%	1.3%	4.5%	6.4%	14.7%

TABLE 3. Prevalence of CAD risk factors in diabetic patients according to EKG changes

		ECG		
		Normal	Abnormal	P value
R.F	Hypertension	39%	63%	0.02
	Smoking	7%	4.6%	0.3
	Dyslipidemia	59.9%	66.7%	0.1
	Retinopathy	73.5%	81.6%	0.3
	Proteinuria	9.7%	22.2%	0.2

TABLE 4. Relative risk of each of the CVD risk factors and their role in producing chest pain in diabetic patients

Chest pain Risk factor	C.P Pro	C.P Yes	P-Value	Relative Risk	95% CI
Hypertension	64.3%	55.6%	0.6%	0.7	0.2-2.4
Dyslipidemia	66.1%	73.7%	0.5%	0.7	0.2-1.8
Smoking	2.3%	11.8%	0.06%	3.3	1.1-9.9
Proteinuria	15.4%	40%	0.2%	2.3	0.5-9.5
Retinopathy	73.1%	100%	0.08%	0.6	0.5-0.8

Only 14.5% of all patients complained of chest pain. Ischemic changes in different age groups were related to increase in age: patients in the MI group, probable MI group, and ischemia group had mean ages of 59.4, 52, and 51.3 years, respectively. The normal group had a mean age of 48.5 years which suggested a significant difference (P<0.05). EKG changes were also significantly different between the two sexes, being greater in women (P<0.05). EKG changes were also studied in the three main surfaces, i.e. anterior, inferior, and lateral. 86.5% of patients with signs of ischemia on the inferior surface had no chest pain and only 13.5% experienced chest pain. 87.5% of patients with signs of ischemia on the anterior surface had no chest pain. 73.9% of patients with ischemic changes on the lateral surface were asymptomatic and 16.1% had chest pain. This difference was significant only on the lateral surface (P<0.01). Among ischemia risk factors, hypertension was found to be significantly associated wit ischemia (table 4). The prevalence of ischemia in hypertensive patients was higher than in normotensive ones (P<0.02). No significant relationship was observed for other risk factors. Overall, 82.2% of men and 87.2% of women with diabetes type II who were ischemic based on Minnesota codes were asymptomatic. Among patients with no symptoms accompanying their EKG changes, 64.3% were hypertensive, 2.3% were cigarette smokers, 33.5% had lipid disorders, 73.1% had retinopathy, and 15.4% had macro-albuminuria. Cigarette smokers stood a nearly three times higher chance of developing chest pain.

However, no significant relative risk was observed for other risk factors (RR=3 CI 1.1-9.9) (table 5).

Discussion

The results of this study demonstrate that silent ischemia is very common in diabetic patients. 85.5% of type II diabetic patients with EKG changes did not complain of chest pain, hence nearly 24% of diabetic patients suffer silent ischemia. This study showed that the prevalence of silent ischemia increases with age. This has been borne out by other studies, however, unlike some studies; EKG changes were seen more often in women than in men. It was also shown that the type of EKG changes is associated with chest pain. A low percentage of patients (4.5%) who were asymptomatic exhibited pathological QS or Q-wave pattern in their EKG and more than one-third of asymptomatic patients (34.6%) had ST-T and T-wave changes favoring ischemia. Thus, ST-T and T-wave changes account for the most frequent EKG changes in diabetic patients with silent ischemia. The figure 4.5% for a major change such as pathological Q-wave suggestive of MI is by no means insignificant and shows that 4.5% of diabetics develop Q-wave MI without experiencing any chest pain. This figure corresponds to those reported by other studies, approximating 5%.

Few studies in Iran have addressed silent ischemia. In the Tehran blood sugar and lipid study which was conducted based on the Rose questionnaire on type II diabetic patients, the prevalence of chest pain was estimated at 14.8%.[13]

A study conducted by Sarrafzadegan et al in Isfahan found the prevalence of ischemic EKG changes in the general population of this central Iranian city to be 12.3% in women and 7.5% in men.[14]

Nonetheless, the present study found the prevalence of ischemic EKG changes in type II diabetic patients to be close to 29%, which is consistent with other studies. Of the 29% with ischemic EKG changes, nearly 85% did not experience chest pain. A 2000 NIH-monitored study investigated the incidence of asymptomatic CVD in diabetic patients. This study found the risk of silent ischemia based on EKG changes to be 54.8 for every 1000 patients per year and had a prevalence of 74%.[16]

The same study showed that the risk of symptomatic CVD is higher in patients with previous history of silent ischemia (RR=2 CI 1.4-2.9).

Another study of diabetic patients using Holter monitoring estimated the prevalence of asymptomatic EKG changes in these patients to be nearly 75%.[19] Another study based on scintigraphy results found 72% of diabetic patients to have asymptomatic ischemia.[20] A recent 2004 study of EKG changes in type II diabetic patients only on basis of Minnesota codes, including Q-wave codes found the prevalence of MI to be 3.9%, 44% of whom were asymptomatic.[21]

Given the oversensitivity of Minnesota codes in diagnosing ischemia and the fact all Minnesota codes for ischemia were used, a prevalence of 29% for ischemia and 85% for asymptomatic ischemia is acceptable.[22,23] The UKPDS study has shown that risk factors such as hypertension, lipid disorders, cigarette smoking, and aging, as well as hyperglycemia result in increased mortality rate of diabetic patients.[15] Some studies have shown an association between silent ischemia and hypertension, hyperglycemia, and other risk factors.[18]

In the present study, a significant relationship was found between hypertension and ischemia. Also a higher prevalence of chest pain and symptomatic ischemia was found in cigarette smoking patients (P<0.05). This finding is not fully consistent with results of other studies. In this study, the weakest and strongest risk factors in asymptomatic patients with EKG changes were cigarette smoking (2.3%) and retinopathy (23.1%), respectively.

This may be accounted for by concomitant microvascular and macrovascular changes in diabetic patients. No significant figures were obtained as regards the relative risk of individual risk factors in causing silent ischemia. This may have been due to small sample size. Only cigarette smoking in diabetics was found to treble the relative risk of chest pain compared to controls (RR=3 CI 1.1-9.9). Overall, the results of this study show that silent ischemia is highly prevalent in type II diabetic patients. This finding is

significant within the context of activities aimed at reducing CVD-related mortality in diabetic patients.

As the onset time of type II diabetes is not known, complications my progress insidiously and result in mortality of diabetic patients.[12] Thus, silent ischemia is one of the hallmarks of symptomatic CVD.

Alertness to silent ischemia, especially in elderly diabetics (at least through obtaining periodical electrocardiograms) can greatly contribute to early detection of CVD and adoption of timely therapeutic measures in these patients. However, as this study was merely based on resting-state EKG changes, the findings may be questionable. Hence, further studies using more accurate ischemia detection methods (including exercise test) are warranted.

*Minnesota codes used in this study:

Definite MI
+ code 1-1-1→ Q-wave > R/3 and Q-wave duration > 0.03 sec. in all surfaces except III and aVR
+ code 1-2-1→ Q-wave > R/3 and 0.02 sec. < Q-wave duration < 0.03 sec.
+ 2-2-1 → Q-wave > 0.03 sec.

Probable MI
+ code 1-2-7 → QS pattern in leads: V1 to V3
+ code 1-2-8 → R-wave decrease to less than 2 mm from one lead to another in leads: V2 to V3 or V3 to V4
+ code 1-3-1 → Q-wave < R/3 and 0.02 sec. < Q-wave < 0.03 sec.

Ischemia
+ code 4-1-1 → ST-segment depression > 2 mm and horizontal or down-sloping ST in any of the leads
+ code 4-1-2 → 1 mm < ST-depression < 2 mm and horizontal or down-sloping ST in any of the leads
+ 4-2 →0.5 mm < ST < 1 mm and horizontal or down-sloping ST in any of the leads
+ 5-2 → inverse or biphasic T-wave with negative phase less than 1 mm in any of the leads
+ 5-3 → flat, negative, or biphasic T-wave or with negative phase less than 1 mm in any of the leads
+ 5-1 → negative T-wave > 5 mm in any of the leads
+ 9-2 → elevated ST-segment > 1 mm in any of the leads

Others
+ code 7-1-1 → complete LBBB
+ code 7-2-1 → complete RBBB
+ code 8-9 → other arrhythmias
+ code 8-1-1 → PAC > 10% of complexes
+ code 8-1-2 → PVC > 10% of complexes
+ code 9 → uncodable

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