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Research Article

The effect of HbA1c on coronary artery bypass grafting mortality and morbidity in concomitant diabetes mellitus and coronary artery disease

Diyabetes mellitus ve koroner arter hastalığı birlikteliğinde hba1c'nin koroner baypas mortalitesi ve morbiditesine etkisi

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Abstract

Aim: In our study, we aimed to comparatively examine the effect of HbA1c levels and diabetes disease on patients undergoing isolated coronary bypass surgery.

Material and Methods: 200 consecutive patients (152 male, 48 female, mean age 61.1) who underwent coronary artery bypass surgery (CABG) in our hospital were included in the study. The patients were divided into two groups. Group 1 consisted of patients with HbA1c ≥6.5 % (n=100) and group 2 consisted of patients with HbA1c <6.5% (n = 100). In group 1 all the patients were diabetic while in group 2, 30 patients were diabetic. There was no difference in preoperative risk factors between the groups.

Results: Both groups had similar mortality rates. There was no difference in postoperative cerebrovascular accident, myocardial infarction, renal dysfunction, reoperation, atrial fibrillation, sepsis and superficial local infections. There was also no statistical difference in operative data, intensive care unit and hospital stay amongst the groups. In group 1, five patients had mediastinitis whilst there were no cases in group 2 and this was statistically significant (p = 0.030). Multivariate analysis revealed that an increase in postoperative blood glucose levels on the second postoperative day was predictive for mediastinitis (p = 0.036). ROC analysis showed that HbA1c >7.65% was the threshold value for occurrence of mediastinitis with a sensitivity of 80% and specificity of 65.6%.

Conclusion: As a result, poor control of blood glucose levels following CABG is a risk factor for infection and HbA1c is a significant marker for identification of preoperative infection risk.

Keywords: HbA1c, coronary artery bypass surgery, diabetes mellitus, mediastinitis

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Öz

Amaç: Çalışmamızda izole koroner bypass ameliyatı uygulanan hastalarda HbA1c düzeyi ve diyabet hastalığının etkisini karşılaştırmalı olarak incelemeyi amaçladık.

Gereç ve Yöntemler: Çalışmaya hastanemizde koroner baypas cerrahisi geçiren ardışık 200 hasta (152 erkek, 48 kadın, yaş ortalaması 61,1) dahil edildi. Hastalar iki gruba ayrıldı. Grup 1, HbA1c seviyesi ≥ %6,5 olan hastalardan (n = 100) ve grup 2, HbA1c seviyesi < %6,5 olan hastalardan (n = 100) oluşuyordu. 1. gruptaki hastaların tamamı diyabetik iken 2. gruptaki hastaların 30'u diyabetikti. Gruplar arasında ameliyat öncesi risk faktörleri açısından fark bulunmamaktaydı.

Bulgular: Her iki grupta da benzer ölüm oranları vardı. Postoperatif serebrovasküler olay, miyokard enfarktüsü, renal disfonksiyon, reeksplorasyon, atriyal fibrilasyon, sepsis ve yüzeyel lokal enfeksiyonlar açısından fark görülmedi. Gruplar arasında operasyon verileri, yoğun bakım ünitesinde kalış süresi ve hastanede kalış süresi açısından da istatistiksel olarak anlamlı fark saptanmadı. Grup 1'de 5 hastada mediastinit görülürken, grup 2'de hiç mediastinit görülmedi ve bu istatistiksel olarak anlamlıydı (p = 0,030). Multivaryant analizlerine göre, ameliyat sonrası ikinci günde kan şekeri düzeyindeki artışın mediastinit açısından öngörücü olduğu saptandı (p = 0,036). ROC analizi HbA1c > %7.65 değerinin, %80 duyarlılık ve %65 özgüllük ile mediastinit için eşik değer olduğunu gösterdi.

Sonuçlar: Sonuç olarak, koroner baypas cerrahisi sonrası kan şekeri düzeylerinin yetersiz kontrolü enfeksiyon için bir risk faktörüdür ve HbA1c preoperatif enfeksiyon riskinin belirlenmesinde önemli bir belirteçtir.

Anahtar Kelimeler: HbA1c, koroner arter baypas cerrahisi, diyabetes mellitus, mediastinit

Introduction

Diabetes mellitus (DM) is a major global contributor to morbidity and mortality, often leading to both microvascular and macrovascular complications [1]. Reducing glycated hemoglobin (HbA1c) levels to below 7%, a key indicator of effective glycemic control, has been shown to significantly decrease diabetes-related complications [2].

Coronary artery bypass grafting (CABG) is a well-established surgical intervention with favorable long-term outcomes, particularly when internal thoracic artery (IMA) grafts are utilized. Optimal management of atherosclerosis-promoting factors is crucial to the success of CABG. Numerous studies have demonstrated that diabetic patients experience higher rates of postoperative mortality and morbidity [3,4].

Postoperative complications such as acute renal failure, deep sternal wound infections, and prolonged hospital stays are more frequently observed in patients with type 1 DM compared to non-diabetic individuals [3]. Diabetic patients are at heightened risk for infections at both the sternotomy and leg graft sites. Aggressive perioperative glycemic control using insulin infusions [4], targeting blood glucose levels below 150 mg/dL postoperatively, has been shown to reduce early mortality and morbidity after cardiac surgery [5].

The American Diabetes Association recommends HbA1c measurement for long-term glucose monitoring in diabetic individuals [6]. HbA1c is a stable glycated hemoglobin complex formed by the irreversible binding of glucose to hemoglobin, reflecting glycemic control over the preceding 90–120 days. In 2008, the International Expert Committee established an HbA1c threshold of 6.5% for diagnosing diabetes, contingent on adherence to international standardization protocols [7].

This study aimed to evaluate the impact of HbA1c levels on outcomes in patients undergoing isolated CABG by stratifying them into two groups based on preoperative HbA1c levels.

Material and Methods

Study population

A total of 200 patients who underwent isolated CABG were enrolled. Patients were divided into two groups based on preoperative HbA1c levels: Group 1 (HbA1c ≥ 6.5%) and Group 2 (HbA1c < 6.5%). All patients in Group 1 had diabetes, whereas 30 patients in Group 2 were diabetic (p < 0.001). There were no statistically significant differences between the groups regarding age, sex, biochemical parameters, or other risk factors (Table 1).

Study end points

Blood glucose levels were measured preoperatively, intraoperatively, and on postoperative days 1, 2, and 3. Lengths of stay in the intensive care unit (ICU) and hospital were recorded. Complications during the follow-up period were considered clinical endpoints and included mortality, cerebrovascular accident (CVA), myocardial infarction (MI), arrhythmia, renal dysfunction, atrial fibrillation (AF), reoperation, deep sternal infection, sepsis, superficial local

infection, and combined infection (deep + superficial). All patients were monitored in the hospital's outpatient clinic for six months postoperatively.

Diabetes treatment

In Group 1, 16 patients received no treatment, 2 were managed with diet alone, 50 were on oral antidiabetic drugs (OADs), 18 on insulin therapy, and 14 on a combination of OADs and insulin. In Group 2, among the 30 diabetic patients, 3 received no treatment, 2 were managed with diet, and 25 were on OAD therapy.

Perioperative glycemic control

Insulin infusion was administered following the Portland Protocol. OADs and/or insulin were continued until the day of surgery, provided fasting blood glucose levels were <200 mg/dL. Patients with higher levels received insulin until stabilization below 200 mg/dL. During surgery, a solution of 25 U crystalline insulin in 250 mL saline was infused intravenously at 10 mL/hour. Blood glucose levels were monitored hourly, with insulin dosing adjusted accordingly.

This study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Türkiye Yüksek İhtisas Training and Research Hospital.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation; categorical variables were presented as frequencies and percentages. Group comparisons were performed using the Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical variables. Intragroup comparisons were analyzed with the Wilcoxon signed-rank test. Receiver operating characteristic (ROC) analysis was used to determine the HbA1c cut-off for predicting mediastinitis. Logistic regression analysis identified independent predictors of mediastinitis. A p-value <0.05 was considered statistically significant. Analyses were conducted using SPSS v15.0 (SPSS Inc., Chicago, IL, USA).

Results

No significant difference in early (30-day) mortality was observed between the groups: 4 deaths (3%) in Group 1 and 3 in Group 2 (Table 2). No group differences were observed in rates of reoperation, CVA, MI, arrhythmia, renal failure, or sepsis (Table 2). Postoperative complications occurred in 21 patients in Group 1 and 13 in Group 2, though this difference was not statistically significant (p = 0.132, Table 3). ICU and hospital stay durations did not differ significantly (Table 3). The groups were comparable regarding the number of distal anastomoses, aortic cross-clamp time, and cardiopulmonary bypass (CPB) duration (Table 4). Off-pump CABG was performed in 3 patients in Group 1 and 5 in Group 2; the rest underwent CPB.

Superficial local infections were documented in 4 patients in Group 1 (1 sternal, 3 saphenous sites) and 2 patients in Group 2 (saphenous site only), with no statistically significant difference (p = 0.341) (Table 5). The only complication found statistically significant in this study was deep sternal infection development. While 5 patients developed deep sternal infection in Group 1, it was not observed in any patient in Group 2 (p: 0.030) (Table 5). In these patients, the diagnosis of medisatinitis was confirmed by computed tomography. Debridement and sternal fixation were performed in 4 patients, and omentoplasty was additionally performed in 1 patient in Group 1. One patient did not undergo surgery, treated with antibiotic therapy for 30 days. One of these patients was a patient revised due to hemodynamic instability in the early postoperative period, and this patient died due to sepsis in the second postoperative month. When the two groups were compared in terms of combined infection development, the difference was observed to be statistically significant (p:0.030) (Table 5).

Multivariate logistic regression analysis identified elevated blood glucose on postoperative day 2 as the sole independent predictor of mediastinitis (p = 0.036) (Table 6).

Group 2 exhibited statistically significant daily fluctuations in blood glucose, whereas Group 1 showed no significant reduction from day 1 to day 2 (p = 0.086), although other changes were significant (Figure 1).

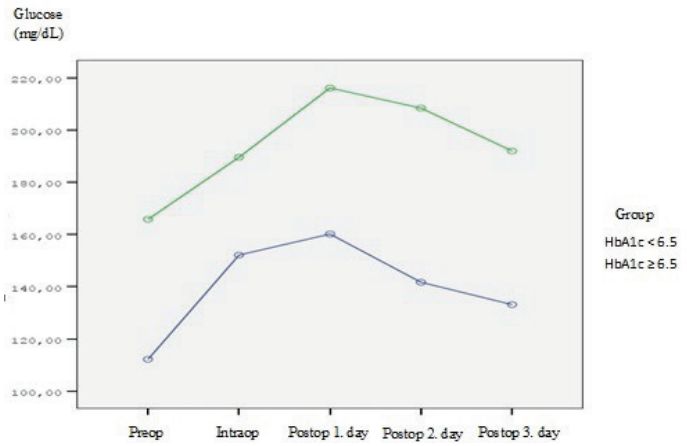

Figure 1. Daily changes of glucose measurement of the study patients according to HbA1c value.

ROC analysis demonstrated an area under the curve (AUC) of 0.737 for HbA1c in predicting mediastinitis. A threshold of 7.65% yielded 80% sensitivity and 65.6% specificity.

Table 1. Baseline clinical and laboratory characteristics of the study patients according to the HbA1c value			
Variable	Group 1 (HbA1c ≥ 6.5)	Group 2 (HbA1c < 6.5)	p value
Age	59.90 ± 8.67	62.30 ± 10.48	0.057
Sex (male/female)	71 / 29	81 / 19	0.098
Diabetes Mellitus	100	30	<0.001
Hypertension	71	75	0.524
Dyslipidemia	35	31	0.547
Peripheral arterial disease	4	1	0.184
Smokers	38	34	0.556
Chronic obstructive pulmonary disease	22	21	0.863
Body mass index (kg/m^2)	28.9 ±4.3	28.3±4.4	0.414
Ejection fraction(%)	53.48 ±9.3	54.18±8.8	0.673
Creatinine (mg/dL)	0.98±0.31	0.97±0.22	0.516
HbA1c (%)	8.87±1.8	5.65±0.5	<0.001
WBC (/mm^3)	8308.80±1983.2	7671.50±1860.4	0.017
Urine proetin(mg/L)	12	8	0.346
Preopertive glucose>180(mg/dL)	49	3	<0.001

Table 2 Postoperative outcomes of the study patients according to the HbA1c value			
Variable	Group 1 (HbA1c ≥ 6.5)	Group 2 (HbA1c < 6.5)	p value
Mortality	4	3	0.702
Cerebrovascular accident	3	1	0.315
Myocardial infarction	3	2	0.653
Arrhythmia	5	1	0.098
Acute renal failure	2	1	0.563
Atrial fibrillation	5	9	0.270
Mediastinitis	5	0	0.030
Sepsis	3	1	0.315
Superficial local infection	4	2	0.341
Reoperation	5	2	0.251

Table 3 Postoperative hospitalization, follow-up and total outcomes of the study patients according to the HbA1c value			
	Group 1 (HbA1c ≥ 6.5)	Group 2 (HbA1c < 6.5)	p value
Intensive care unit stay (hr)	91.34± 348.39	31.99± 64.93	0.437
Length of stay (day)	10.58± 17.25	7.24± 5.84	0.201
Follow-up(month)	3.32± 1.40	3.61± 1.45	0.119
Postoperative complications(n)	21	13	0.132

Table 4 Intraoperative variables of the study patients according to the HbA1c value			
Variable	Group 1(HbA1c ≥ 6.5)	Group 2(HbA1c < 6.5)	P value
Number of bypass graft			
1	10	12	
2	18	17	0.955
3	35	31	
4 and over	37	40	
CPB time(min)	99.18±32.51	98.18±33.05	0.890
Cross-clamp time (min)	67.10±27.23	63.66±24.21	0.476
CPB: Cardiopulmonary bypass			

Table 5 Postoperative infective complications of the study patients according to the HbA1c value			
Variable	Group 1 (HbA1c ≥ 6.5)	Group 2 (HbA1c < 6.5)	P value
Deep wound infection	5	0	0.030
Superficial local infection	4	2	0.341
Total (deep + superficial inf.)	9	2	0.030

Table 6 Multivariate analysis for prediction of mediastinitis in all patients

Variable	P value	OR	95.0%C.I. for EXP
Preoperative glucose	0.642	0.993	0.964 – 1.023
Intraoperative glucose	0.697	0.994	0.962 – 1.026
Postoperative 1. day glucose	0.554	1.007	0.983 – 1.033
Postoperative 2. day glucose	0.036	1.037	1.002 – 1.072
Postoperative 3. day glucose	0.069	0.969	0.936 – 1.003
Age	0.285	1.090	0.930 – 1.278
Sex	0.845	0.787	0.071 – 8.685
Diabetes mellitus	0.997	0.0	
Hypertension	0.273	3.512	0.372 – 33.197
HbA1c	0.614	1.151	0.665 – 1.992
Cardiopulmoner bypass time	0.568	0.990	0.956 – 1.025
Ejection fraction	0.696	0.979	0.882 – 1.087

Discussion

Cardiovascular mortality is two to five times higher in diabetic patients than in non-diabetic individuals [8]. Several studies have shown elevated postoperative mortality and morbidity in this population [9,10]. However, tight perioperative glycemic control via insulin infusion has been associated with improved outcomes [11,12]. These results draw attention to the importance of strict glycemic control in the period after CABG.

Our findings revealed similar early mortality in both HbA1c groups. Although some previous studies reported no significant effect of diabetes on CABG outcomes [7], Bundhun et al. found increased mortality among diabetic patients in a meta-analysis of 11 studies involving 12,965 patients [9].

Pathophysiologic mechanisms underlying poorer outcomes in diabetic patients include end-organ damage, metabolic derangements, electrolyte disturbances, increased myocardial oxygen demand, and immune dysfunction. Hyperglycemia impairs neutrophil function, increases infection susceptibility, and disrupts coagulation and endothelial function. Some studies [13,14] found that high glucose values were an important risk factor for wound site infections, and there was a high correlation between maintaining glucose control and reduction in infection and sternal opening rates. In our study, deep sternal infection was significantly more common in the high-HbA1c group. Although superficial infections were not statistically different, the combined infection rate was. One of the 5 patients with mediastinitis underwent reoperation due to hemodynamic instability in the early postoperative period and the etiology may be re-surgery instead of poor glycemic control in this patient. Logistic regression identified postoperative day 2 hyperglycemia as a significant risk factor, underscoring the importance of tight glycemic control after CABG. Therefore, maintaining blood glucose control with aggressive treatment after surgery is of great importance in terms of reducing the risk of postoperative infection development. Alserius et al. reported that HbA1c > 6% was associated with an increased risk of superficial sternal infection and mediastinitis after CABG in a study of 605 patients [15]. Halkos et al. reported that HbA1c elevation was significantly associated with an increased risk of deep sternal infection after CABG and found the cut-off value as 7.8% for this complication [16]. In our study, we found the cut-off value of HbA1c as 7.65% for deep sternal infection with a sensitivity of 80% and specificity of 65.6%. In contrast, Göksedef et al. reported that HbA1c elevation did not pose a risk for mediastinitis development after CABG, but mediastinitis and local sternal infection were more common in the patients with high intraoperative blood glucose levels [17]. In our study, we found that high blood glucose levels on the 2nd postoperative day were significantly continued in the HbA1c ≥ 6.5% group with more common mediastinitis and superficial local infection compared to the other group. Interestingly, 30% of patients in the low-HbA1c group had diabetes but experienced no mediastinitis, suggesting that well-controlled diabetes may not pose an increased infection risk. Our findings support the notion that poor glycemic control, rather than the diagnosis of diabetes itself, is the primary risk factor.

Diabetes is also considered as an independent risk factor for neurological complications after CABG, and delirium and stroke are the most common of these complications. Zhongmin Li et al. [18] argued that there was no increase in neurological complications in diabetic patients. In our study, neurological events were observed in 3 patients in Group 1 and 1 patient in Group 2, but this difference was not statistically significant.

According to the results of the Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) study of 1800 patients, revascularization was more observed in diabetic patients after both CABG and percutaneous coronary intervention (PCI) compared to non-diabetic patients [19]. In this study, postoperative MI findings were observed in 3 patients in the HbA1c ≥6.5% group and 2 patients in the other group, but this difference was not statistically significant. Long-term follow-up studies will be more appropriate to evaluate revascularization after coronary bypass surgery. Therefore, our study is not suitable for evaluating this complication since it involves the early period after CABG.

Atrial fibrillation is the most common arrhythmia observed after cardiac surgery [20,21]. Apart from the proven classical risk factors, new mechanisms have now been introduced especially considering the role of inflammation in AF pathophysiology. One of the newly identified risk factors is the HbA1c levels in diabetic patients. There are studies demonstrating an inverse correlation between HbA1c levels and postoperative AF and showing that the incidence of AF is decreased in the presence of high HbA1c levels [22]. Iguchi et al. [23] showed that the incidence of AF was higher in patients with HbA1c level below 6.5% in a population study. Contrary to these data, Dublin et al. [24] showed that the risk of developing AF increased with increasing HbA1c levels in a population-based study on 1410 patients newly diagnosed with AF. In our study, although it was not statistically significant, AF was observed in 9 patients in the HbA1c <6.5% group, while it was observed in 5 patients in the other group. Although the effect of HbA1c level on AF is still controversial, one alleged mechanism is the emergence of higher doses of insulin need for postoperative blood glucose regulation is protective for AF development.

Given the high morbidity and mortality of mediastinitis, delaying elective CABG in patients with HbA1c ≥ 7.65% to allow for better glycemic optimization may be advisable. Tight glycemic regulation is endorsed by the American Heart Association, particularly targeting blood glucose <180 mg/dL perioperatively [25]. It will be possible on the day of surgery with high doses of insulin therapy even in patients with poor glycemic control. As in our study, the patients with good blood glucose regulation in the long term have a lower risk of developing complications after CABG. Thus, HbA1c, which is an indicator of long-term glycemic control, is a valuable method that can be used to evaluate preoperative risks for cardiac surgery, especially infection.

Limitations of the study

This study was conducted at a single center with a limited sample size. The findings pertain to early postoperative outcomes; long-term effects of HbA1c on CABG complications warrant further investigation in larger, multicenter studies.

In conclusion, effective glycemic control significantly reduces the risk of infection following CABG. HbA1c is a reliable measure of long-term glucose regulation and may serve as a useful preoperative risk stratification tool.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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Ethics approval

This study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Türkiye Yüksek İhtisas Training and Research Hospital.

Authors' contributions

ST; Designed and performed experiments, analyzed data and co-wrote the paper. HZİ, AÖ, EUÜ,VB,CLB.; Performed experimentes. EUÜ; Performed bioinformatic analyzes. BTT; Designed experiments and co-wrote the paper. HZİ., UÜ, CLB; Supervized the research.

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