Association between HbA1c levels and clinical outcomes in patients undergoing isolated coronary artery bypass grafting

İzole koroner arter bypass cerrahisi uygulanan hastalarda HbAIC düzeyleri ile klinik sonuçlar arasındaki ilişki

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Abstract

Purpose: Several studies have indicated that elevated HbA1c levels may increase adverse postoperative outcomes in cardiac surgery. However, the consistency of this relationship remains unclear. This study aimed to evaluate the impact of preoperative HbA1c levels on postoperative clinical outcomes in patients undergoing isolated coronary artery bypass grafting (CABG).

Materials and methods: A total of 169 patients who underwent elective, primary, isolated CABG under cardiopulmonary bypass (CPB) between January 2022 and January 2024 were retrospectively analyzed. Patients were divided into three groups based on their preoperative HbA1c levels: Group I (<5%), Group II (5-6.5%), and Group III (>6.5%). Demographic characteristics, preoperative risk factors, operative details, and postoperative complications were recorded. Logistic regression analysis was used to assess the relationship between HbA1c levels and postoperative outcomes such as atrial fibrillation, sternal wound infection, and chest tube drainage.

Results: The prevalence of diabetes mellitus (82.1%) and peripheral arterial disease (32.8%) was significantly higher in Group III ($p<0.05$). Postoperative complications, including sternal wound infection ($p=0.036$), atrial fibrillation ($p=0.006$), and higher 24-hour drainage volume ($p=0.01$), were more frequent in this group. HbA1c >6.5% was an independent predictor of sternal wound infection (OR:3.81; 95% CI:1.25-11.5) and atrial fibrillation (OR:2.25; 95% CI:1.17-4.32). Additionally, HbA1c positively correlated with drainage volume ($r=0.172$, $p=0.026$) and erythrocyte suspension usage ($r=0.201$, $p=0.01$).

Conclusion: High preoperative HbA1c levels are associated with increased risk of postoperative complications. HbA1c may serve as a valuable predictor of adverse outcomes, and optimizing glycemic control before surgery could improve prognosis.

Keywords: CABG, HbA1c, complications.

Öz

Amaç: Bazı çalışmalar, yüksek HbA1c düzeylerinin kalp cerrahisi sonrası olumsuz postoperatif sonuçları artırabileceğini göstermiştir. Ancak, HbA1c düzeyleri ile klinik sonuçlar arasındaki ilişki halen net değildir. Bu çalışmada, izole koroner arter bypass greftleme (CABG) uygulanan hastalarda preoperatif HbA1c düzeylerinin postoperatif klinik sonuçlar üzerindeki etkisinin değerlendirilmesi amaçlanmıştır.

Gereç ve yöntem: Ocak 2022 - Ocak 2024 tarihleri arasında kardiyopulmoner bypass (KPB) altında elektif, primer, izole CABG uygulanan 169 hasta retrospektif olarak analiz edildi. Hastalar preoperatif HbA1c düzeylerine göre üç gruba ayrıldı: Grup I (<%5), Grup II (%5-6,5) ve Grup III (>%6,5). Demografik veriler, preoperatif risk faktörleri, cerrahi ayrıntılar ve postoperatif komplikasyonlar kaydedildi. HbA1c düzeyleri ile atriyal fibrilasyon, sternal yara enfeksiyonu ve drenaj gibi postoperatif komplikasyonlar arasındaki ilişki lojistik regresyon ile değerlendirildi.

Bulgular: Diyabet (%82,1) ve periferik arter hastalığı (%32,8) Grup III'te anlamlı olarak daha yüksekti ($p<0,05$). Sternal yara enfeksiyonu ($p=0,036$), atriyal fibrilasyon ($p=0,006$) ve 24 saatlik drenaj miktarı ($p=0,01$) Grup III'te daha fazlaydı. HbA1c >%6,5, sternal enfeksiyon (OR:3,81) ve atriyal fibrilasyon (OR:2,25) için bağımsız risk faktörüydü. Ayrıca HbA1c, drenaj ($r=0,172$, $p=0,026$) ve eritrosit süspansiyonu kullanımı ($r=0,201$, $p=0,01$) ile pozitif korelasyon gösterdi.

Sonuç: Yüksek preoperatif HbA1c düzeyleri, postoperatif komplikasyon riskinin artmasıyla ilişkilidir. HbA1c, olumsuz sonuçların değerli bir öngörücüsü olabilir ve ameliyat öncesi glisemik kontrolün optimize edilmesi prognozu iyileştirebilir.

Anahtar kelimeler: CABG, HbA1c, komplikasyonlar.

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Introduction

Diabetes mellitus (DM) is a well-established risk factor for cardiovascular disease and is present in approximately 20% of patients undergoing coronary artery bypass grafting (CABG). Among diabetic patients, the prevalence of coronary artery disease reaches 55% [1].

Hemoglobin A1c (HbA1c), a glycated form of hemoglobin, serves as a key indicator of long-term glycemic control. This test reflects the average blood glucose levels over the past 90 days and is widely used for both monitoring and diagnosing diabetes [2]. Studies suggest that elevated HbA1c levels are strongly associated with increased morbidity and mortality. In particular, when HbA1c levels exceed 8.6%, the mortality risk after CABG is estimated to be four times higher than in patients with well-controlled glucose levels. Therefore, except in emergency cases, optimizing glycemic control before surgery is recommended to minimize postoperative risks [3].

Despite DM being widely acknowledged as a risk factor for adverse surgical outcomes, the impact of preoperative HbA1c levels on postoperative clinical outcomes remains controversial. While some studies have reported an association between high HbA1c levels and increased complications such as atrial fibrillation, wound infections, and renal dysfunction, others have found no significant relationship. Further research is needed to clarify the role of HbA1c as a predictor of postoperative outcomes in CABG patients.

This study aims to evaluate the relationship between preoperative HbA1c levels and postoperative clinical outcomes in patients undergoing CABG with cardiopulmonary bypass (CPB). Specifically, we seek to determine whether elevated HbA1c levels are associated with an increased risk of postoperative complications, including atrial fibrillation, sternal wound infections, and renal function deterioration.

Metarials and methods

Patients and selection criteria

A total of 203 patients who underwent open-heart surgery between January 2022 and January 2024 at the cardiovascular surgery clinic of Bandırma Training and Research Hospital were retrospectively reviewed. Inclusion criteria consisted of elective, first-time coronary artery bypass surgery performed with cardiopulmonary bypass (CPB) in adult patients. Exclusion criteria were reoperations, emergency cases, patients undergoing off-pump procedures, patients with multiple preoperative comorbidities (liver failure, renal failure, respiratory failure, or advanced malignancy), procedures involving additional surgeries (e.g., valve surgery), and patients with incomplete medical records. A total of 169 patients who underwent elective, primary, isolated coronary artery bypass grafting were included in the final analysis, with HbA1c levels recorded regardless of diabetes diagnosis.

This study was approved by the Bandırma Onyedi Eylül University Health Sciences Non-Interventional Research Ethics Committee (approved date: 13.06.2024, approval number: 2024-134). The study was conducted in accordance with the Declaration of Helsinki. The study flowchart is presented in Figure 1.
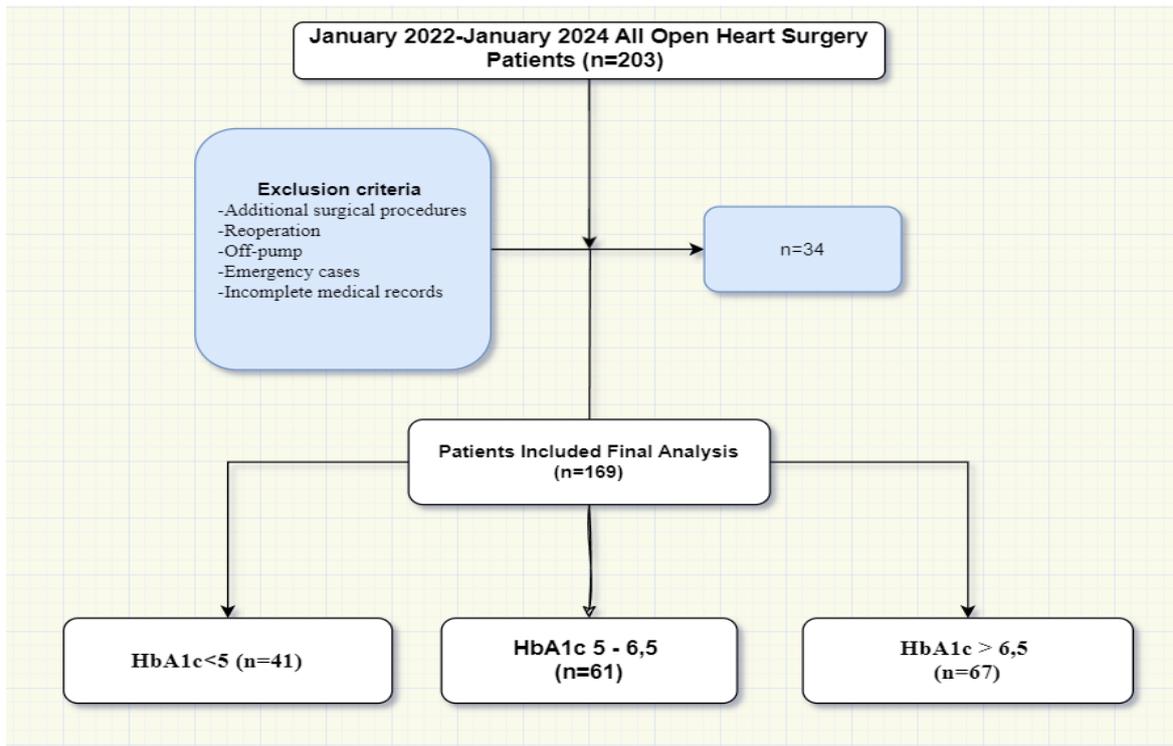
Figure 1. The flowchart of study

In our study, patients undergoing coronary revascularization who had preoperative HbA1c levels measured within 3 days before the procedure were identified. Patients were categorized into three groups based on their HbA1c levels: <5% (Group I), 5%-6.5% (Group II), and >6.5% (Group III). These three groups were compared in terms of demographic data, surgical methods, diabetes status, and postoperative clinical outcomes.

Definitions

Renal failure was defined as renal dysfunction requiring renal replacement therapy. Cerebrovascular events were defined as new focal or global neurological deficits confirmed by clinical findings and computed tomography scanning. Atrial fibrillation (AF) was defined as new-onset AF within 30 days postoperatively. Chest tube drainage was defined as postoperative drainage exceeding the median value of 500 mL for all patients. Additionally, intensive care unit (ICU) stay duration and sternal wound infection status were recorded.

Surgical technique

Patients were monitored upon admission to the operating room using a five-lead electrocardiogram, pulse oximetry, invasive arterial blood pressure via an arterial catheter connected to a pressure transducer, capnography, a central venous catheter placed in the internal jugular vein, a nasopharyngeal temperature probe, and a urinary catheter. After preoxygenation, general anesthesia was induced using fentanyl (2-10 mg/kg), pancuronium (0.1 mg/kg), and midazolam (0.05-0.1 mg/kg). Anesthesia was maintained with isoflurane, fentanyl (1-2 µg/kg), and pancuronium (0.01 mg/kg). Anticoagulation was initiated with heparin (300-400 IU/kg) to maintain activated clotting time (ACT) above 400 seconds, and additional heparin was administered during CPB as needed. Median sternotomy and ascending aorta-right atrium venous cannulation were performed. Patients were maintained at 28-32°C. Cardioplegic arrest was achieved with isothermic blood cardioplegia, and heparin neutralization was performed using protamine sulfate at the end of CPB.

Statistical analysis

All statistical analyses were performed using IBM SPSS (Statistical Package for the Social Sciences), version 25.0 (IBM Corp., Armonk, NY, USA). The normality of continuous data distribution was evaluated using the Kolmogorov–Smirnov test and confirmed by visual inspection of histogram and box plot graphs. Levene's test was used to evaluate the homogeneity of variances. Normally distributed continuous variables were presented as mean ± standard deviation, whereas non-normally distributed variables were expressed as median (25th–75th percentile). Categorical variables were summarized as frequencies and percentages. For comparisons between groups, One-way ANOVA (F-test) was used for normally distributed variables, and the Kruskal–Wallis H test was used for non-normally distributed variables. Categorical variables were compared using the Pearson Chi-square (χ^2) test. Spearman's rank correlation coefficient (Spearman's rho) was used to evaluate the relationship between non-normally distributed continuous variables. Test statistics and corresponding exact p-values were reported in all tables, and statistically significant values were marked with an asterisk (*). To identify independent predictors of postoperative complications, binary logistic regression analysis was performed, and results were expressed as Odds Ratios (OR) with 95% confidence intervals. A two-tailed p-value <0.05 was considered statistically significant.

Results

Among the 169 patients included in the study, the mean age was 63 (59-66.5) years in Group I, 68 (62-73) years in Group II, and 65 (60-71) years in Group III. All three groups predominantly consisted of male patients. None of the patients in Group I had DM. The number of patients diagnosed with DM was significantly higher in Group III (82.1%). Additionally, the prevalence of peripheral artery disease was also higher in Group III (32.8%). However, the incidence of hypertension and chronic obstructive pulmonary disease (COPD) was similar across the groups (Table 1).

Table 1. Demographic data of the patients

Variables	Groups			p
	HbA1c <5 (n=41)	HbA1c 5-6.5 (n=61)	HbA1c >6.5 (n=67)	
Age	63 (59-66.5)	68 (62-73)	65 (60-71)	[a]0.06 (4.724)
Gender (Male)	33 (80.5%)	43 (70.5%)	40 (59.7%)	[b]0.072 (5.258)
BSA	1.87 (1.99-1.73)	1.88 (1.98-1.78)	1.88 (2-1.78)	[a]0.786 (0.480)
Euroscore	5.3 (3.99-7.22)	5.87 (5.21-6.97)	7.63 (5.9-9.24)	[a]<0.001* (18.818)
CABG (count)	3 (2.5-4)	3 (3-4)	3 (2-4)	[a]0.458 (1.560)
EF	50 (47.5-55)	50 (45-50)	50 (45-40)	0.051 (5.412)
DM	0 (0%)	39 (63.9%)	55 (82.1%)	[b]<0.001* (72.110)
HT	28 (63.8%)	46 (75.4%)	55 (82.1%)	[b]0.256 (2.275)
PAH	3 (7.3%)	10 (16.4%)	22 (32.8%)	[b]0.004* (11.170)
COPD	5 (12.2%)	8 (13.1%)	9 (13.4%)	[b]0.354 (2.074)

[a] Kruskal Wallis, [b] Pearson Chi-square, BSA: Body Surface Area, EF: Ejection fraction, DM: Diabetes mellitus, HT: Hypertension
PAH: Peripheral arterial disease, COPD: Chronic obstructive pulmonary disease, * $p<0.05$

The operative details of the patients are presented in Table 2. In the HbA1c >6.5 group, relatively higher levels of postoperative chest tube drainage (*p*=0.01), the amount of erythrocytes used (*p*=0.018), atrial fibrillation (*p*=0.006), and sternal wound infection (*p*=0.036) were observed. No differences were identified between the groups regarding other operative variables (Table 2).

Table 2. Operational data of the patients

Variables		HbA1c <5 (n=41)	HbA1c 5-6.5 (n=61)	HbA1c >6.5 (n=67)	*p*
		Groups			
CPB time (min)	Mean ± SD	110.2±29.2	113.6±23.4	120.5±23.5	[c]0.091 (2.429)
ACC time (min)	Mean ± SD	60.5±22.5	61.1±17.9	67.8±17.4	[c]0.07 (2.704)
CABG (number)	Median (IQR)	3 (2.5-4)	3 (3-4)	3 (2-4)	[a]0.458 (1.560)
PO 24-h drainage (mL)	Median (IQR)	400 (362.5-600)	400 (350-500)	500 (400-700)	[a]0.002* (11.925)
ES used (mL)	Median (IQR)	400 (250-500)	400 (212.5-800)	600 (400-800)	[a]0.018* (8.018)
Extubation time (h)	Median (IQR)	9 (6-10.75)	10 (8-12)	10 (8-14)	[a]0.136 (3.994)
ICU stay (days)	Median (IQR)	3 (2-3)	2 (2-3)	3 (2-3)	[a]0.388 (1.892)
POAF	n (%)	6 (14.6)	21 (34.4%)	30 (44.8)	[b]0.006* (10.359)
Sternal wound infection	n (%)	0 (0%)	4 (6.6%)	9 (13.4%)	[b]0.036* (6.832)

[a] Kruskal Wallis, [b] Pearson Chi-square, [c] One way ANOVA, CPB: Cardiopulmonary bypass, ACC: Aortic cross clamp, PO: Postoperative
CABG: Coronary artery bypass grafting, ES: Erythrocyte suspension, ICU: Intensive care unit, POAF: Postoperative atrial fibrillation
IQR: Interquartile range, * *p*<0.05

Although the correlation was weak, a statistically significant positive association was found between HbA1c levels and both 24-hour drainage volume (r=0.172; *p*=0.026) and erythrocyte suspension use (r=0.201; *p*=0.01) (Table 3).

Binary logistic regression models were used to demonstrate the relationship between HbA1c >6.5% and certain postoperative complications. In univariate analysis, HbA1c >6.5% was found to increase the risk of atrial fibrillation (OR=2.25; 95% CI:1.17-4.32; *p*=0.015), postoperative bleeding exceeding 500 cc (OR=2.65; 95% CI:1.37-5.12; *p*=0.004), and sternal wound infection (OR=3.81; 95% CI:1.12-12.8; *p*=0.032) (Table 4).

Table 3. Correlation of operative variables with HbA1c

Variables		HbA1c
Postoperative 24-hour drainage (mL)	r	0.172
	p	0.026*
Erythrocytes used (mL)	r	0.201
	p	0.01*
Extubation time (hours)	r	0.071
	p	0.380
Lactate at end of CPB	r	-0.095
	p	0.238

HbA1c: Hemoglobin A1c, CPB: Cardiopulmonary bypass, r: Spearman Correlation Test

Table 4. Logistic regression analysis for the association between HbA1c >6.5 and postoperative complications

Variables	Odds Ratio (OR)	Wald	95% C.I	p
Atrial fibrillation	2.25	5.953	1.17-4.32	0.015*
Postoperative bleeding (>500 cc)	2.65	8.418	1.37-5.12	0.004*
Sternal wound infection	3.81	4.590	1.12-12.8	0.032*

Discussion

Diabetes mellitus (DM) is recognized as a risk factor for the development of coronary artery disease [4]. HbA1c levels are expressed as an index of long-term blood glucose control in diabetic patients and as predictors of outcomes. In a large cohort, a 1% increase in HbA1c levels was reported to be associated with an 18% increased risk of cardiovascular disease events and a 19% increased risk of myocardial infarction [5]. All patients included in our study presented with angina pectoris and angiographically confirmed critical coronary artery disease and were admitted for coronary artery bypass grafting (CABG).

Numerous studies have been conducted to evaluate the relationship between HbA1c levels and postoperative clinical outcomes and major adverse cardiac events, yielding diverse results. While some studies have suggested that elevated HbA1c levels are associated with increased complications, others have reported conflicting findings [6-8].

In our study, 82.1% of patients with HbA1c >6.5% had a DM diagnosis. This ratio was 63.9% in patients with HbA1c levels between 5% and 6.5%. None of the patients with HbA1c levels <5% had DM. Among the patients included, there were also individuals with elevated HbA1c levels but without a DM diagnosis. These patients with high HbA1c levels require careful monitoring and observation of potential risk factors to reduce their future risk of developing diabetes. The relationship between HbA1c levels and peripheral artery disease has been clearly demonstrated [9]. In our study, the presence of peripheral artery disease was significantly higher in patients with HbA1c >6.5%.

We observed a positive correlation between postoperative 24-hour chest tube drainage and HbA1c levels (r=0.172; p=0.026), and HbA1c >6.5% was identified as a risk factor for postoperative bleeding exceeding 500 mL (OR=2.65; p=0.004). Similarly, a parallel study reported a significant correlation between 24-hour postoperative drainage and HbA1c levels [10].

Sternal wound infections are among the complications that can occur following cardiac surgery. A meta-analysis by Wang et al. [11] reported a strong association between preoperative elevated HbA1c levels and sternal wound infections. However, another study comparing HbA1c measurements with postoperative outcomes found no association between HbA1c levels and sternal wound infections [3]. In our study, the incidence of sternal wound infections was higher in patients with elevated HbA1c levels (p=0.036), and HbA1c >6.5% was identified as a risk factor for sternal wound infections (OR=3.81; CI=1.25-11.5; p=0.018).

New-onset atrial fibrillation (AF) is a common complication after cardiac surgery. Studies by Kinoshita et al. [12] and Halkos et al. [13] reported an increased incidence of AF at lower HbA1c levels. In contrast, Wang et al. [11] meta-analysis indicated no significant difference in AF incidence between diabetic patients with lower preoperative HbA1c levels and those with higher levels. However, in our study, the frequency of AF was significantly higher in the high HbA1c group (p=0.006). Furthermore, univariate analysis identified elevated HbA1c as a risk factor for postoperative AF (OR=2.25; CI=1.17-4.32; p=0.015).

Schnack et al. [14] reported a correlation between the incidence of pneumopathy and HbA1c levels. Finger et al. [15] found no differences in HbA1c levels regarding intensive care unit (ICU) stays, while Sato et al. [16] reported that HbA1c levels >6.5% were associated with prolonged ICU stays. In our study, HbA1c was not found to be associated with ICU stay duration (p=0.388).

At our clinic, we manage cardiac surgery patients with a multidisciplinary approach, from the preoperative period to outpatient follow-up. For elective surgeries, preoperative referral to endocrinology for glycemic control adjustment is a routine practice. Intraoperative glycemic control is optimized with insulin during anesthesia and cardiopulmonary bypass management, and close monitoring is performed in the ICU to prevent rapid glycemic spikes. We believe this approach minimizes postoperative morbidity and mortality.

The use of HbA1c as a predictor of postoperative complications remains controversial in the literature. While some studies have shown a relationship, others have demonstrated no effect, and some have suggested that HbA1c could predict certain complications.

Our study has some limitations. First, the small sample size of the groups necessitates larger cohorts to clarify conflicting results in the literature. Second, HbA1c levels were not evaluated alongside fasting blood glucose levels. Third, the short postoperative follow-up period highlights the need for longer-term monitoring to capture different outcomes.

In conclusion, this study reveals that HbA1c may be a predictor of some complications after cardiac surgery. These complications include atrial fibrillation, sternal wound infection, and postoperative chest tube drainage. However, our study had no predictive value for the duration of mechanical ventilation and intensive care unit stay. We recommend that the HbA1c value should be carefully evaluated in the preoperative period to reduce some of the possible postoperative complications.

Authors contributions: D.D. and M.Ö. constructed the main idea and hypothesis of the study. D.D. developed the theoretical background and arranged the material and method section. M.Ö. performed the statistical analysis and interpreted the data in the Results section. The Discussion section of the article was written by D.D., and M.Ö. reviewed, corrected, and approved the final version.

Conflict of interest: No conflict of interest was declared by the authors.

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