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ORIGINAL ARTICLE

Exercise ECG for Detection of Asymptomatic Coronary Artery Disease in Patients with Type 2 Diabetes Mellitus

Omar Mowaffaq Fadhil [1,*] and Sabah Mohammed Zangana [2]

[1] *Department of Internal Medicine, Azadi Teaching Hospital, Kirkuk, Iraq.*
[2] *Department of Internal Medicine, College of Medicine, University of Kirkuk, Kirkuk, Iraq.*

[*] *Corresponding author email: omarrrry4@gmail.com*

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ABSTRACT

Background: Around 425 million (6%) of humans are diabetics all over the world, and most of them are T2DM(>85%). Diabetes increases the incidence of asymptomatic coronary artery disease (CAD) by two to seven times when compared to non-diabetics. The study aimed to find out how common asymptomatic (subclinical) coronary artery disease (CAD) is in people with diabetes and how it connects to glucose management and the duration of type 2 diabetes using TMT in order to improve the detection rate of CAD.

Methods: This observational research was conducted from October 2021 to April 2022 at Azadi Teaching Hospital in Kirkuk. This research comprised 103 individuals with a mean duration of 5.2 ± 4.2 years since complications starting from diagnosis of T2DM, a mean HbA1C of 7.9 ± 1.3 mg/dl who had been diagnosed with T2DM and were having a treadmill test. Patients with preexisting cardiac disease have been excluded from the study.

Results: The exercise ECG finding showed that 23% of patients had positive Exercise ECG findings and being elderly, long duration of DM, having high HbA1C level, and having high diastolic blood pressure were found to be associated significantly with positive exercise ECG ($p<0.05$). For the categorical variables, being on insulin was associated significantly with positive exercise ECG in which patients on insulin have higher risk (Risk ratio=4.9), other factors did not demonstrate significant association with positive TMT.

Conclusion: The prevalence of positive TMT was comparable to worldwide studies and being elderly, long duration of DM, high HbA1C level showed significant association with asymptomatic CAD findings.

Key words: Type 2 Diabetes; Exercise ECG; Coronary artery disease.

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INTRODUCTION

Recent studies showed that around 425 million (6%) are diabetics all over the world, and most of them are T2DM(>85%) [1]. Diabetes increases the incidence of asymptomatic coronary artery disease (CAD) by two to seven times when compared to non-diabetics [2].

Research has shown that more than one in five diabetics (22%) experience asymptomatic CAD, which is linked to autonomic neuropathy affecting sympathetic afferent nerves [3].

Because myocardial ischemia takes longer to diagnose and treat, there is a higher chance of consequences like myocardial infarction [4]. In addition, following their first myocardial infarction, people with T2DM have an increased risk of cardiovascular events and mortality [3].

Last research found that in 25–29% of diabetics who lack symptoms of CAD, non-invasive CAD screening reduced their cardiac morbidity and mortality [3].

According to Wacker's et al [2] . about 41% of individuals with silent ischemia would have gone unidentified if patients had only been chosen based on compliance with American Diabetes Association recommendations. Current guidelines support CAD screening in high-risk asymptomatic diabetics[5].

Theoretically, cardiovascular disease is more common in people with diabetes, particularly in those who have poor long-term glucose control. Even so, the presence of specific risk factors—such as macroangiopathy, which does not exhibit clinical symptoms, changes in the resting electrocardiogram, micro-macroalbuminuria, cardiac autonomic neuropathy, prolonged diabetes, and an early family history of CAD in men younger than 55 and women younger than 65—as well as obesity, dyslipidemia, smoking, and high blood pressure—increase the likelihood that the patient will experience an acute cardiovascular event [6].

Although an overall analysis of the available studies does not show fully conclusive results or have limited applicability, the American Diabetes Association does not recommend routine screening for CAD in asymptomatic diabetic patients because it believes that survival does not improve in correlation with intensive clinical treatment of cardiovascular risk factors. Consequently, these techniques are limited to patients who exhibit aberrant resting ECG or who have conventional or atypical cardiac symptoms [7]. The diagnosis of coronary artery disease in diabetics is less reliable when based solely on clinical symptomatology. In comparison to the general population, coronary atherosclerotic plaques grow earlier, more diffusely, and more quickly in diabetic patients. For this reason, more thorough CAD screening is warranted in order to increase patient survival [8].

MATERIALS AND METHODS

This observational research was conducted from October 2021 to April 2022 at Azadi Teaching Hospital in Kirkuk and involved all adults who met the following criteria (Adult patients 30 -70 years old who have no symptoms of angina or angina equivalents, diagnosed with Type-2 Diabetes Mellitus using ADA criteria (HbA1c 6.5%, FBS 126 mg/dl, PPBS 200 mg/dl) and have normal baseline 12-lead ECG) excluding (Those with pre-existing congenital heart diseases, renal impairment, Coronary Artery Disease, Valvar Heart disease, and unstable angina, individuals with physical limitations, such as severe osteoarthritis, those who were unable to complete the treadmill test, and patients who declined to provide the study with written informed consent).

Data was collected by direct interview with all respondents, the interview is done by a questionnaire that includes questions regarding demographic data and examination (age, gender, comorbidities such as hypertension and hyperlipidemia, smoking history, antidiabetic medication (Oral or insulin) Vital signs Last HbA1C measurement) and TMT result.

Every participant has had a baseline 12-lead electrocardiogram, an echocardiography, and a TMT performed. Using a 12-lead ECG, TMT was carried out in accordance with the Bruce Protocol. If the patient's heart rate reached 85% of the maximum predicted rate (220 minus age), if they experienced significant chest pain, a drop in systolic blood pressure of 10 mmHg or more, neurologic symptoms like vertigo or dizziness, blood flow problems like cyanosis, continuous ventricular arrhythmia, or an increase in the ST segment of less than 1.0 to 1.5 mm, TMT was stopped.. More than a 1-mm horizontally downsloping or upsloping ST-segment depression that occurred at least 0.08 seconds after the J point was considered a favorable outcome. Results were deemed "uncertain" when a treadmill exercise test was positive but the outcome was unsuitable—that is, when there were abnormalities in heart rate or exercise capacity. Its typical values for specificity and sensitivity are 77% and 68%, respectively. During TMT, coronary artery angiography was performed in situations where the results were positive or unclear.[9]

The Local Scientific Council of the Iraqi Board of Medical Specialization granted ethical approval for this study after it was discussed and each participant gave their verbal agreement. Version 23 of the Statistical Package for social sciences (SPSS) program was utilized for data entry and analysis. For contin-

uous data in the descriptive statistics for sociodemographic traits, the means, standard deviations, min, and max values were utilized. For countable data, numerical and percentage values were employed. Chi-square and the t-test were employed to examine the group differences. The cutoff point for statistical significance was set at P<0.05.

RESULTS

There were 103 patients with type 2 diabetes mellitus have been included in this study. The mean age of patients was 53.8 ± 8.5 years (range 33 – 69 years). Regarding the gender of participants, males were representing 56.3% of patients .

The majority of patients (69.9%) have hypertension and 14 (13.6%) patients have hyperlipidemia. Smoking status showed 23 (22.3%) patients currently smokers. For diabetic medication, the majority of patients (96.1%) take oral antidiabetic medication. The average duration of DM was 5.2 ± 4.2 years and the mean HbA1C was 7.9 ± 1.3 mg/dl. The characteristics of vital signs are given in below (Table 1.)

Table 1. Descriptive statistics for all patients' vital signs and DM features.

	Mean	SD	Minimum	Maximum
Duration of DM (years)	5.2	4.2	0.5	20.0
HbA1c	7.9	1.3	5.5	12.0
PR	84	13	60	130
SBP	134	13	110	170
DBP	83	8	60	100
RR	15	2	12	26

PR=Pulse rate, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, RR=Respiratory rate

The exercise ECG finding showed that 23% of patients had positive Exercise ECG findings as illustrated in (Figure 1).

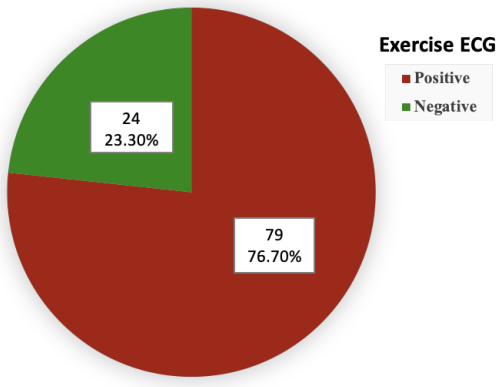

Figure 1. Exercise ECG finding among DM patients

By running the independent sample t-test to find the association between the continuous variable and positive exercise ECG, the test showed that being elderly, long duration of DM, high HbA1C level, and high diastolic blood pressure found to be associated significantly with positive exercise ECG (p<0.05) as shown in (Table 2).

For the categorical variables, the association between positive exercise ECG and given variables showed that only being on insulin associated significantly with positive exercise ECG in which patients on insulin have a higher risk (Risk ratio=4.9) to have a positive exercise ECG in comparison to patients on oral medication (p=0.001), other factors(sex, hypertension, hyperlipidemia, smoking history) did not demonstrate significant association with positive exercise TMT.

Table 2. Comparison of different parameters between HS and CT techniques.

	Negative Mean	SD	Positive Mean	SD	P value*
Age	51	9	58	7	**0.001**
Duration of DM	4.2	3.6	8.7	4.4	**0.0001**
HbA1C	7.5	.9	9.4	1.4	**0.0001**
PR	83	13	88	15	0.091
SBP	133	14	137	11	0.13
DBP	82	8	88	7	**0.01**
RR	15	2	15	3	0.65

* Independent sample t-test, DM=Diabetes mellitus, PR=Pulse rate, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, RR=Respiratory rate

DISCUSSION

The study demonstrated that 56% of patients were males and the mean age of patients was 53 years. This outcome is consistent with a sizable cohort research carried out in Iraq by Abbas's [10] which showed 50% of patients were males and the mean age was 51 years.

Around two-thirds of the patients included in this study had comorbidities, which was hypertension. This is in line with a large primary care cohort study in the UK [11] which demonstrated around 65% of patients with DM had at least one comorbidity and hypertension was the most prevalent condition among all patients. The lipid profile characterization for the patients included in this study showed that dyslipidemia was seen in 13% of the study population, which is lower in comparison to Das et al and Narindrarangkura et al studies [12, 13]. It is proven that dyslipidemia prevalence is higher among DM patients [14] and dyslipidemia is frequently higher among DM patients in comparison to hypertensive patients (reported to be 40% with hypertensive patients) [15], and this could be due

to difference in sample size and study design among studies [16]

About 20% of the patients smoked, which is less than the 30% smoker rate among Iraqis overall found in research by Ibrahim et al. [17].

This discrepancy may be caused by variations in study sample sizes. The average duration of diabetes mellitus was over 5.2 years, consistent with research conducted by Abdulghani et al.that found 63% of DM patients had a duration of more than 10 years [18]. The importance of duration is related to the complication, especially occlusive arterial disease.

Glycemic control was bad in the studied sample, in which the mean HbA1C was 7.9 mg/dl. And more than 90% of patients had HbA1C more than 7. This was in line with Abbas's study [10] which demonstrated achievement of good control in only 13.8% of their patients and 87% were in poor control. In Saudi Arabian research by Alzaheb RA et al. [19], showed the prevalence of good control was 25%, while in Africa and China and USA, the control patients were higher (40%, 35%, and 46% respectively) [20, 21], The difference may be related to HbA1C measurements which associated with variability depending on test procedure used to measure it and also, can vary further with race and ethnicity [22].

Diabetes patients with asymptomatic CAD can be screened using a variety of non-standardized techniques. The gold standard for diagnosing CAD is coronary angiography, an invasive procedure that is only performed on patients who exhibit persistent heart symptoms or who show signs of ischemia on a stress test [23]. Because of this, a number of non-invasive techniques have been suggested for the first screening of diabetics with asymptomatic CAD., one of them is CACs score but exercise stress testing ECG (TMT) may be considered [24].

In this study, the exercise ECG finding showed that, 23% of patients had positive Exercise ECG finding among patients with DM type 2.This was in line with a study conducted by Sharma M etal showed that 26.66% of asymptomatic T2DM had positive TMT results [25] , and comparable outcomes from another research carried out by Joshi AS et al. that showed that 24% of patients with asymptomatic T2DM had positive TMT results [26]. 22% of the asymptomatic type II diabetic patients in the Identification of Silent Myocardial Ischemia in Asymptomatic Diabetics (DIAD) trial showed signs of ischemia on stress myocardial perfusion imaging [27]. Myocardial contrast Echocardiography (MCE) abnormalities were seen in 60% of asymptomatic diabetic individuals, and follow-up coronary angiography abnormalities were present in 65% of these patients [8]. It is important to note that the difference in the prevalence of asymptomatic CAD in these studies can be attributed to selection bias in study design and the fact that retrospective studies showed higher prevalence than prospective studies. These results provide credence to the need for screening diabetics for asymptomatic CAD.

By running the independent sample t test to find the association between the continuous variable and positive exercise ECG, the test showed that, being elderly, long duration of DM, and high HbA1C level found to be associated significantly with positive exercise ECG. In Huang ES et al study [28] , they found that being elderly and have long duration of DM were associated with more prevalence in CAD in DM patients. Furthermore, the 2011 American Diabetes Association (ADA) guidelines advise against routinely monitoring the asymptomatic diabetic population for coronary artery disease (CAD) [29]. The ADA supported screening those who had more risk factors in their medical history; however, this stance was contentious and was changed in 2007 [30]. Nonetheless, the theory that people with extremely high CAD risk may eventually benefit from screening is still in place.

CONCLUSION

Based on study results, we concluded that the prevalence of positive TMT results in patients with type Diabetes was 23% of patients and being elderly, prolonged history of diabetes mellitus, elevated HbA1C, and elevated diastolic blood pressure were strongly linked to positive exercise electrocardiogram ($p<0.05$).Insulin users are more likely to have a positive exercise electrocardiogram (Risk ratio=4.9) than those on oral medication ($p=0.001$).

RECOMMENDATION

More attention should be given for patients with type 2 DM for asymptomatic CAD, adopt a local guideline for screening of asymptomatic CAD among type 2 DM patients and high risk DM patients group should have regular checkup for asymptomatic CAD.

ETHICAL DECLARATIONS

- **Acknowledgements**

  None.

- **Ethics Approval and Consent to Participate**

  This study was approved by the Local Scientific Council of the Iraqi Board of Medical Specialization of Internal Medicine.

- **Consent for Publication**

  Non.

- **Availability of Data and Material**

  The datasets are available from the corresponding author upon reasonable request.

- **Competing Interests**

  The authors declare that there is no conflict of interest.

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- **Authors' Contributions**

  All stated authors contributed significantly, directly, and intellectually to the work and consented it to be published.

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