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The Relationship Between Coronary Artery Disease and Undiagnosed Glucose Metabolism Disorders in Patients who Have Undergone Angiography

Anjiyografi Geçiren Hastalarda Bilinmeyen Glukoz Metabolizma Bozuklukları ve Koroner Arter Hastalıkları ile Olan İlişkisi

Halil Akbulut, Aydoğan Aydoğdu*, Ümit Aydoğan, Cem Barçın**, Serkan Tapan***, Yusuf Çetin Doğaner, Türker Türker****, Tuncer Çaycı***, Ersoy Işık**, Hürkan Kürşatlıoğlu**, Kenan Sağlam

Gülhane Military Medical Academy, Department of Family Medicine, Ankara, Turkey
*Gülhane Military Medical Academy, Department of Endocrinology and Metabolic Disorders, Ankara, Turkey
**Gülhane Military Medical Academy, Department of Cardiology, Ankara, Turkey
***Gülhane Military Medical Academy, Department of Biochemistry, Ankara, Turkey
****Gülhane Military Medical Academy, Department of Epidemiology, Ankara, Turkey

Abstract

Purpose: Diabetes mellitus (DM) and coronary artery disease (CAD), seen frequently in the general population, are major causes of morbidity and mortality. DM, controllable through treatment, is one of the most important risk factors for the development of cardiovascular diseases.

Material and Method: Our study included patients who had undiagnosed glucose metabolism disorders and had undergone an angiography under elective conditions. To diagnose the glucose metabolism disorders, these patients were given the oral glucose tolerance test (OGTT) (75 g) within 5-10 days after angiography.

Results: In our study, 24.5% (n=79) of patients had isolated impaired fasting glucose, 9.3% (n=30) had isolated impaired glucose tolerance, 21.1% (n=68) had both impaired fasting glucose and impaired glucose tolerance, and 5% (n=16) had DM. None of these patients knew about their condition beforehand. Only 40.1% (n=129) of patients had normal OGTT results.

Discussion: If patients with suspected CAD found to have blocked arteries after an angiography are screened for DM, glucose metabolism disorders can be diagnosed early. When caught early, the long-term complications can be avoided, resulting in significant savings for health care costs. *Turk Jem 2013; 17: 111-5*

Key words: Diabetes mellitus, coronary artery disease, oral glucose tolerance test

Özet

Amaç: Diabetes Mellitus (DM) ve koroner arter hastalıkları (CAD) toplum genelinde sık olarak görülen ve ciddi oranda morbidite veya mortaliteye neden olan hastalıklardır. DM kontrol edilemediği takdirde uzun dönemde başta kardiyovasküler sistem olmak üzere bir çok sistemde komplikasyonlar meydana getirmektedir. Çalışmamızda koroner arter hastalarındaki bilinmeyen DM, bozulmuş açlık glukozu (BAG) ve glukoz toleransı bozukluğu (GTB) sıklığı ve aralarındaki ilişkisi araştırılmıştır.

Gereç ve Yöntem: Çalışmamız elektif şartlarda anjiyografi işlemi uygulanan ve öncesinde bilinen DM, BAG veya GTB hastalığı bulunmayan bireyler üzerinde gerçekleştirilmiştir. Tüm hastalara anjiyografi sonrası 5.-10. günlerde 75 g oral glukoz tolerans testi uygulanmıştır.

Bulgular: Çalışmamızda katılımcıların %24,5'inde (n=79) izole BAG, %9,3'ünde (n=30) izole GTB, %21,1'inde (n=68) BAG ve GTB birlikteliği ve %5'inde (n=16) ise DM saptanmıştır. Anjiyografi geçiren hastaların yanlız %40,1'inin (n=129) OGTT sonuçları normal yorumlanmıştır.

Tartışma: DM erken saptandığı takdirde uzun dönemde meydana gelen ciddi komplikasyonlarından korunulabilir. Özellikle koroner arter hastalığı ile DM arasındaki ilişki bilinmeli ve koroner anjiyografi geçiren tüm hastalar altta bulunabilecek glukoz metabolizma hastalıkları açısından araştırılmalıdır. *Turk Jem 2013; 17: 111-5*

Anahtar kelimeler: Diabetes mellitus, oral glukoz tolerans testi, koroner arter hastalığı

Address for Correspondence/Yazışma Adresi: Halil Akbulut MD, Gülhane Military Medical Academy, Department of Family Medicine, Ankara, Turkey
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Introduction

Diabetes Mellitus (DM) and cardiovascular diseases are chronic diseases seen frequently in our day, especially in developed countries. According to data from 2008, there are approximately 13 million people with coronary artery disease (CAD) in the U.S. Cardiovascular disease, in particular, is the leading cause of death in adults all over the world (1,2,3). Furthermore, two thirds of these deaths are due to CAD. DM is responsible for 5% of deaths in adults all over the world (3). According to the World Health Organization (WHO) there are more than 220 million people with DM in the world. This number is expected to increase by more than two-fold in the year 2030 (3). Studies have shown that many factors, including gender, race, age, and family history contribute to the development of CAD. In addition to these factors which predetermine one's risk of developing CAD, there are also factors that can be changed or treated, such as high levels of low-density lipoprotein (LDL) cholesterol and triglycerides, low levels of high-density lipoprotein (HDL) cholesterol as well as DM, obesity, hypertension, smoking, and a sedentary lifestyle (4,5,6).

DM, which can be controlled through treatment, is one of the most important risk factors for the development of cardiovascular diseases. DM patients are two to four times more likely to develop a cardiovascular disease (7). In a study conducted by Türkiye Diyabet Epidemiyoloji Araştırma Projesi-2 (TURDEP-2), it was found that the prevalence of DM in the Turkish population was 13.7%. However, 45.5% of those with DM are not getting treatment because they are not aware that they have the disease (8). In the GAMI (Glucose in Acute Myocardial Infarction) study, it was seen that patients with acute myocardial infarction in Sweden had abnormal blood glucose metabolism (9). CAD occurs at an earlier age in DM patients and coronary lesions tend to be both more complex and extensive in these patients (10). The cause of death in more than 80% of DM patients is due to CAD and the complications that result from CAD (11).

In summary, we aimed to determine the frequency of glucose metabolism disorders in patients with undiagnosed CAD and the relationship between glucose metabolism disorders and CAD.

Material and Methods

How Patients were Selected for İnclusion in this Study

We included patients with suspected CAD and who had undergone an angiography under elective conditions, from June 2009 to June 2010 in the Department of Cardiology at Gülhane Military Medical Academy Hospital (GATA). In order to determine who would be included in this study, while waiting in the clinic after their angiography, the patients were given one to one interviews. Furthermore, we evaluated the results of the routine preoperative laboratory tests. During the interviews, the purpose of this study was explained to the patients and signed consent forms were collected from those who agreed to participate. Following this, questionnaires containing socio-demographic data were given to the patients to fill out and the results from routine blood tests and complete blood count tests that were requested prior to angiography, were recorded. Each patient was given the oral glucose tolerance test (OGTT) (75 g) within 5-10 days after the angiography. After the OGTT, the results of the blood tests were recorded. In total, 322 patients, who had undergone angiography for suspected CAD, were included in this study. We aimed to research unknown glucose metabolism disorders (Diabetes Mellitus, impaired fasting glucose and, impaired glucose tolerance) and their effects on the coronary arteries.

2.2 Conditions that Need to be met by the Patient for Inclusion in this Study

1. Patient must have willingly had an angiography
2. Patient must have undiagnosed glucose metabolism disorder
3. Patient must have had no acute myocardial infarction at least 3 months prior to the angiography
4. Patient must willingly consent to the study
5. Patient must have no history of autoimmune disease and/or cancer

The patients went to the Endocrinology and Metabolism Diseases Department in GATA to have the OGTT administered. The doctor responsible for the patients in this study performed a systemic examination and had the patient rest sitting down, in a quiet room, for a 15-minute period before taking his/her blood pressure. In patients where no problems were found, the OGTT was administered. During the OGTT, 0- and 2-hour venous blood samples were taken from patients and sent to the Department of Biochemistry in GATA where they were immediately analyzed.

The Examination Process of Laboratory Parameters

The patients were told not to introduce a new diet to their daily regimen for a period of three days before OGTT and to continue eating what they have always been eating. In order to avoid a false-negative test result, the patients were reminded to eat at least 150 g of carbohydrates per day. The patients were not asked to limit their physical activity. After fasting for a 10-hour period, a blood sample was taken from each patient and glucose and insulin levels were examined. The patients were given a 75 g oral glucose in 300 ml water and asked to drink it within 5 minutes, in a sitting position. At the 120 minute mark, measured from the time the patients started drinking, another blood sample was taken and blood glucose levels were measured for the second time. The patients' states of glucose metabolism were evaluated.

Evaluation of Coronary Angiography Results

Critical CAD is defined as ≥50% narrowing of the luminal diameter of any epicardial artery and/or a side branch with a diameter greater than 2.5 mm. Patients with CAD were grouped according to the number of blocked vessels. After examining angiography reports, the severity of the blockages was recorded separately.

Statistical Analysis

At the end of this study, when evaluating the findings, SPSS 15.00 for Windows (Chicago-USA) was used. Descriptive statistical methods for categorical variables are given in the form of numbers and percentages, and for continuous variables arewere given in the form of mean±standard deviation. The Chi-square test was used when examining the relationship between glucose metabolism disorders and the number of clogged arteries. The compliance of the data with normal dispersion was examined using the Shapiro-Wilk test. The results of the Shapiro Wilk test show that there is no

normal distribution because p<0.001 in all groups. The Mann-Whitney U test was used to compare the normal and the impaired fasting glucose groups whereas the Kruskal-Wallis test was used to compare the normal, impaired glucose tolerance and the DM groups. A p value of less than 0.05 was considered significant. The Bonferroni adjusted Mann-Whitney U test was used to determine the subgroup pairs that caused the differences between the three groups. In this case, a p value of less than 0.017 was considered significant.

Ethics Committee Approval

Ethical approval for our study was given by the ethics committee of our hospital. During the study period, the patients were informed about the study and written informed consent forms were signed by the patients. All patients' data have been kept confidential. Furthermore, nothing was implemented on the patients except those stated in the ethics committee application form. No conflict of interest exists in this study.

Results

The mean age of the patients was 54.04±11.52 years. 66.2% (n=213) of patients were male and 33.8% (n=109) of patients were female. The medical history revealed that 76.4% (n=246) of patients had no history of cardiovascular disease or had undergone any procedure. 15.5% (n=50) of patients have had a myocardial infarction, 5% (n=16) had undergone a percutaneous transluminal coronary angioplasty (PTCA) and 3.1% of patients had undergone a coronary artery bypass. When the history of smoking was examined, we saw that 31.05% (n=100) of patients had never smoked, 49.8% (n=159) of patients had smoked, but had quit at least one year before participating in this study, and 19.57% (n=63) of patients continued to smoke. None of the patients were diagnosed with DM or a glucose metabolism disorder. However, 28.6% (n=92) suffered from hypertension.

In our study, 24.5% (n=79) of patients had isolated impaired fasting glucose, 9.3% (n=30) had isolated impaired glucose tolerance, 21.1% (n=68) had both impaired fasting glucose and impaired glucose tolerance, and 5% (n=16) had DM. None of these patients knew about their condition beforehand. The rate of patients newly diagnosed with DM, after being diagnosed with CAD based on their angiography results, was 6.78%.

According to the measurements at 0 minute during the OGTT, the patients were divided into two groups: impaired fasting glucose group and normal group. When the left anterior descending artery, circumflex artery and the right coronary artery of blocked arteries were compared between the two groups, there was a statistically significant difference between the two (in order p=0.001, p=0.001, p=0.003). However, a statistically significant difference was not found in the left coronary artery (p=0.300) (Table 1).

According to the measurements at 120 minute after the OGTT test, the patients were divided into three groups: impaired glucose tolerance group (IGT), DM group and a normal group. When the left coroner artery, left anterior descending artery, circumflex artery and the right coronary artery of blocked arteries were compared between the three groups, there was a statistically significant difference (p=0.005, p=0.031, p=0.037, p=0.021, respectively) (Table 2). The Bonferroni adjusted Mann-Whitney U test was used to determine the subgroup pairs that caused the differences between the three groups. No statistically significant difference was not found in the coronary arteries between the normal and IGT groups (p=0.431, p=0.705, p=0.469, p=0.154, respectively); only a difference in the left anterior descending artery was found between the IGT and DM groups (p=0.041, p=0.08, p=0.041, p=0.077, respectively), and a difference was found in the coronary arteries between the normal and DM group (p=0.001, p=0.013, p=0.010, p=0.009).

When the number of coronary arteries affected by glucose metabolism disorder that detected at the 0 and 120 minute measurements during the OGTT was compared, a statistically significant difference was found between the two groups (p=0.001, p=0.002, respectively) (Table 3).

Discussion

In our study, we found that 5% of patients who have undergone coronary angiography had previously unknown DM. Furthermore, 59.9% of our patients had a glucose metabolism disorder (DM, impaired glucose tolerance or impaired fasting glucose). According

Table 1. Comparison of the average rates of blocked coronary arteries between the impaired fasting glucose group and the normal group and the statistically significant difference between the two groups

Name of Coronary Artery	Normal		Impaired Fasting Glucose		P*
	Mean Median	Std. Deviation Min - Max	Mean Median	Std. Deviation Min - Max	
LCA	0.11 0	1.06 0-20	0.81 0	5.81 0-60	0.300
LAD	19.20 10	27.91 0-100	31.95 20	36.92 0-100	0.001
CX	11.06 0	24.68 0-100	24.65 10	34.83 0-100	0.001
RCA	10.11 0	20.31 0-100	24.31 10	24.31 0-100	0.003

LCA: Left Coronary Artery LAD: Left Anterior Coronary Artery CX: Circumflex Artery RCA: Right Coronary Artery *: Mann-Whitney U Test

to the angiography results in all patients who were diagnosed with DM, we found a blockage in the coronary arteries. This is an important finding because it shows the frequency of CAD in DM patients. When we examined the number of pathological coronary arteries in our patients who were newly diagnosed with DM, we observed that in 75% of 3 arteries, in 12.5% of 2 arteries and in 12.5% of 1 artery were blocked. None of our patients had normal angiography results. 23% were found to have healthy coronary arteries. In addition, 50% of patients who were newly diagnosed with DM had serious blockage and 50% had mild blockage in their arteries. In participants with normal glucose metabolism, only one in four had serious blockage. Furthermore, there was a statistically significant difference in the degree of stenosis between the DM and normal groups. These findings are important because they seem to indicate that DM increases the severity of CAD. Moreover, in our study, we detected a statistically significant difference between the state of coronary artery blockage and blood sugar levels.

The Funagata Diabetes study has clearly shown the increased mortality rates in patients with impaired glucose tolerance and CAD (12). The DECODE study has shown that the risk of developing CAD increases as a result of chronic hyperglycemia. The results of these two studies support the findings of our study (13). According to the TURDEP-2 study, 7.5% of the Turkish population (approximately 5.5 million people) has undiagnosed DM (8). According to Harris et al., the prevalence of undiagnosed DM in the U.S. is 2.7% (approximately 5.4 million people) and according to Garancini et al., the prevalence of undiagnosed DM in Italy is 2.5% (approximately 1.5 million people) (14,15). In our study, newly diagnosed DM rates in patients who have undergone angiography are about twice of that of the studies mentioned above. In our study, the prevalence of DM in newly diagnosed patients was similar to the that found in the TURDEP-2 study. However, in contrast to the TURDEP-2 study, the prevalence of other glucose metabolism disorders that were diagnosed in our study was twice as high. The rate of patients newly diagnosed with DM after being diagnosed with CAD based on their angiography results, was 6.78%. This result is about three times higher than that of the US population study results. The high frequency of undiagnosed DM in patients with CAD who have undergone angiography, in comparison to the normal population, is an important finding. However, the rate of newly diagnosed DM

Table 2. Comparison of the average rates of blocked coronary arteries between the impaired fasting glucose group, the normal group, and DM group and the statistically significant difference between the three groups

Name of Artery	Normal		IGT		DM		P*
	Mean Median	Std. Dev. Min-Max	Mean Median	Std. Dev. Min-Max	Mean Median	Std. Dev. Min-Max	
LCA	0.10 0	0.97 0-20	1.02 0	7.10 0-60	1.25 0	3.41 0-10	**0.005**
LAD	24.38 10	31.97 0-100	24.06 10	34.15 0-100	40.00 25	36.14 10-100	**0.031**
RCA	15.57 0	28.48 0-100	18.71 0	33.19 0-100	31.25 10	36.30 0-100	**0.037**
CX	15.00 0	27.97 0-100	18.76 10	30.17 0-100	25.00 20	24.22 0-75	**0.021**

IGT: Impaired Glucose Tolerance DM: Diabetes Mellitus LCA: Left Coronary Artery LAD: Left Anterior Coronary Artery CX: Circumflex Artery RCA: Right Coronary Artery Std. Dev.: Standard Deviation *: Kruskal-Wallis Test

Table 3. Number of blocked arteries according to the results of the Coronary Angiography and its relationship with the results of the OGTT

Number of Blocked Coronary Arteries	OGTT 0				P*	OGTT 120						P*
	Normal		IFG			Normal		IGT		DM		
	n	%	n	%		n	%	n	%	n	%	
0	56	17.4	30	9.3	0.001	58	18.0	28	8.7	0	0	0.002
1	42	13.0	26	8.1		46	14.3	20	6.2	2	0.6	
2	37	11.5	27	8.4		48	14.9	14	4.4	2	0.6	
3	39	12.1	63	19.6		56	17.4	34	10.6	12	3.7	
4	0	0	2	0.6		0	0	2	0.6	0	0	

OGTT: Oral Glucose Tolerance Test IFG: Impaired Fasting Glucose
IGT: Impaired Glucose Tolerance DM: Diabetes Mellitus *: Chi-square test

patients in our study is lower than the rate found in the GAMI study performed in Sweden (9). The GAMI study consisted of patients with acute myocardial infarction whereas our study consisted of patients who had undergone angiography in elective conditions. Therefore, we assume that the difference resulted from the differences in the patient groups used in both studies. According to the Society of Endocrinology and Metabolism of Turkey, impaired glucose intolerance and impaired fasting glucose could be described as pre-diabetes (16). In general, patients with impaired glucose tolerance receive the diagnosis of DM within 4-6 years. Therefore, if glucose metabolism disorders are identified early, complications as a result of these disorders can be avoided. As seen in our findings, one in five patients who have undergone angiography and who have normal fasting blood glucose, have impaired glucose tolerance.

In the TURDEP-2 study, the researchers reported that 7.1% of the general population had impaired glucose tolerance levels. According to the results of our study, impaired glucose tolerance levels in the general population were five times greater than this. The results from a study by Gui et al. conducted in China in 2010 support the results of our study (17). The results from the Gui et al. study indicated that 50% of patients who had CAD had normal OGTT results, 9.3% had isolated impaired fasting glucose, 23.02% had isolated impaired glucose tolerance, and 17.62% had both impaired fasting glucose and impaired glucose tolerance. In our study, 24.5% (n=79) of patients had isolated impaired fasting glucose, 9.3% (n=30) had isolated impaired glucose tolerance, and 21.1% (n=68) of patients had both impaired fasting glucose and impaired glucose tolerance. When viewed from this aspect, both studies had similar findings.

In conclusion, we found that 69.45% of patients diagnosed with impaired glucose tolerance had blockage, in various diameters, in at least one coronary artery. Only 26.71% of patients with normal OGTT results were diagnosed with CAD. This result is particularly important because it shows the relationship between impaired glucose tolerance and CAD. Another noteworthy finding in our study was that approximately one in three patients who had undergone coronary angiography had a positive family history of CAD. In addition, 62.5% of patients who were newly diagnosed with DM had at least one first-degree relative diagnosed with DM. These results prove once more the importance of family history.

Approximately one in three DM patients are unaware that they have the disease (8,18,19). This leaves patients vulnerable to complications down the line (19,20,21). Complications related to CAD tops the list. Disability and death resulting from impaired glucose metabolism can be avoided if caught early (20,22). Therefore, even if patients who have undergone angiography have no complaints, their fasting and postprandial glucose levels should be examined. Furthermore, when early diagnosis is made, annual health care spending on DM and CAD will decrease. This issue is particularly important for primary health care providers as they are often the first point of contact with these patients.

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