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Evaluation of Cardiac Events in Diabetic Patients with Inadequate Exercise Test and Normal Myocardial Perfusion Scan Compared to the Control Group

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Abstract

Objective: Ischemic heart disease is one of the most important complications of diabetes mellitus. This study aimed to compare the incidence of cardiovascular events in diabetic patients with inadequate exercise testing and normal myocardial perfusion scans with those who had adequate exercise testing and normal scans.

Materials and Methods: This retrospective study was conducted at Shahid Sadoughi Hospital in Yazd, Iran. Medical records of patients referred to the nuclear medicine department were reviewed. Patients were divided into two groups: those with inadequate exercise tests but normal myocardial perfusion scans and those with adequate exercise tests and normal scans. Patients' contact information was obtained from their medical records, and follow-up was performed by telephone to determine the occurrence of cardiovascular events, including cardiovascular-related death, coronary angiography, percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG), myocardial infarction, and hospitalization due to cardiovascular disease. Data were analyzed using SPSS version 20, and statistical analyses were performed using the independent t-test and Chi-square test.

Results: A total of 210 patients were included in the study, of whom 86 (41%) were male. Dyslipidemia was present in 120 patients (57.1%), hypertension in 89 (42.4%), and smoking in 48 (22.9%). Hypertension and smoking were significantly more common in the study group than in the control group. Cardiovascular events occurred in 18 patients (17.1%) in the study group and 10 patients (9.5%) in the control group; however, this difference was not statistically significant (P= 0.10). Although the risk of cardiovascular events in the study group was 1.35 times higher than in the control group, this difference was not statistically significant (P= 0.60).

Conclusion: Although the incidence of cardiovascular events was higher among diabetic patients with inadequate exercise testing and normal myocardial perfusion scans, the difference compared with patients with adequate exercise testing and normal scans was not statistically significant.

Keywords: Cardiovascular events, Diabetes, Mortality, Ischemic heart disease, Myocardial perfusion scan

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Introduction

The cardiovascular system consists of the heart and blood vessels and plays a vital role in maintaining blood circulation throughout the body. Various disorders can affect this system, including endocarditis, rheumatic heart disease, and abnormalities of the cardiac conduction system (1). Although cardiovascular diseases may arise from different causes, atherosclerosis is the most common underlying pathological process.

Lifestyle-related factors such as physical inactivity and diets high in calories, saturated fats, and sugars contribute significantly to the development of atherosclerosis and metabolic disorders such as diabetes mellitus, hypertension, and metabolic syndrome (2). These conditions are major risk factors for cardiovascular diseases, which remain among the leading causes of morbidity and mortality worldwide and impose a substantial economic burden on healthcare systems (3).

Myocardial infarction (MI), commonly known as a heart attack occurs when blood flow to a part of the myocardium is reduced or completely interrupted. Most myocardial infarctions result from coronary artery disease (CAD), which leads to decreased oxygen supply to the myocardium and subsequent myocardial necrosis. Clinically, patients often present with chest discomfort that may radiate to the neck, jaw, shoulder, or arm. Diagnosis is based on clinical findings, electrocardiographic (ECG) changes, and elevated cardiac biomarkers such as troponins (4,5).

Several imaging techniques are used to evaluate myocardial perfusion, viability, and cardiac function, including echocardiography, radionuclide imaging, and cardiac magnetic resonance imaging (MRI). Echocardiography can detect regional wall motion abnormalities shortly after the onset of ischemia, while cardiac MRI provides detailed structural and functional assessment of the myocardium (6).

Nuclear myocardial perfusion imaging using single-photon emission computed tomography (SPECT) or positron emission tomography (PET) is widely used for evaluating suspected coronary artery disease. These methods provide more detailed diagnostic information than exercise electrocardiography alone. Although the definitive diagnosis of CAD requires coronary angiography demonstrating significant coronary stenosis, stress testing is useful for estimating disease probability, risk stratification, and guiding further diagnostic decisions (7).

Cardiovascular diseases remain among the leading causes of death worldwide (8). Therefore, accurate and timely diagnosis is essential. Stress testing combined with myocardial perfusion imaging is a relatively noninvasive method used to evaluate patients with suspected cardiovascular disease (9).

Myocardial perfusion imaging assesses myocardial blood flow and ventricular function, often by calculating left ventricular ejection fraction (LVEF). Single-photon emission computed tomography (SPECT), commonly performed using Thallium-201 or Technetium-99m tracers, can identify ischemic areas, infarcted tissue, and viable myocardium (10).

Exercise stress testing evaluates the heart's performance during physical activity, typically using treadmill protocols or bicycle ergometry. As exercise intensity increases, myocardial oxygen demand rises, requiring increased coronary blood flow (11-14). However, exercise stress testing alone has limitations, particularly in detecting diffuse atherosclerosis, as it mainly identifies flow-limiting coronary stenosis (15,16).

In clinical practice, some patients are unable to achieve an adequate exercise workload during stress testing, yet their myocardial perfusion scans may appear normal. The prognostic significance of this finding, particularly in diabetic patients who are at

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higher risk for cardiovascular complications, is not fully understood.

Therefore, this study aimed to evaluate the one-year incidence of cardiovascular events in diabetic patients with inadequate exercise tests but normal myocardial perfusion scans compared with those who had adequate exercise tests and normal scans. Cardiovascular events in this study included cardiac death, coronary angiography, percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), myocardial infarction, and hospitalization due to cardiovascular causes (9).

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Therefore, this study aimed to evaluate the one-year incidence of cardiovascular events in diabetic patients with inadequate exercise tests but normal myocardial perfusion scans compared with those who had adequate exercise tests and normal scans. Cardiovascular events in this study included cardiac death, coronary angiography, percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), myocardial infarction, and hospitalization due to cardiovascular causes (9).

Previous studies have evaluated the diagnostic value of different stress imaging techniques. Hung et al. (2010) reported that thallium imaging and cardiac fluoroscopy provided more diagnostic information than exercise electrocardiography in symptomatic women without previous myocardial infarction (17). Paetsch et al. (2004) showed that dobutamine stress magnetic resonance imaging was superior to adenosine stress methods for detecting ischemia in patients with suspected coronary artery disease. Additionally, Fragasso et al. (2000) compared myocardial perfusion SPECT with stress echocardiography techniques in hypertensive patients with chest pain and positive exercise tests, demonstrating the diagnostic value of these imaging modalities compared with coronary angiography (5).

Materials and methods

This retrospective study was conducted at the Nuclear Medicine Center of Shahid Sadoughi Hospital in Yazd, Iran, during 1401 (2022-2023). The study population consisted of diabetic patients who had undergone myocardial perfusion imaging and had normal scan results. These patients had previously performed an exercise stress test that was classified as either complete (adequate) or submaximal (incomplete). A submaximal exercise test was defined as achieving 70-84% of the age-predicted maximal heart rate during treadmill testing.

Patients were identified through a review of medical records in the nuclear medicine department. Individuals with incomplete demographic information or those who declined to participate in the follow-up were excluded from the study. After identifying eligible patients, their contact information was extracted from medical records, and follow-up was performed via telephone to determine the occurrence of cardiovascular events after the initial evaluation.

For the purposes of this study, cardiovascular events were defined as any of the following outcomes: cardiovascular-related death, coronary angiography, percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG) surgery, myocardial infarction, or hospitalization due to cardiovascular causes. During follow-up calls,

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patients were asked standardized questions regarding the occurrence of these events, and when possible, additional clinical details were confirmed through available medical records.

A total of 200 patients meeting the inclusion criteria were enrolled in the study using convenience sampling based on similar previous studies. The participants were divided into two groups: patients with inadequate (submaximal) exercise tests and normal myocardial perfusion scans (study group), and patients with adequate exercise tests and normal myocardial perfusion scans (control group).

In addition to outcome variables, demographic and clinical characteristics were collected for all participants. These included age, sex, and smoking status, presence of hypertension, hyperlipidemia, and duration of diabetes. Blood pressure and other clinical parameters were obtained from the patients' medical records.

All collected data were entered into SPSS software version 20 for statistical analysis. Continuous variables were expressed as mean ± standard deviation and compared using the independent t-test. Categorical variables were presented as frequencies and percentages and were analyzed using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

The study had several limitations. Due to its retrospective design, some medical records contained incomplete or missing information. In addition, follow-up relied partly on telephone interviews, and some patients could not be reached or declined to provide information, which may have introduced response bias. Despite these limitations, the study provides useful insight into the clinical outcomes of diabetic patients with inadequate exercise testing but normal myocardial perfusion imaging.

Ethical considerations

The study protocol was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences, Yazd (ethics code: IR.SSU.MEDICINE.REC.1402.147).

Results

A total of 210 diabetic patients were enrolled in this study, including 105 in the study group and 105 in the control group. Overall, 86 patients (41%) were male and 124 patients (59%) were female. Among the participants, 120 patients (57.1%) had dyslipidemia and 89 patients (42.4%) had hypertension. A total of 48 patients (22.9%) reported a history of smoking. Baseline qualitative variables are summarized in Table 1. Hypertension and smoking were significantly more frequent in the study group compared to the control group. The frequency distribution of qualitative baseline variables was analyzed using the Chi-square test (Table 1).

The mean age of all patients was 55.5± 7.1 years (range: 44-72 years). The mean age was 55.8 ± 7.4 years in the study group and 55.2± 6.7 years in the control group. The difference in age between the two groups was not statistically significant (*P*= 0.56). The mean duration of diabetes was 8.6± 2.3 years (range: 4-15 years). The mean duration of diabetes was significantly longer in the study group (7.2± 2.8 years) compared to the control group (6.5± 1.7 years) (*P*= 0.04) (Table 2).

Regarding cardiac outcomes, 18 patients (17.1%) in the study group and 10 patients (9.5%) in the control group reported cardiovascular events. However, this difference was not statistically significant (*P*= 0.10) (Table 3).

When comparing cardiovascular events by gender, mortality and event frequency were significantly higher in men than in women (*P*= 0.007) (Table 4).

Since hypertension, smoking, and duration of diabetes differed significantly between groups, a multivariate logistic regression analysis was conducted. The duration of diabetes was categorized into two groups: less than 10 years and 10 years or more. After adjusting for hypertension, smoking, and diabetes duration, the study group showed a 1.35-fold higher

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odds of developing cardiovascular events compared to the control group; however, this difference was not statistically significant (*P*= 0.60) (Table 5). Based on the p-values, no statistically significant difference was observed between the two groups in terms of cardiovascular events.

Discussion

In the present study, 210 diabetic patients with normal myocardial perfusion scans were evaluated. The majority of participants were women. The prevalence of hypertension, smoking, and longer duration of diabetes was significantly higher in the study group compared with the control group. The incidence of cardiovascular events was 17.5% in the study group and 9.5% in the control group; however, this difference was not statistically significant.

Coronary artery disease (CAD) remains one of the leading causes of mortality worldwide, including in Iran. The Tehran Lipid and Glucose Study reported a CAD prevalence of 21.8% (22.3% in women and 18.8% in men), based on angina symptoms, medical history and electrocardiographic findings. This prevalence is higher than that observed in the present study (18). Similarly, the prevalence of CAD was reported about 28% among diabetic patients in Isfahan, which is also higher than the rate observed in our study. This discrepancy may be explained by methodological differences, as the present study evaluated only major cardiovascular events (18).

Diabetes mellitus is a well-established independent risk factor for ischemic heart disease. Kannel et al. demonstrated that the incidence of coronary events in diabetic individuals is significantly higher than in non-diabetic populations, being approximately

Table 1.Frequency distribution of qualitative baseline variables in total and by study group

Qualitative variables		Total	Study group	Control group	*P*-value
Gender	Male	86 (41%)	61 (49.2%)	63 (50.8%)	0.77
	Female	44 (51.2%)	44 (51.2%)	42 (48.8%)	
Dyslipidemia		120 (57.1%)	60 (50%)	60 (50%)	0.99
Hypertension		89 (42.4%)	53 (59.6%)	53 (59.6%)	0.01
Smoking		48 (22.9%)	31 (64.6%)	17 (35.4%)	0.02

Table 2. Distribution of quantitative baseline variables by study group

Quantitative variables	Total	Study group	Control group	*P*-value
Age (years)	55.5± 7.1	55.8± 7.4	55.2± 6.7	0.56
Duration of type 2 diabetes (years)	8.6± 2.3	7.2± 2.8	6.5± 1.7	0.04

Table 3. Distribution of cardiovascular events by study group

	Negative	Positive	*P*-value
Study group	87 (82.9%)	18 (17.1%)	0.10
Control group	95 (90.5%)	10 (9.5%)	

Table 4. Distribution of cardiovascular events according to gender

Gender	Number	Percentage	*P*-value
Male	18	20.9%	0.007
Female	10	8.1%	

Table 5. Logistic regression analysis of cardiovascular events between the study and control groups

Model	Odds Ratio	*P*-value
Unadjusted	1.96	0.10
Adjusted	1.35	0.60

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two times higher in men and three times higher in women (19). These findings emphasize the substantial role of diabetes in increasing cardiovascular risk.

Weckbach et al. reported a CAD prevalence of 37% among diabetic patients, which is higher than the prevalence observed in the present study. Their study population consisted of 65 patients with type 1 and type 2 diabetes who had the disease duration more than 10 years (20), which supports our findings that the longer duration of diabetes, particularly type 2 diabetes, may contribute to an increased risk of cardiovascular complications and events.

In contrast to the findings of the present study, Huxley et al., in a meta-analysis of cohort studies, reported that diabetic women had a 1.5-fold higher risk of cardiovascular events compared with diabetic men (21). Differences in study design, population characteristics, sample size, and distribution of cardiovascular risk factors may explain these inconsistent findings.

Furthermore, hypertension showed a significant association with the occurrence of cardiovascular events in our diabetic cohort. This finding is consistent with previous studies which demonstrated a significant relationship between hypertension and cardiovascular outcomes (21-22). However, unlike those studies, the present analysis did not demonstrate a significant association between dyslipidemia and cardiovascular events. This discrepancy may be related to differences in sample size, study design, patient characteristics, or the widespread use of lipid-lowering medications among the study participants.

Conclusions

In conclusion, the results of the present study showed that the incidence of cardiovascular events was higher among diabetic patients with inadequate exercise tests compared with those who achieved adequate exercise tests; however, this difference was not statistically significant when myocardial perfusion scans were normal. These findings suggest that a normal myocardial perfusion scan may indicate a relatively favorable prognosis in diabetic patients, regardless of whether the target heart rate is achieved during exercise testing.

Furthermore, several clinical factors were found to be associated with an increased risk of cardiovascular events. In particular, a longer duration of diabetes, smoking, and the presence of hypertension were more common among patients who experienced cardiovascular events. These findings are consistent with previous studies that have identified these variables as major cardiovascular risk factors in diabetic populations. Therefore, appropriate management and control of these modifiable risk factors are essential for reducing the risk of adverse cardiovascular outcomes.

Recommendations

Based on the findings of this study, further research with larger sample sizes and more diverse study populations is recommended to improve the statistical power and generalizability of the results. Including patients with different comorbid conditions and varying clinical characteristics may provide a more comprehensive understanding of cardiovascular risk factors in diabetic individuals.

Additionally, prospective studies with longer follow-up periods are recommended to better evaluate the long-term prognostic value of myocardial perfusion imaging in patients with inadequate exercise tests. Future studies should also consider assessing additional variables such as medication use, glycemic control, and other metabolic risk factors in order to improve risk stratification and provide a clearer understanding of predictors of cardiovascular events in diabetic patients.

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Author contributions
AM.H, E.A: Conceptualization, Project administration, Methodology, Investigation, collecting the data, Writing-Review & Editing. Z.S, N.N: collecting the data. Methodology, Investigation, Writing-Review & Editing. SK.R, MA.J: Formal Analysis, Investigation, Writing-Review & Editing.

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