ORIGINAL RESEARCH

IN-HOSPITAL MORTALITY IN PATIENTS WITH IMPAIRED FASTING GLUCOSE AND ACUTE CORONARY SYNDROMES

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ABSTRACT

Objectives: Diabetes mellitus is considered to be equivalent to coronary artery disease(CHD). Both impaired fasting glucose(IFG) and impaired glucose tolerance (IGT) are risk factors for cardiovascular disease. We aimed to compare the mortality during hospitalization between IFG and diabetes in patients with acute coronary syndrome (ACS).
Methods: The patients under 65 years of age, who had been diagnosed as ACS; were evaluated for mortality during the first 7 days. The patients were divided into three groups as the first group diabetic, the second group non-diabetic patients , the patients with IFG.
Results: A total of 375 patients were enrolled. The mortality rate was found to be 6.7% in patients with diabetes, 2.6% in patients without diabetes , 7.0% in patients with an IFG. The mortality rate of the patients with IFG and the patients with diabetes were approximately the same and this rate was significantly higher than in those with normal blood glucose during the acute phase of ACS.
Conclusion: The IFG affects mortality as much as diabetes. Fasting plasma glucose is beneficial, in determining the cardiovascular risks and in the modification of the therapy to reduce the risk of CHD.

Keywords: Acute coronary syndrome, Impaired fasting glucose, Diabetes, Mortality

BOZULMUŞ AÇLIK GLUKOZU OLAN AKUT KORONER SENDROMLU HASTALARDA HASTANE İÇİ MORTALİTE

ÖZET

Giriş: Diyabet artık koroner arter hastalığının eşdeğeri sayılmaktadır.Ayrıca hem bozulmuş açlık glukozu(IFG) hemde bozulmuş karbonhidrat toleransı (IGT) kardiyovasküler hastalık için birer risk faktörüdür.Bu çalışmada akut koroner sendrom (AKS) tanısı alan; diyabetli ve IFG li hastalar arasında hastane içi mortalitenin karşılaştırılması amaçlanmıştır.
Yöntem: Çalışmaya akut AKS tanısı alan 65 yaş altı hastalar alındı ,ilk 7 gündeki mortaliteleri değerlendirildi.Hastalar açlık kan şekerine göre diyabeti olan, diyabeti olmayan ve bozulmuş açlık glukozu olanlar olmak üzere üç gruba ayrıldı.
Bulgular: Toplam 375 hasta çalışmaya dahil edildi. Tüm hastalarda hospitalizasyon dönemindeki mortalite; diyabeti olan hastalarda % 6.7, diyabeti olmayanlarda % 2.6, bozulmuş açlık glukozu olanlarda %7.0 olarak bulundu.AKS sonrası erken dönemde mortalite IFG ve diyabetli hastalarda yaklaşık aynı oranda tespit edildi. Bu oran normal kan şekeri olanlardan anlamlı derecede yüksek tespit edildi.
Sonuç: Dolayısıyla IFG; diyabet gibi koroner kalp hastalığı için risk faktörüdür ve mortalite üzerinde onun kadar etkilidir.Sonuç olarak,açlık plazma glukozu,kardiyovasküler hastalık riskinin belirlenmesinde ve koroner arter hastalık riskini azaltıcı yaklaşımların belirlenmesinde son derece faydalıdır.

Anahtar Kelimeler: Akut koroner sendrom, Bozulmuş açlık glikozu, Diyabet, Mortalite

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INTRODUCTION

Diabetes mellitus is an important cardiovascular risk factor. The rate of death due to cardiovascular disease in diabetic patients is 2 – 4 times higher than in non-diabetic population. In diabetics, 70-80% of deaths occur because of cardiovascular diseases.

Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) are conditions where the plasma glucose level is lower than the required level for diabetes mellitus(DM) diagnosis but higher than normal. The etiology of type 2 DM and IGT is abdominal obesity, insulin resistance and impaired insulin secretion, but the etiology of IFG has not yet been determined. IGT and IFG are believed to be two different disorders affecting two different populations, and these disorders are risk factors for diabetes and cardiovascular disease development[1].

In this study, we aimed to investigate the mortality during the hospitalization period (the first 7 days) by dividing patients admitted to coronary intensive care unit due to acute coronary syndrome (ACS) into three groups as the patients with diabetes, patients without diabetes, and patients with IFG.

MATERIAL AND METHOD

Three hundred seventy five patients admitted with acute coronary syndrome (ACS) diagnosis to the coronary intensive care unit between January 2006 – January 2007 were included in the study. As diabetes prevalence is higher in the population aged 65 and older, the patients in this age group were not included in the study. The blood samples of the patients were taken the first morning following admission. The blood samples were analyzed using standard biochemistry tubes in the biochemistry laboratory of our hospital. The age, gender, diagnosis, anamnesis, medical history, fasting blood glucose level and course of the MI in the acute phase (in the first 7 days) of each patient were recorded. The blood sugar levels of the patients were grouped into three groups according to the results : Normal group; patients with no previous diagnosis of diabetes and with a fasting glucose level of <100 mg/dl; IFG group; patients with a fasting glucose level of 100 – 125 mg/dl; and DM group; patients with a fasting glucose level of >125 mg/dl. The patients in these three groups were monitored during their hospitalization periods (7 days on average) and mortality was investigated. The SPSS for the Windows 10.0 statistical package program was used in the evaluation of the data. The quantitative data of the groups were compared using ANOVA and Tukey's HSD and the qualitative data were compared using chi-square tests. $P<0.05$ was considered significant.

Our study was approved by local ethic commite of our hospital.

RESULTS

A total of 375 patients, 66 women (17.6%) and 309 men (72.4%) under the age of 65, who were hospitalized for ACS diagnosis in the coronary intensive care unit were included in the study. 18.4% of the patients were under 45 years of age (69), 59.73% of the patients were between 45-60 years of age (224) and 21.86% of the patients were between 60-65 years of age (82). Of these patients, 72 (19.2%) had a previous diagnosis of diabetes, 17 (4.53%) were newly diagnosed with diabetes and in 56 (14.93%) patients impaired fasting glucose and in 230 patients (61.33%) normal blood glucose was detected(Table I). Sixteen patients died during the hospitalization period.

- The number of men (309) was significantly higher than the number of women (66).
- Although 72.4% of the patients were male, diabetes was more common in women with acute myocardial infarction ($p < 0.028$).
- While the prevalence of diabetes for all patients was 19.2% during the first admission, it was 23.73% after the study.
- Among the patients with ACS, 83.8% had myocardial infarction (MI) with ST elevation, 6.1% had MI without ST elevation and 10% had unstable angina pectoris(USAP).
- With respect to the ACS classification no statistically significant difference in mortality

was seen during the hospitalization period (p = 0.532).

• It was found that the mortality in all patients during the hospitalization period was 6.7% in patients with diabetes, 2.6% in patients without diabetes and 7.0% in patients with impaired fasting glucose(Table II). In conclusion, mortality in the diabetic patients during the acute phase (first 7 days) of acute coronary syndrome was significantly increased compared to the patients without diabetes. However, no statistically significant differences were found between the patients with impaired fasting glucose and the diabetic patients with respect to the mortality in the acute phase of MI. (p = 0.192)

Table I: The clinical and demographic characteristics of patients

	Non DM	IFG	DM
Age	52,3±8.3	54.98±7.43	52.9 ±8.64
FPG	88.67 ±21.5	117.82 ±5.75	219.21±75.07
Total cholesterol(mg/dl)	195,1±44,97	195±43,8	197±40,3
Triglycerides(mg/dl)	167,29±102,16	165±100,5	250±42,5*
Low densitiy cholesterol(mg/dl)	113,43±38,56	100,55±18,93	165±28,93*
High densitiy cholesterol(mg/dl)	40,11±10,69	38,05±10,09	42±18,9
Smoking (%)	34	35	31
Body mass index (kg/m²)	27,61± 5,47	26,09±3,09	32,03±3,2*
SAB(mm/hg)	**115,7±7,39**	113±8,13	139± 6,35*
DAB(mm/hg)	69,3±5,79	71,55±8,31	88±5,9*

*The parameters are significantly higher in diabetic group (p<0,05).
(SAB:sistolic arterial pressure, DAB:diastolic arterial pressure)

Table II: Mortality rate of patients

	Non DM		IFG		DM	
	n	%	n	%	n	%
Patients who survived	224	97.4	52	93	83	93.3
Patients who died	6	2.6	4	7	6	6.7

χ^2=3,91 p=0,192

DISCUSSION

It is reported that dyslipidemia, hypertension, obesity, and cerebrovascular and coronary artery diseases are commonly seen in diabetic patients. In diabetics, coronary artery atherosclerosis is aggressive and has an early-onset[2]. It is thought that in the pathogenesis of diabetes, long before overt hyperglycemia occurs and diabetes is diagnosed, there is a long period of insulin resistance, when the blood glucose is maintained at normal levels by compensatory hyperinsulinemia. Events associated with atherosclerosis start to develop long before the stages when this can be detected as IFG and IGT[3]. It was demonstrated that cardiovascular risk increases also in this prediabetic period[4,5]. Detecting patients in this stage and protecting them against the harmful effects of insulin resistance helps to prevent coronary heart disease. Also in our study, the early stage mortality rates of the acute MI patients with diabetes (6.7%) and with IFG (7.0%) were almost the same and significantly higher compared to patients without diabetes (2.6%). This shows that the atherosclerotic process starts well before the impaired fasting glucose stage, which is the earliest stage of DM. The risk of cardiac mortality in type 2 diabetes patients is at a similar level with the risk in patients who have had myocardial infarction[6]. The fact that complications develop in the prediabetic period in an important proportion of the patients has increased the interest in impaired fasting glucose, impaired glucose tolerance and postprandial hyperglycemia[7]. The high cardiovascular disease risk in these patients is the result of atherosclerosis development[8]. The cause of the accelerated atherosclerosis development observed in diabetes is multifactorial; hyperglycemia, dyslipidemia and high oxidative stress were demonstrated to play important roles in the etiology.[9,10]

The fact that impairments are observed in the endothelial functions in individuals with cardiovascular risk factors before overt cardiovascular disease development shows that the endothelial dysfunction is the main factor in atherosclerosis development[11]. In the hyperinsulinemia period before type 2 diabetes occurs, endothelial dysfunction and proliferation in the vascular smooth muscle occurs with the effect of increasing levels of insulin and insulin-like growth factors in the blood. Endothelial dysfunction is an important factor in thrombosis formation and contributes to increased coronary artery disease risk in individuals with impaired fasting glucose and impaired glucose tolerance.

Although hyperinsulinemia was shown to cause endothelial dysfunction in healthy persons, it was found that the insulin treatment given to diabetic patients corrects endothelial dysfunction. In UKPDS study, it was reported that no significant change was observed in the macrovascular disease incidence, while a decrease was observed in the incidence of microvascular disease with the aggressive insulin treatment given to diabetic patients.

The study which provided the most comprehensive information about the diabetes – macrovascular disease relationship, is the DECODE study[12]. In this study, which aimed to determine the diabetes prevalence as well as to demonstrate all-cause mortality and cardiovascular prognosis, it was found that there was a linear relationship between postprandial glucose level and coronary heart disease, and cardiovascular mortality. It was found that mortality increased if the postprandial glucose level exceeded 200 mg/dl[13]. In some studies in the literature, fasting blood glucose level alone is inadequate in indicating the mortality risk associated with hyperglycemia and it was stated that oral glucose tolerance test(OGTT) would provide additional prognostic information indicating impaired glucose tolerance[14]. In a FUNAGATA study, it was suggested that impaired glucose tolerance presents a cardiovascular risk while impaired fasting glucose does not cause any risk[15].

In the study they conducted, Nurkalem Z. and Sargın M. investigated acute coronary syndrome cases. As a result of this study, they found a correlation between the number of

affected coronary arteries and both IGT and diabetes frequency. They also detected a positive correlation between the number of involved coronary arteries and the postprandial glucose level[16]. The studies published in other countries also show that the prevalence of previously undiagnosed diabetes is increasing. This demonstrated that impaired glucose tolerance and undiagnosed diabetes is an important public health problem[17]. Considering the fact that IGT and IFG present similar cardiovascular risks and IGT is detected in nearly 50% of patients with IFG, similar results are expected in patient groups with IFG. As previously discussed, how IFG and IGT causes coronary artery disease has not been clarified yet. In many patients, IGT is accompanied by risk factors such as hypertension, obesity and dyslipidemia. In a study conducted in Japan, it was demonstrated that in 225 cases on whom coronary angiography was performed, the proportion of diabetic patients and IGT patients who developed coronary artery disease was higher compared to non-diabetic patients and it was claimed that in the IGT group, hypertension and hypertrigliceridemia played an important role in the atherosclerosis development[18]. Moreover, hyperglycemia may also represent an individual risk factor. Hyperglycemia causes changes in the coagulation mechanism, which again causes thrombosis.In hyperglycemic patients, increases in prothrombin, fibrinopeptide A and factor 7 levels together with an increase in platelet aggregation are observed[19,20].

Consequently, in our study it was interesting to observe that the rate of impaired fasting glucose was higher in patients with ACS than in the normal population. The findings that in the early phase after the ACS (hospitalization phase) the mortality rate was almost the same in patients with IFG and diabetes and that this rate was significantly higher when compared to the patients with normal fasting glucose are important. Recognizing that the atherosclerosis process has already started in the IFG period, which is the earliest phase of diabetes and that it presents a cardiovascular risk, early detection of patients with IFG would be a useful approach in the determination of the cardiovascular risks and modification of the treatment. It is recommended that more aggressive treatment approaches should be used in diabetics or in patients with IFG, also considering the concomitant risk factors such as hypertension, dyslipidemia and obesity. It is thought that when this is provided, the complications may be prevented more successfully. In individuals with risk factors for diabetes (obesity, family history of diabetes, history of giving birth to a macrosomic baby), it is beneficial to determine whether IFG is present by testing the fasting blood sugar, to prevent or delay the development of diabetes with recommended treatment approaches in patients with detected IGT by OGTT if necessary will be beneficial in reduction of the CHD risk.

Our study showed that; in patients hospitalized in our coronary intensive care unit with a diagnosis of acute myocardial infarction, the prevalence of diabetes and IFG was higher compared to that of the normal population. In the early phase after AMI, the rate of mortality was approximately the same in patients with IFG and diabetes, and this rate was significantly higher compared to the individuals with normal glucose levels and therefore like diabetes, IFG was also a risk factor for CHD and it affected mortality as much as diabetes.

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