

Assessment of the relationship between silent myocardial ischemia, microalbuminuria, and left ventricular function in asymptomatic subjects with non-insulin dependent diabetes mellitus

Asemptomatik insüline bağımlı olmayan diabetes mellitusta sessiz miyokart iskemisi, mikroalbüminüri ve sol ventrikül fonksiyonları arasındaki ilişkinin değerlendirilmesi

Recep Demirbağ, M.D.

Harran University Faculty of Medicine, Department of Cardiology, Sanliurfa

Silent myocardial ischemia (SMI) is defined as ischemic findings established by tests, in the absence of chest pain or any equivalent symptom related to myocardial ischemia. SMI is more common in patients with diabetes mellitus (DM) (6.4 to 56.7%) compared to nondiabetics (0.5 to 4.7%). The wide range of incidence in diabetics may be explained by age, gender, type and duration of DM, micro and macrovascular complications, coronary risk factors and techniques used to diagnose ischemia.^[1] Prognosis is worse and the incidence of a cardiovascular event is 4-5 fold in diabetics with silent myocardial ischemia.^[2] Only 30-60% of diabetics diagnosed with silent myocardial ischemia had severe coronary stenosis. And $\leq 50\%$ of patients with normal coronary arteries are also known to have decreased coronary flow reserve.^[3] Therefore, early diagnosis of SMI in patients with type 2 DM is vital.

Several mechanisms are considered responsible for the development of silent myocardial ischemia including (a) endothelial dysfunction characterized by vasomotor tone dysfunction and inadequate coronary blood flow to meet the increased metabolic requirement, and (b) elevated pain threshold due to increase in beta-endorphin. In addition, SMI is closely associated with diabetic cardiomyopathy. Diabetic cardiomyopathy is characterized by conduction retarda-

tion in sensory and motor nerve fibers of the myocardium, and sympathetic and parasympathetic denervation. Diabetic cardiomyopathy may also cause myocardial ischemia and sudden cardiac death, like it prevents the recognition of chest pain.^[1]

Table 1. Characteristics of high-risk asymptomatic patients with type 2 diabetes recommended for SMI scan according to SFC/ALFEDIAM 2004 guidelines

1. Patients >60 years or with a 10-year history of diabetes with at least 2 risk factors of coronary artery disease (CAD):
 - a. Total cholesterol >2.5 g/L, LDL cholesterol >1.6 g/L or HDL cholesterol <0.35 g/L, triglyceride >2 g/L or using lipid lowering drugs
 - b. Blood pressure >140.90 mmHg or using antihypertensives
 - c. Cigarette smoking or a history of cigarette smoking within the last 3 years
 - d. Premature CAD (before age 60) in first degree relatives
2. Peripheral or carotid artery disease
3. Proteinuria
4. At least 2 cardiovascular risk factors except microalbuminuria and age
5. Patients >45 years with a sedentary life style, and who would perform severe exercise

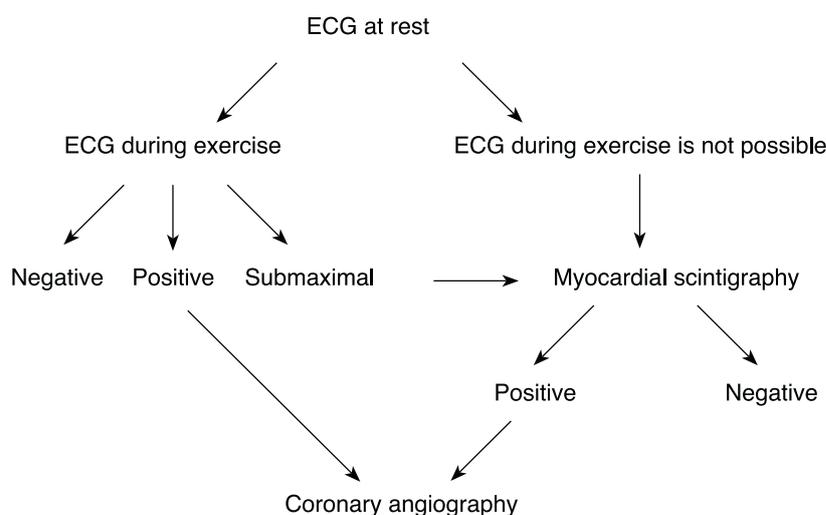


Figure 1. Algorithm for silent myocardial ischemia in patients with type 2 diabetes

Three types of SMI have been described:^[4] Type I, is the least common, and is seen in totally asymptomatic patients and in patients with coronary artery disease (CAD) having no previous anginal complaints. Type II is seen in asymptomatic patients with a history of myocardial infarction. Type III is the most common, and is seen in patients with stable, unstable and variant angina.

Conditions that require SMI scan in asymptomatic diabetics are listed in Table 1 and the algorithm is shown in Figure 1.^[5] On the other hand, it was reported that elevated HbA1c level, microvascular complications such as erectile dysfunction and retinopathy and angiotensin-converting enzyme gene polymorphism particularly with D allele are associated with SMI in type 2 diabetic patients.^[6]

Assessment of SMI should be initiated by performing ECG at rest in asymptomatic patients with type 2 diabetes. A 24-hour rhythm Holter analysis can be performed to evaluate ST-segment changes; however, the specificity and sensitivity of this method is poor. Effort ECG test is widely used since it is a cheap test and is easy to perform. It may be necessary to evaluate most of the patients by myocardial perfusion scintigraphy since majority of diabetic patients have obesity and low exercise capacity, and the probability of false-negative or false-positive results are high in diabetics due to the medicinal products used. Stress echocardiography is another technique used to assess SMI which gives similar results to myocardial scintigraphy. Magnetic resonance imaging, which

does not possess any contrast or radiation effect can be preferred to multislice computed tomography since it is a non-invasive imaging technique and also provides information about coronary anatomy and functional structures.^[2] Coronary angiography should be performed in patients whose non-invasive test results are positive and who have ischemia or infarction in their ECG at rest. Diabetic patients without any finding of silent myocardial ischemia should also be followed up biennially.^[3]

Nearly 25% of patients with type 2 diabetes have microalbuminuria (MA). Diabetic patients with microalbuminuria have a 2-fold mortality rate related to CAD. MA levels are known to be higher in diabetics with silent myocardial ischemia. Microalbuminuria is an important parameter in predicting CAD in a 2.8 year follow-up in patients with type 2 diabetes.^[7] In the absence of coronary artery disease, it was observed that MA was associated with myocardial systolic and diastolic functions, QT dispersion and left ventricular mass index in diabetics.^[8,9]

Silent ischemia in diabetics is associated with left ventricular functions and other coronary risk factors. SMI scan is essential for the early diagnosis and treatment of CAD in high risk asymptomatic patients with type 2 DM. The treatment goal for diabetic patients with microalbuminuria is to eradicate all ischemic attacks and to correct all CAD risk factors. Preferentially, medical therapy, and revascularization with coronary angioplasty or bypass surgery in available cases is recommended.

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