Research Square

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Influence of preoperative glycosylated Hemoglobin (HbA1c) level on long-term outcomes after coronary artery bypass grafting

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Abstract

Background: Diabetes mellitus is highly prevalent among patients undergoing coronary artery bypass grafting (CABG), yet the prognostic significance of preoperative glycemic control remains uncertain. Thus, this study aims to investigate the association between hemoglobin A1c (HbA1c) and long-term outcomes following CABG.

Methods: We conducted a retrospective cohort study of 8,147 adults who underwent isolated CABG between 2009 and 2025. Patients were included based on available HbA1c samples and categorized by preoperative HbA1c as ≤5.8%, 5.8-6.5%, or ≥6.5%. The primary outcome was all-cause mortality. Secondary outcomes included postoperative complications and intensive care unit (ICU) length of stay. Multivariable Cox proportional hazards models were used to evaluate associations between HbA1c and mortality after adjustment for demographic, clinical, and procedural factors. Subgroup analyses assessed result robustness.

Results: Of the cohort, 2,630 were included with 1,022 (39%) having a HbA1c ≤5.8%, 501 (19%) 5.8-6.5%, and 1,107 (42%) ≥6.5%. Over a median follow-up of 5.2 years, mortality increased across HbA1c categories. After adjustment, HbA1c ≥6.5% was independently associated with higher mortality (HR 1.74; 95% CI 1.43-2.11; p<0.001), whereas intermediate HbA1c was not (HR 0.97; 95% CI 0.74-1.27; p=0.82). Elevated HbA1c was also associated with longer ICU stay and higher rates of sternal wound infection. Findings were consistent across age, sex, and body mass index subgroups.

Conclusions: Poor preoperative glycemic control is independently associated with increased long-term mortality and postoperative morbidity after CABG. HbA1c provides important prognostic information and may inform perioperative risk stratification in patients undergoing surgical revascularization.

Research Insights

What is currently known about this topic?	• Diabetes mellitus is highly prevalent among patients undergoing coronary artery bypass grafting (CABG) and is associated with worse postoperative and long-term outcomes. • Preoperative hemoglobin A1c (HbA1c) reflects chronic glycemic exposure and has been linked to postoperative complications such as infection and impaired wound healing. • However, the prognostic significance of preoperative HbA1c for long-term survival after CABG remains inconsistent across prior studies.
What is the key research question?	Does preoperative HbA1c independently predict long-term mortality and postoperative morbidity after isolated coronary artery bypass grafting?
What is new?	• In a cohort of 2,630 patients undergoing CABG, HbA1c ≥6.5% was independently associated with increased long-term mortality. • Intermediate HbA1c levels (5.8–6.5%) were not associated with excess mortality after multivariable adjustment. • Higher HbA1c was also associated with increased postoperative morbidity, including longer ICU stay and a higher rate of sternal wound infection.
How might this study influence clinical practice?	Preoperative HbA1c provides practical prognostic stratification before CABG and may support intensified perioperative and longitudinal metabolic management for patients with HbA1c ≥6.5%, without necessarily delaying surgery for modest HbA1c elevation.

Introduction

Diabetes mellitus (DM) is a major determinant of adverse cardiovascular outcomes and remains highly prevalent among patients undergoing coronary artery bypass grafting (CABG) [1,2]. Despite advances in surgical techniques and perioperative care, patients with DM continue to experience higher rates of perioperative complications, graft failure, and long-term mortality following revascularization [1–4].

Glycemic control, commonly assessed by hemoglobin A1c (HbA1c), reflects cumulative metabolic exposure and has emerged as a potential modifiable risk factor influencing surgical outcomes [5,6]. Elevated HbA1c levels are associated with endothelial dysfunction, impaired wound healing, heightened inflammatory responses, and increased susceptibility to infection, pathophysiological mechanisms that may adversely affect both short- and long-term outcomes after CABG [5,6]. Prior studies have demonstrated associations between poor preoperative glycemic control and postoperative complications, including sternal wound infection, renal dysfunction, and prolonged hospitalization [7,8].

However, evidence regarding the prognostic value of HbA1c for long-term survival and major adverse cardiovascular events after CABG remains inconsistent [3,4]. Moreover, current clinical guidelines provide limited guidance on optimal preoperative HbA1c targets for patients referred for surgical revascularization [3,4,8]. Whether HbA1c represents a continuous risk marker, a modifiable therapeutic target, or simply a surrogate of systemic disease severity in this setting remains uncertain [7,8]. Clarifying the relationship between HbA1c and CABG outcomes is particularly relevant given the growing

burden of DM and the increasing complexity of contemporary surgical candidates. We aimed to evaluate whether HbA1c independently predicts mortality and major postoperative complications after comprehensive adjustment for demographic, clinical, and procedural factors.

Methods

Study Design and Data Sources

This retrospective cohort study included 8,147 adults undergoing CABG at Sheba Medical Center between 2004 and 2025. Data were obtained from the institutional cardiovascular surgery registry and linked electronic medical records, including perioperative variables, laboratory testing, echocardiography, and longitudinal follow-up [10]. The study was approved by the institutional review board with a waiver of informed consent due to the retrospective design and use of de-identified data.

Exposure Assessment

Preoperative HbA1c was measured using standardized high-performance liquid chromatography assays. The most recent HbA1c value obtained within 1 week before surgery was used. Patients were categorized into 3 prespecified groups: ≤5.8% (reference), 5.8-6.5%, and ≥6.5% [6-8]. HbA1c was additionally analyzed as a continuous variable in sensitivity analyses.

Statistical Analysis

Continuous variables are presented as median (interquartile range) and categorical variables as counts (percentages). Comparisons across HbA1c groups were performed using one-way ANOVA or the Kruskal-Wallis test, according to data distribution. Survival was assessed using Kaplan-Meier estimates and compared using the log-rank test. Log-minus-log survival plots were also visually inspected for key covariates. Schoenfeld residual testing indicated maintenance of the proportional hazards assumption. Associations between HbA1c and mortality were evaluated using Cox proportional hazards models. Univariate and multivariable models were constructed, with covariates entered simultaneously in adjusted analyses. The proportional hazards assumption was assessed using Schoenfeld residuals. Prespecified subgroup analyses were conducted according to age, sex, body mass index, and comorbidity burden, with interaction terms used to test effect modification. Variables with more than 40% missingness were excluded. Sensitivity analysis was conducted to confirm robustness of findings. Analyses based on age group classification, with patients ≥ 80 being classified as octogenarians or older and < 80 as non- octogenarians was conducted. Furthermore, sex based and obesity statues evaluations were undertaken, with body mass index (BMI) of ≥ 30 kg/m2 being classified as obese.

All statistical analyses were conducted in R (version 4.5.0, R Foundation for Statistical Computing). All results are presented as HRs with 95% confidence intervals (CIs). Statistical significance was defined as a two-sided p value <0.05.

Results

Baseline Characteristics

Among 2,630 CABG patients with available HbA1c, 1,022 (39%) had ≤5.8%, 501 (19%) had 5.8-6.5%, and 1,107 (42%) had ≥6.5%. Median age was 67 years (IQR 61-74), and 82.7% were males. Higher HbA1c was associated with greater cardiometabolic and renal comorbidity burden, including progressively higher BMI (26.9 vs 27.7 vs 27.8 kg/m²), hypertension prevalence (51% vs 62% vs 68%), and hyperlipidemia (57% vs 69% vs 71%) across increasing HbA1c categories (all $p<0.05$). 1,065 (40.5%) were treated with insulin therapy preoperatively, increasing with HbA1c groups (Table 1).

Table 1

Variable	Total (N = 2,630)	HbA1c <=5.8 (N = 1,022)	HbA1c - 5.8-6.5 (N = 501)	HbA1c >=6.5 (N = 1,107)	P value
Age (Y)	67.0 [61.0, 74.0]	67.0 [60.0, 74.0]	68.0 [62.0, 75.0]	67.0 [61.0, 73.0]	0.022
Male (%)	2174 (82.7%)	873 (85.4%)	394 (78.6%)	907 (81.9%)	0.003
HbA1c (%)	6.2 [5.6, 7.4]	5.5 [5.2, 5.7]	6.1 [6.0, 6.3]	7.7 [7.0, 8.9]	<0.001
BMI (kg/m2)	27.4 [24.8, 30.5]	26.9 [24.5, 29.7]	27.7 [25.1, 30.9]	27.8 [25.0, 31.1]	<0.001
COPD (%)	142 (5.8%)	49 (5.0%)	38 (8.2%)	55 (5.4%)	0.046
Hyperlipidemia (%)	1678 (65.5%)	573 (57.4%)	340 (69.1%)	765 (71.4%)	<0.001
Hypertension (%)	1541 (60.1%)	507 (50.8%)	304 (62.0%)	730 (67.8%)	<0.001
Renal Failure (%)	229 (10.0%)	58 (6.5%)	46 (10.2%)	125 (13.1%)	<0.001
Dialysis (%)	20 (1.6%)	8 (1.6%)	5 (2.0%)	7 (1.4%)	0.820
Number of conduits grafts	2.0 [0.0, 2.0]	2.0 [0.0, 2.0]	2.0 [0.0, 2.0]	2.0 [0.0, 2.0]	0.116
Previous Cardiac Operation (%)	73 (2.8%)	26 (2.5%)	15 (3.0%)	32 (2.9%)	0.675
Previous CABG (%)	39 (1.5%)	16 (1.6%)	6 (1.2%)	17 (1.5%)	0.541
Echocardiography					
LVEF (%)	55.0 [43.0, 60.0]	60.0 [45.0, 60.0]	55.0 [45.0, 60.0]	55.0 [40.0, 60.0]	<0.001
LVEDD (cm)	4.8 [4.4, 5.2]	4.8 [4.4, 5.3]	4.8 [4.4, 5.2]	4.8 [4.4, 5.2]	0.522
LVESD (cm)	3.1 [2.7, 3.7]	3.1 [2.7, 3.6]	3.2 [2.7, 3.8]	3.2 [2.8, 3.8]	0.023
SPAP (mmHg)	31.2 [26.0, 39.0]	31.0 [26.0, 36.0]	32.0 [27.0, 40.0]	32.0 [26.5, 41.0]	0.005
LA Area (cm2)	20.0 [17.0, 23.3]	19.3 [16.6, 23.0]	20.0 [17.0, 24.0]	20.0 [17.0, 23.3]	0.010
Blood Test					
Sodium (mmol/L)	141.0 [139.0, 143.0]	141.0 [139.0, 143.0]	141.0 [140.0, 143.0]	141.0 [139.0, 142.0]	<0.001
Direct Bilirubin (mg/dL)	0.1 [0.1, 0.2]	0.1 [0.1, 0.2]	0.1 [0.1, 0.2]	0.1 [0.1, 0.2]	0.061

Creatinine (mg/dL)	**1.1 [0.9, 1.4]**	**1.1 [0.9, 1.2]**	**1.1 [0.9, 1.3]**	**1.1 [0.9, 1.5]**	**<0.001**
Potassium (mmol/L)	**4.7 [4.4, 5.1]**	**4.6 [4.3, 4.9]**	**4.7 [4.4, 5.1]**	**4.8 [4.5, 5.2]**	**<0.001**
Urea (mg/dL)	**46.0 [37.0, 60.0]**	**43.0 [35.0, 53.0]**	**46.0 [38.0, 58.0]**	**51.0 [39.0, 72.0]**	**<0.001**
Uric (mg/dL)	**6.7 [5.6, 8.0]**	**6.6 [5.7, 7.7]**	**6.9 [5.8, 8.2]**	**6.7 [5.4, 8.3]**	**0.047**
Albumin (g/dL)	**4.2 [3.9, 4.5]**	**4.2 [4.0, 4.5]**	**4.2 [4.0, 4.4]**	**4.2 [3.9, 4.4]**	**0.083**
Hemoglobin (g/dL)	**14.2 [12.6, 15.3]**	**14.5 [13.3, 15.5]**	**14.1 [12.3, 15.2]**	**13.9 [11.7, 15.1]**	**<0.001**
Treatments					
DM Medications (%)	**1,763 (67%)**	**239 (23%)**	**473 (94%)**	**1,051 (95%)**	**0.045**
Insulin (%)	**1,065 (40.5%)**	**78 (7.5%)**	**142 (28%)**	**845 (75%)**	**<0.001**
Complications					
Leg Infection (%)	**32 (1.3%)**	**8 (0.8%)**	**11 (2.3%)**	**13 (1.2%)**	**0.046**
Sternal Infection (%)	**75 (2.9%)**	**20 (2.0%)**	**14 (2.8%)**	**41 (3.7%)**	**0.001**
TIA/CVA (%)	**43 (1.6%)**	**15 (1.5%)**	**10 (2.0%)**	**18 (1.6%)**	**0.746**
Cardiac Reoperation (%)	**88 (3.3%)**	**27 (2.6%)**	**18 (3.6%)**	**43 (3.9%)**	**0.1**
CABG Reoperation (%)	**19 (0.7%)**	**8 (0.8%)**	**4 (0.8%)**	**7 (0.6%)**	**0.897**

BMI - Body Mass Index

COPD - Chronic Obstructive Pulmonary Disease

CVA - Cerebrovascular Accident

DM - Diabetes Mellitus

HbA1c - Hemoglobin A1c (Glycated Hemoglobin)

LA - Left Atrium

LVEDD - Left Ventricular End-Diastolic Diameter

LVEF - Left Ventricular Ejection Fraction

LVESD - Left Ventricular End-Systolic Diameter

SPAP - Systolic Pulmonary Artery Pressure

TIA - Transient Ischemic Attack

In hospital and long-term outcomes

Median follow-up was 5.5 years (IQR 2.5-8.5), 5.04 years (IQR 2.1-8.5), and 5.02 years (IQR 2.0-8.5) in the ≤5.8%, 5.8-6.5%, and ≥6.5% HbA1c groups, respectively. One-year mortality increased across categories (3.5%, 7%, and 7%), as did 5-year mortality (9%, 11%, and 17%), with the highest rates observed among patients with HbA1c ≥6.5% (Figure 1). ICU stay increased stepwise with worsening glycemic control (22 vs 22 vs 24 hours, p<0.001). Postoperative sternal wound infection (2% vs 3% vs 4%) and tracheostomy reopening (1% vs 3% vs 3%) were more frequent in higher HbA1c strata (p≤0.01), whereas in-hospital mortality did not differ (2% vs 3% vs 2.5%).

Prognostic Association of HbA1c for Long-Term Survival

In univariate Cox analysis, HbA1c ≥6.5% was associated with significantly higher mortality compared with HbA1c ≤5.8% (HR 1.75; 95% CI 1.45-2.12; p<0.001), whereas HbA1c 5.8-6.5% was not (HR 1.10; 95% CI 0.85-1.42; p=0.47). After multivariable adjustment, HbA1c ≥6.5% remained independently associated with mortality (HR 1.74; 95% CI 1.43-2.11; p<0.001), while intermediate HbA1c was not associated with excess risk (HR 0.97; 95% CI 0.74-1.27; p=0.82) (Figure 2).

Sensitivity and subgroup analysis

Several subgroup analyses confirmed the robustness of our findings. In multivariable models, HbA1c ≥6.5% remained independently associated with higher mortality in patients aged <80 years (HR 1.79; 95% CI 1.44-2.21), those aged ≥80 years (HR 1.78; 95% CI 1.20-2.64), patients with BMI <30 kg/m² (HR 1.68; 95% CI 1.35-2.09) and ≥30 kg/m² (HR 1.96; 95% CI 1.26-3.05), and in males (HR 1.88; 95% CI 1.46-2.42) (all p<0.01). No significant association was observed for intermediate HbA1c (5.8-6.5%) in any subgroup.

Discussion

In this large contemporary cohort of patients undergoing coronary artery bypass grafting, elevated preoperative HbA1c was independently associated with increased long-term mortality and higher rates of postoperative complications, even after comprehensive adjustment for demographic, clinical, and procedural factors. In contrast, intermediate HbA1c levels were not associated with excess mortality. These findings suggest that poor glycemic control identifies a subgroup of surgical patients at persistently increased risk, whereas modest elevations in HbA1c may not confer adverse long-term prognostic implications.

Several biological mechanisms may explain the adverse prognostic impact of poor glycemic control in this setting. Chronic hyperglycemia promotes endothelial dysfunction, oxidative stress, and systemic inflammation, all of which may accelerate graft atherosclerosis and impair microvascular perfusion [10]. In addition, impaired immune function and altered collagen metabolism in diabetes contribute to delayed wound healing and increased susceptibility to infection [11–14].

Consistent with these mechanisms, we observed higher rates of sternal wound infection and prolonged ICU stay among patients with elevated HbA1c. These early postoperative complications may serve as intermediaries linking metabolic dysregulation to adverse long-term outcomes [10,15]. Furthermore, chronic hyperglycemia is associated with autonomic dysfunction, platelet activation, and adverse myocardial remodeling, which may further amplify long-term cardiovascular risk after revascularization [10,15].

Our study demonstrates a clear threshold effect, whereby only HbA1c values in the diabetic range were associated with adverse survival. Patients with HbA1c ≥ 6.5% experienced nearly a 75% higher adjusted mortality risk compared with those with normal glycemic control. This association remained consistent across age, sex, and body mass index strata, underscoring the robustness and generalizability of the findings. Importantly, intermediate HbA1c values were not associated with increased mortality in either primary or sensitivity analyses. This observation suggests that mild dysglycemia or prediabetes may not substantially influence long-term outcomes following CABG when contemporary surgical and medical care is provided [16]. Together, these findings argue against a linear relationship between HbA1c and postoperative risk and instead support a clinically relevant risk threshold [16,17].

These findings have several important clinical implications. First, preoperative HbA1c measurement provides valuable prognostic information that extends beyond short-term surgical risk. Patients with HbA1c ≥ 6.5% represent a high-risk subgroup that may benefit from intensified perioperative monitoring, optimization of metabolic control, and closer long-term follow-up [16–18]. Second, the absence of excess risk among patients with intermediate HbA1c suggests that routine surgical delay for modestly elevated values may not be warranted in otherwise stable patients [15–18]. This observation may help inform shared decision-making and avoid unnecessary postponement of revascularization. Third, whether aggressive preoperative glycemic optimization can improve long-term outcomes remains uncertain. While our findings support HbA1c as a prognostic marker, they do not establish causality. HbA1c may reflect cumulative metabolic injury, disease duration, or broader systemic vulnerability rather than a directly modifiable surgical risk factor. Prospective studies are needed to determine whether targeted glycemic interventions before CABG translate into improved survival [19–23].

Future research should focus on integrating HbA1c with other metabolic and inflammatory biomarkers to improve risk stratification in surgical candidates. Randomized or pragmatic trials evaluating structured preoperative and postoperative glycemic optimization strategies are needed to determine whether modifying HbA1c can meaningfully improve outcomes. Additionally, studies exploring the interaction between glycemic control, graft patency, and long-term cardiovascular remodeling may further clarify underlying mechanisms.

Strengths and Limitations

This study has several strengths, including its large sample size, long-term follow-up, detailed clinical characterization, and comprehensive multivariable modeling. The consistent findings across subgroups

further support their robustness. However, several limitations merit consideration. First, the observational design precludes causal inference, and residual confounding cannot be excluded. HbA1c may capture unmeasured factors such as diabetes duration, medication adherence, or socioeconomic status. Second, we lacked data on perioperative glucose variability and postoperative glycemic management, which may also influence outcomes. Third, HbA1c was measured at a single preoperative time point and may not reflect longitudinal glycemic control. Finally, the study was conducted within a single healthcare system, which may limit generalizability to other populations.

Conclusion

In this large cohort of patients undergoing CABG, poor preoperative glycemic control, defined by HbA1c ≥ 6.5%, was independently associated with increased long-term mortality and higher postoperative complication rates. In contrast, intermediate HbA1c levels were not associated with adverse outcomes. These findings support the role of HbA1c as an important prognostic marker in surgical revascularization and highlight the need for targeted risk stratification and longitudinal metabolic management in patients with diabetes undergoing CABG.

Abbreviations

BMI - Body mass index

CABG - Coronary artery bypass grafting

COPD - Chronic obstructive pulmonary disease

DM - Diabetes mellitus

HbA1c - Hemoglobin A1c (glycated hemoglobin)

ICU - Intensive care unit

LA - Left atrium

LVEF - Left ventricular ejection fraction

SPAP - Systolic pulmonary artery pressure

Declarations

Ethics approval and consent to participate

The study was approved by the Sheba Medical Center Institutional Review Board (Ethics Committee approval 02.12.2014; Protocol 4257). The requirement for informed consent was waived due to the retrospective design and use of de-identified data. The study was reported according to the STROBE guidelines.

Consent for publication
Not applicable.

Data availability statement
The datasets generated and analyzed during the current study are not publicly available due to institutional data governance and patient privacy restrictions, though are available from the corresponding author on reasonable request and subject to approval by the Sheba Medical Center Institutional Review Board and data-sharing agreements.

Competing interests
The authors declare that they have no competing interests.

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Authors' contributions
VC contributed to study conception and design, data analysis and interpretation, and drafted the manuscript. AK contributed to study conception and design, clinical interpretation, critical revision and drafted the manuscript. RPK, SA, and EZF contributed to data acquisition/curation and critical revision. ER and LS contributed to senior oversight, clinical interpretation, and critical revision. All authors read and approved the final manuscript.

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Trial registration: Ethical Committee of Sheba Medical Centre, Israel, on 02.12. 2014, Protocol 4257.

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Figures

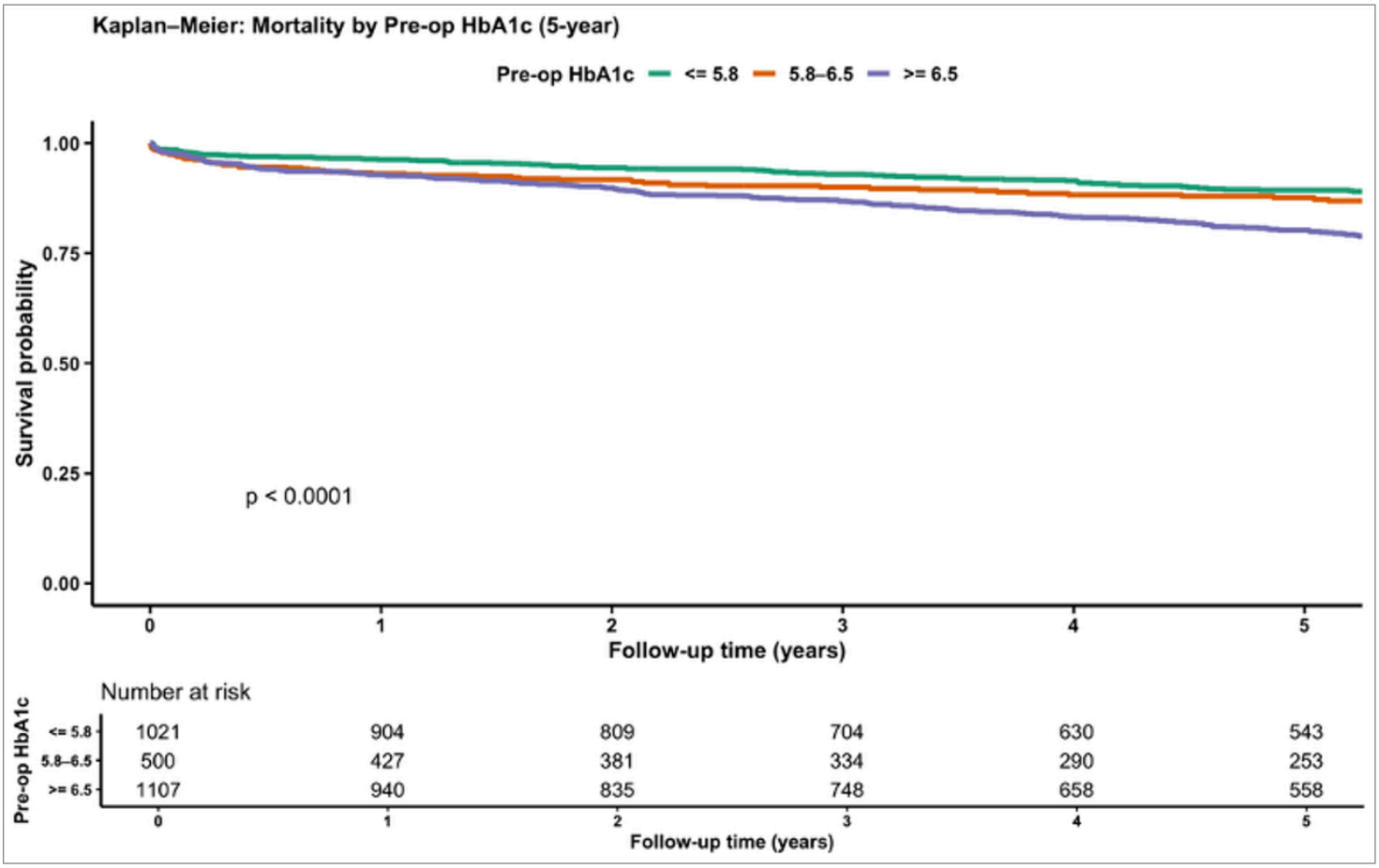


Figure 1

Kaplan-Meier 5 Year Survival Curves by HbA1c Category: Kaplan-Meier estimates of all-cause mortality according to preoperative hemoglobin A1c category.

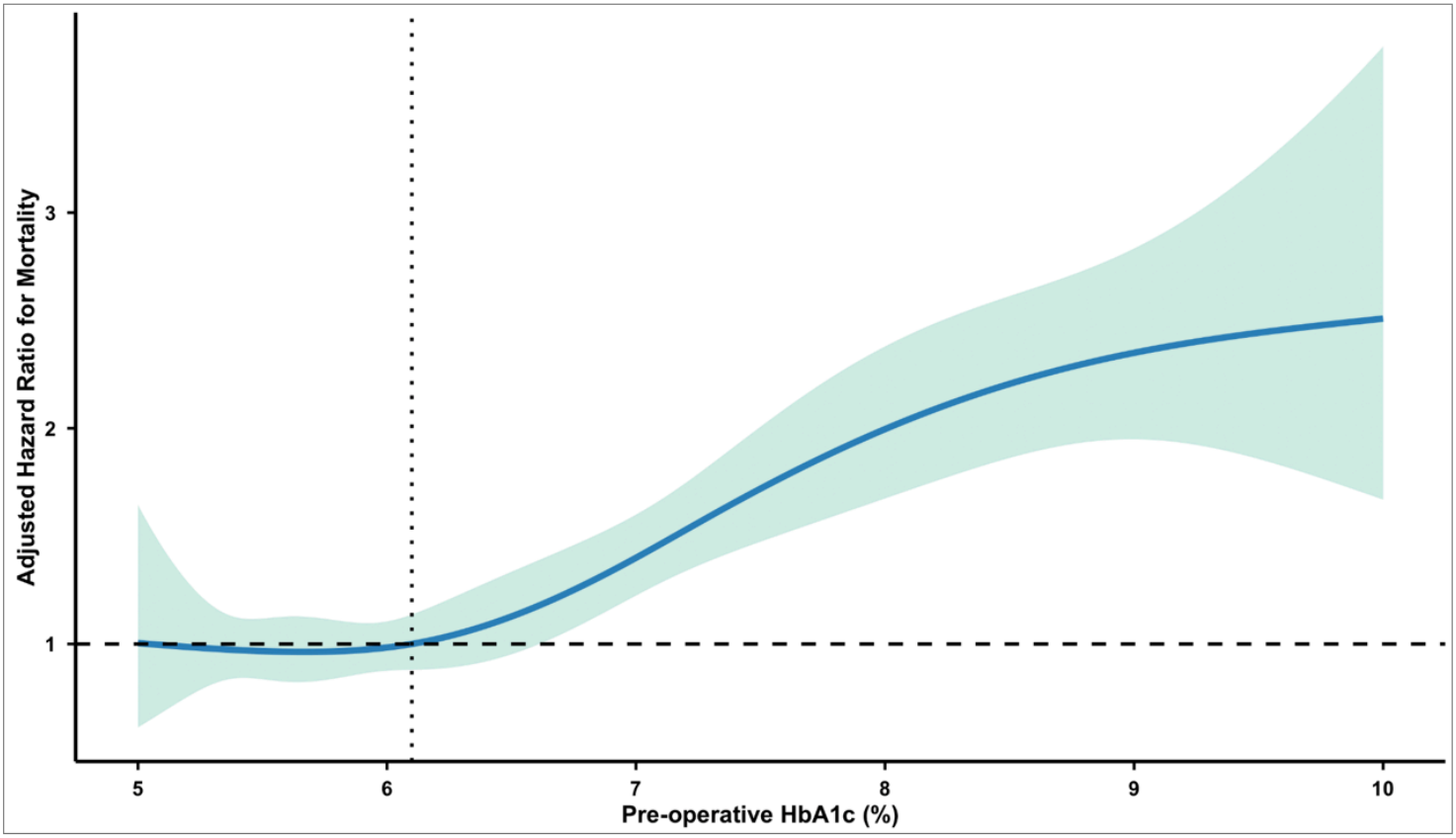


Figure 2

Adjusted Association Between Preoperative HbA1c and Mortality - Restricted cubic spline demonstrating the adjusted hazard ratio for all-cause mortality across the continuous spectrum of preoperative HbA1c.

Supplementary Files

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- GraphicalAbstract.png