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THE IMPORTANCE AND THE RELATİONSHİP OF BLOOD GLUCOSE LEVEL İN THE DEVELOPMENT OF ATRİAL FİBRİLLATİON İN CORONARY BYPASS SURGERY İN DİABETİC PATİENTS

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ABSTRACT

Aim: Currently, coronary artery bypass graft surgery (CABG) is the most commonly performed open heart surgery. Diabetes mellitus (DM) causes morbidity and mortality in patients undergoing CABG as in other surgeons. In this study, we aimed to explain the relationship between blood glucose level and Atrial Fibrillation (AF) after CABG operations in DM patients.
Material and Method: In this study we included, 456 patients, whom underwent elective isolated CABG operation between January, 2015 and August 2017, retrospectively. 219 of these patients had DM. These patients were divided into two groups as Group 1 (no postoperative AF developed) and Group 2 (postoperative AF, developed). Preoperative demographics, amount of drainage after operation, amount of blood usage during and after operation were recorded and statistically evaluated.
Results: Group 1 had 135 patients (58 F, 77 M) and Group 2 had 84 patients (31 F, 53 M). The mean time for the diagnosis of DM in patients was 5.2 ± 2.3 years in Group 1 and 6.7 ± 2.6 years in Group 2. 92 of the group 1 patients (68.2%) were receiving standard insulin therapy, 43 (31.8%) were receiving oral antidiabetic treatment, 65 of the group 2 patients (77.4%) were receiving standard insulin therapy, 19 (22.6%) were receiving oral antidiabetic treatment. There was no significant difference between the groups in terms of smoking habit, COPD and HT. The mean age was 62.4 ± 8.2 years in Group 1 and 61.5 ± 6.3 years in Group 2. Blood glucose levels of the patients were measured 182 ± 56 mg / dl preoperative, in perioperative period as 224 ± 48 mg / dl and 162 ± 41 mg / dl postoperatively in Group 1. Blood glucose levels of the patients in Group 2 were measured 210 ± 44 mg / dl preoperatively, 256 ± 38 mg / dl in perioperative period, 195 ± 63 mg / dl postoperatively. The mean duration of hospitalization in intensive care unit was 2.3 ± 0.5 days in Group 1 and 4.4 ± 1.2 days in Group 2.
Conclusion: Diabetes mellitus is still an important risk factor for morbidity and mortality in coronary bypass surgery. Although not directly, increased glucose levels cause a significant increase in the rate of postoperative AF development. As a result of this study, lowering and following up of blood glucose levels in DM patients before and after the operation will decrease the rate of postoperative AF development and hence the duration of hospital stay and cost.

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INTRODUCTION

AF is the most common among the rhythm disorders after coronary artery bypass surgery (CABG) (Suresh Nair, 2010). This rhythm disturbance, characterized by irregular contractions of atrium tissue and irregular R-R distances on the electrocardiogram, can be seen in 30-40% after cardiac surgery operations (Sumeet *et al.,* 2014). Normal sinus rhythm, after open heart surgery, can return to AF on the second postoperative day. Old age, male sex, impaired left ventricular function, enlarged atrium diameters in valve diseases, obesity, concomitant renal disease, post-operative electrolyte imbalance or blood usage plays an important role in the development of this arrhythmia. Patients usually do not feel this rhythm disturbance unless there is a hemodynamic problem during AF development.

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However, if the cardiac functions of patients are at the limit, it can lead to increased mortality and morbidity after hemodynamic instability. Atrium tissue provides a 30% contribution to left ventricular ejection fraction (EF). Therefore, AF patients with low EF experience more problems (Peretto *et al.,* 2014). The most catastrophic complication of acute AF development is the development of hemiplegic or quadriplegic disease following an embolism in brain tissue. Patients' duration of hospitalization prolongs after morbidity increase, depending this health expenditure and resource utilization also increases. DM is a systemic disease. Angio pathy of the vessel endothelium and its walls may cause stenos is (Aronson and Edelman, 2014).

Therefore, DM patients with coronary stenos is should be investigated for peripheral arterial disease, renal artery stenos is, and carotid artery stenos is. Peripheral vascular examinations should be done carefully, carotid Doppler USG should be taken, urea and creatinine values should be seen before the surgery of patients with DM. Blood glucose levels should be monitored on an hourly basis during open heart surgery of patients with DM. Insulin resistance, one of the systemic effects of cardiopulmonary bypass (CPB), can alter blood glucose levels after surgery. Unstable blood glucose levels after surgery can lead to problems such as bleeding disorders, diabetic ketoacidosis, delayed wound healing, and increased infection rates. DM increases morbidity and mortality after CABG (Holzmann *et al.,* 2015). For this reason, 2 points are given to patients with DM in EUROSCORE (Nashef *et al.,* 1999). There is no clear reason for increased AF rates after CABG in patients with DM. In our study, we aimed to clarify the significance of glucose levels which were measured four times a day starting three days prior to the operation, preoperative blood glucose levels and glucose levels when AF first developed after surgery in relation to postoperative AF development.

MATERIALS AND METHODS

In this study we included, 456 patients, who underwent elective isolated CABG operation between January 2015 and August 2017, retrospectively. Preoperative demographic data of all patients were recorded in detail. Patients who underwent additional surgery, aortic surgery, valve surgery, preoperative arrhythmia, emergency surgery, revision surgery due to hemorrhage, and patients with low cardiac output were excluded from the study. 219 of 456 patients had DM. These patients were divided into two groups as Group 1 (no postoperative AF developed) and Group 2 (postoperative AF developed). Group 1 had 135 patients (58 F, 77 M) and Group 2 had 84 patients (31 F, 53 M). Patients' preoperative demographic data and other risk factors were compared in detail by assessing hypertension (HT), chronic obstructive pulmonary disease (COPD), smoking, hypercholesterolemia, aortic cross clamp time and blood product use (Table 1). EUROSCORE risk score was used prior to the patients' operation. The blood gas values of the patients were checked every half an hour under CPB and hourly for the other phases of the operation. After the median sternotomy, full-dose heparin was administered in accordance with their weight. All of the patients were operated under cardiopulmonary bypass. Right jugular vein was used for central vein catheterization of all patients. All patients were treated with Left Internal Mammary Artery (LMA) graft for LAD (Left Anterior Descending) vessel.

The number of distal anatomizes performed in the operation, the use of isotropic agent, the time of CPB (minutes), and the time of cross clamping (minutes) were recorded and evaluated.

Statistics

For the statistical analysis of the data, SPSS13.0 statistical package program was used. The Shapiro-Walk test was used to examine whether the data showed normal distribution, Mann-Whitney U test was used for two groups comparison for normal non-dispersive data. Pearson's Chi-square test and Fisher's exact Chi-square test were used to examine the categorical data. Statistical significance level of $p < 0.05$ was used.

RESULTS

Patients were divided into two groups as Group 1 (no postoperative AF developed) and Group 2 (postoperative AF developed). Group 1 had 135 patients (58 F, 77 M) and Group 2 had 84 patients (31 F, 53 M). The mean age was 62.4 ± 8.2 years in Group 1 and 61.5 ± 6.3 years in Group 2. Mean DM diagnostic time of the patients was 5.2 ± 2.3 years in Group 1 and 6.7 ± 2.6 years in Group 2. 92 patients (68.2%) received standard insulin therapy, 43 (31.8%) received oral ant diabetic therapy in Group 1, 65 patients (77.4%) received standard insulin therapy and 19 (22.6%) received oral ant diabetic therapy in Group 2. HbA1c levels were 7.2 ± 1.8 in Group 1 and 6.7 ± 1.7 in Group 2. There was no significant difference between the groups in terms of smoking habit, COPD and HT. The mean duration of aortic cross clamping (ACC) in patients with CPB was 58.6 ± 15.1 minutes in Group 1, in Group 2 it was 69.7 ± 17.3 minutes.

The mean number of distal anasto moses was 3.2 ± 1.4 in group 1 and 2.5 ± 3.7 in group 2. There was no statistically significant difference in COPD, hypertension, hypercholesterolemia and smoking among the two groups. ($p > 0.05$) Intraoperative and postoperative findings are presented in Table 2 and Table 3. 48 of Group 1 patients (35.5%) had 1, 28 patients (20.7%) had 2, 15 patients (11.1%) had 3 units of blood was given, 55 of Group 2 patients (%65.4) had 1, 21 patients (26.1%) 2, 8 patients (9.5%) had 3 or more units of blood was given to them and this was not statistically significant ($p > 0.05$). Blood glucose levels of the patients in Group 1 were measured 182 ± 56 mg / dl preoperatively, 224 ± 48 mg / dl in perioperatively, 162 ± 41 mg / dl postoperatively. Glucose levels of the patients in Group 2 were measured 210 ± 44 mg / dl preoperatively, 256 ± 38 mg / dl perioperatively, 228 ± 63 mg / dl postoperatively (Table 4). Postoperative measurement was statistically significantly higher in group 2 ($p < 0.05$).

The mean duration of hospitalization in intensive care unit was 2.3 ± 0.5 days in Group 1 and 4.4 ± 1.2 days in Group 2. The average length of stay in hospital 6.4 ± 1.5 days in Group 1 was 9.7 ± 1.2 days in Group 2. Found statistically significant ($p < 0.05$). The mean level of glucose in blood gas test, taken at the time of AF first observed, in group 2 patients was measured as 285 ± 117 mg / dl. As a result of this significant increase, AF is predicted to be associated with elevated blood glucose level. When compared with Group 1, it was found that the difference was statistically significant ($p < 0,05$). In group 2 patients, medical treatment agents (Amiodarone ampoule 900 mg loading dose and maintenance treatment and

Table 1. Preoperative Patient Data

Variable	Total (n=219)	Group 1 (n=135)	Group 2 (n=84)	p value
Mean Age (Year)	61.4 ± 5.7	62.4 ± 8.2	61.5 ± 6.3	>0.05
Sex (Female / Male)	89 F, 130 M	58 F, 77 M	31 F, 53 M	>0.05
Mean BMI(kg/m^2)	23.8 ± 4.05	23.4 ± 4.8	24.2 ± 3.3	>0.05
past myocardial infarction n (%)	45 (% 20.5)	26 (% 19,2)	19 (% 22,6)	>0.05
Mean EF (%)	47 ± 3.8	45 ± 4.8	49 ± 2.9	>0.05
Use of Acetyl Salicylic Acid n (%)	170 (% 77.6)	102 (% 75,5)	68 (% 80,9)	>0.05
Hipertension n (%)	167(% 76.2)	96 (% 71,1)	71 (% 84,5)	>0.05
COPD n (%)	82(% 37.4)	44 (% 32,5)	38 (% 45,2)	>0.05
Smoking habit n (%)	155(% 70.7)	92 (% 68,1)	63 (% 75)	>0.05
HbA1c Levels	6.95 ± 1.7	7,2 ± 1,8	6,7 ± 1,7	>0.05
Preoperative Hemoglobin Levels (gr/dl)	13.2 ± 2,6	14 ± 2.4	13 ± 3.1	>0.05
Preoperative INR value	1.2 ± 0,2	1.3 ± 0.22	1.2 ± 0.31	>0.05
Preoperative Platelet Levels	275.000 ± 30.500	235.000 ± 45.000	315.000 ± 16.000	>0.05
NYHA Functional Class (1-5)	2.80 ± 0.8	2.79±0.88	2.89±0.98	>0.05
EUROSCORE	3.56 ± 2.51	3.27±2.48	3.86±2.52	>0.05

Valuesare n (%) for categorical variables and mean ± SD for continuous variables
COPD: Chronic Obstructive Pulmonary Disease, MI: Myocardial Infarction, INR: International Normalized Ratio, NYHA: New York Heart Association, BMI: Body Mass Index, ICU: Intensive Care Unit

Table 2. Operative Data

Variable	Total (n=219)	Group 1 (n=135)	Group 2 (n=84)	p value
Number of Anastomoses	2.85 ± 2.55	3.2 ± 1.4	2.5 ± 3.7	>0.05
Total By-pass Duration (minutes)	93.15 ± 17.3	89.5 ± 18.7	96.8 ± 15.9	>0.05
Aortic Cross Clamp Duration (minutes)	54.1 ± 16.2	58.6 ± 15.1	69.7 ± 17.3	>0.05
Aspirated Blood Amount During Operation (cc)	409 ± 152	394 ± 143	425 ± 161	>0.05
Amount of Blood Product Used During Operation (Units)	1.2 ± 1.6	1.2 ± 1.5	1.3 ± 1.6	>0.05

Values are n (%) for categorical variables and mean ± SD for continuous variables

Table 3. Post-operative Patient Data

Variable	Total (n=219)	Group 1 (n=135)	Group 2 (n=84)	p value
Total Amount of Drainage	797 ± 187	855 ± 125	740 ± 250	>0.05
Total amount of blood used (units)	1,3 ± 0,4	1.1 ± 0.3	1.6± 0.4	>0.05
Hemoglobin	8.8 ±2.1	9.6 ± 2.1	8.1 ± 2.0	>0.05
Revision surgery due to hemorrhage	3 (% 1.3)	2 (% 1.4)	1 (% 1.1)	>0.05
Pleural Effusion	20 (%4.5)	12 (% 8.8)	8 (% 9.5)	>0.05
Platelet Count	206.000 ± 20.000	220.000 ± 22.000	192.000 ± 18.000	>0.05
Duration of patient intubated and under general anesthesia (hours)	5.7 ±1,4	5.3±1.5	6.1±1.2	>0.05
Duration of hospitalization in ICU (days)	3.35 ± 0.8	2.3 ± 0.5	4.4 ± 1,2	<0.05
Total hospitalization duration (days)	8.05 ± 1.4	6.4 ± 1.5	9.7 ± 1.2	<0.05
Meanremoval time of drains (days)	2.8 ± 0.6	2.4 ± 0.5	3.1 ± 0.8	>0.05
Mediastinitis / Deep Sternal Infection		-	-	>0.05

Values are n (%) for categorical variables and mean ± SD forcontinuousvariables

Table 4. Blood Glucose Levels

Variable	Total (n=219)	Group 1 (n=135)	Group 2 (n=84)	p value
Preoperative	196 ± 52	182 ± 56	210 ± 44	>0.05
Perioperative	241 ± 43	224 ± 48	256 ± 38	>0.05
Postoperative	195 ± 52	162± 41	228 ± 63	<0,05

afterwards amiodarone 200 mg tablets and Metoprolol 50 mg tablets at the onset of AF) in the same protocol were started for treatment after diagnosis with ECG. ECG showed normal sinus rhythm during the discharge of the patients and at the first month follow-up.

DISCUSSION

Diabetic patients are divided into two types: Type 1 diabetes is a result from the lack of adequate insulin secretion and Type 2 diabetes is due to insulin resistance. Type 1 DM patients receive standard insulin therapy while Type 2 DM patients receive oral ant diabetic treatment. However, patients undergoing major surgery need to take standard insulin therapy in the preoperative period (Giakoumidakis *et al.,* 2013). All the patients in our study were treated with standard insulin treatment before surgery.

During their discharge, the patients were consulted to the Endocrinology Department. Patients were recommended to continue their previous treatment. According to literature, 30-35% of CABG patients are diabetic (Vinod *et al.,* 1999). In our study, 219 (48%) of 456 patients, who underwent CABG operation, were diabetic. The vascular wall structure and morphology of diabetic patients are affected diffusely, rather different from the effects of atherosclerosis. Therefore, left ventricular dysfunction is more frequent (Whang, and Bigger, 2000). Unlike other surgical branches, the fluctuation of glucose levels after cardiac surgery is more frequent. This fluctuation is caused by the effects of the heart-lung machine on the organs (Punke *et al.,* 2014). CPB leads to changes in glucose and insulin balances and levels in both diabetic and non-diabetic patients. Glucose levels can vary, especially during surgery.

Abnormal fluctuations in glucose levels can be seen when the patient is hypothermic or when the patient is taken off pump and re warmed (Knapik *et al.,* 2009). These fluctuations tend to be high in glucose levels. While patients are hypothermic, blood glucose levels may be slightly elevated. However, elevation of stress hormones during rewarming can lead to even higher blood glucose levels (Floh *et al.,* 2015). In a study conducted by Blaha *et al.* (Blaha *et al.,* 2009), maintaining blood glucose levels of 80-120 mg / dl in patients in intensive care unit after cardiac surgery have been shown to reduce mortality and morbidity. However, hypoglycemia after insulin therapy significantly increased mortality. For this reason, it is predicted that the glucose levels should be kept flexible after cardiac surgery in the same study. We did not have any patients with hypoglycemia in both groups. We have tried to keep blood glucose levels of our patients between 100-150 mg / dl in the postoperative period and the insulin doses have been adjusted for this purpose.

All the patients who are to be operated in our clinic are monitored in accordance with the recommendations given by the Endocrinology Department in the preoperative period and patient is taken to surgery after proper preoperative blood sugar regulation is achieved. The measurement of the concentration of glycohemoglobin (HbA1c), which gives an idea of the mean blood glucose concentration over the last 3-4 months, should be checked in the preoperative period. For all surgical procedures, it is recommended to keep the HbA1c levels below 7% for reducing diabetic complications (15). Different opinions have been put forward in the work done with HbA1c. A study by Iguchi et al. (Iguchi *et al.,* 2012) showed that the incidence of AF is higher in patients with an HbA1c level below 6.5%. Contrary to this study, Kinoshita et al. (Kinoshita *et al.,* 2012) have shown that the incidence of AF decreases in the presence of high levels of HbA1c. AF is the most common rhythm disturbance after heart surgery. Postoperative AF may be due to multifactorial causes. Obesity, presence of valve disease, postoperative electrolyte imbalances, low cardiac output, incomplete revascularization, postoperative blood transfusion are among the proven risk factors. Recently, there have been intensive researches on white blood cell count, C-reactive protein, HbA1c levels, serum uric acid level stating or colchicines use (Memetoglu *et al.,* 2015).

As a result of a meta-analysis by Fauchier et al. (Fauchier *et al.,* 2013), preoperative stating use significantly reduced the risk of postoperative AF. Post-operative hyperglycemia results in susceptibility to infection due to impaired polymorpho nuclear leukocyte function and delay in wound healing, sternal discharge or mediastinitis, coagulation and fibrinolytic activity deterioration due to increased platelet activity, deterioration of lipid metabolism and endothelial function can be seen (Lemaignen *et al.,* 2015; Ranucci *et al.,* 2014; Hiroshi *et al.,* 2013). For this reason, blood glucose levels should be closely monitored after cardiac surgery operations. Blood and blood products are often given to patients due to low haematocrit levels during and after cardiac surgery operations. Changes in blood glucose levels due to blood transfusions can occur. Several reports have documented the development of AF due to blood transfusion. In a study conducted by Almandine *et al.* (Alameddine *et al.,* 2014), 879 patients were examined and blood transfusion was performed in 564 patients. It was observed that the rate of AF was increased by 61% in each transfusion performed.

In a study conducted by Vlahos *et al.* (Vlahou *et al.,* 2016) on 446 patients against this data, the use of blood and blood products during and after the operation was reported to have no role in postoperative AF development. The acid-citrate-dextrose mixture in blood storage bags increases the need for exogenous insulin. In this case, hyperglycemia occurs also in non-DM patients, but this increase is more pronounced in DM patients. In our patients there was no difference in blood transfusion rates for both groups. In patients with poor cardiac function, isotropic agents may cause changes in blood insulin levels leading to deviations in glucose levels (Mansur *et al.,* 2015). In particular, changes in serum glucose levels are observed with the use of catecholamine. In our study, we found that glucose levels were high in blood gas parameters, especially at the initial onset of AF. Blood glucose levels are high during AF formation, usually seen in the morning of the second postoperative day. This may be due to steroid hormones secreted in the morning. The result of our study is that strict control of blood glucose levels in diabetic patients may reduce the incidence of postoperative AF.

Conclusion

Diabetes mellitus is still an important risk factor for morbidity and mortality in coronary bypass surgery. It has been shown that increased glucose levels lead to a significant increase in the incidence of postoperative AF, although not directly. As a result of our study, we concluded that the blood glucose levels should be closely monitored in DM patients before and after the operation and that they should be kept at normal intervals to decrease AF, which is a direct cause of morbidity and mortality.

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