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RESEARCH

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# Effect of elevated HbA1c on outcomes in on-pump versus off-pump coronary artery bypass grafting

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## Abstract

**Background** Diabetic patients are at an increased risk of cardiovascular morbidities. We aimed to examine if elevated pre-operative glycosylated hemoglobin (HbA1c) levels are associated with higher likelihood of experiencing adverse events in on-pump (ONCAB) versus off-pump (OPCAB) coronary artery bypass graft (CABG) procedures. We examined characteristics of patients undergoing CABG using our institutional STS Adult Cardiac Surgery Database (ACSD) from 2014 to 2020. Descriptive statistics and univariate analyses were used to compare postoperative outcomes between ONCAB and OPCAB based on preoperative HbA1c levels: (1) HbA1c ≤ 6.0%, (2) 6.0% < HbA1c ≤ 7.0%, (3) 7.0% < HbA1c ≤ 8.5%, (4) HbA1c > 8.5%. Multivariable models were built to assess risk factors associated with adverse events. Primary outcomes were operative mortality and stroke.

**Results** For ONCAB, statistically significant associations were found between increasing HbA1c and new post-operative dialysis ($p$=0.01), rates of readmission ($p$=0.003) and greater lengths of stay ($p$=0.002). For OPCAB, statistically significant associations were found between increasing HbA1c and rates of operative mortality ($p$=0.04), post-operative renal failure ($p$=0.0001), new post-operative dialysis ($p$=0.0001), sternal wound infection ($p$=0.01), and greater lengths of stay ($p$=0.03). No significant relationship was noted between HbA1c and stroke, reoperation due to bleeding, or post-operative transfusion.

**Conclusions** Increasing HbA1c positively correlated with numerous adverse patient outcomes in both ONCAB and OPCAB, and differences were noted in which outcomes were most impacted between the two techniques. Pre-operative medical optimization from a diabetes standpoint is paramount to improve CABG outcomes in both on-pump or off-pump techniques.


**Keywords** Coronary artery bypass grafting, Hemoglobin A1c

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## Background

Heart disease accounts for one in every four deaths in the United States, and for those who die of heart disease, coronary artery disease (CAD) is the most frequently cited cause [1]. Common risk factors for CAD include diabetes mellitus, hypertension, smoking, hyperlipidemia, obesity, and psychosocial stress. With an increasing prevalence of obesity and the expected worsening of cardiovascular risk factors, the incidence of CAD is expected to rise among the general population [2]. Coronary artery bypass graft

(CABG) surgery is an effective way to restore blood flow to ischemic tissues, prevent myocardial infarction, and reduce post-myocardial infarction complications, and current guidelines consider it a standard of care for patients with specific anatomical distribution of coronary artery disease [3, 4].

Diabetes mellitus is a well-established independent risk factor for the development of CAD, and approximately 25% of all patients who undergo coronary revascularization have diabetes [5, 6]. Diabetes mellitus is associated with a two-to-four-times higher risk of developing cardiovascular disease, and these patients have an up to three times higher risk of mortality [7]. In addition to increased CAD development, the literature has shown that clinical outcomes following CABG surgery are significantly worse in diabetic patients when compared to non-diabetic patients [8, 9]. It is imperative that diabetic patients' glycemic control is monitored in order to track disease progression and to establish a patient's risk for developing CAD or deleterious outcomes following CABG. Glycosylated hemoglobin A1c (HbA1c) is commonly used to track diabetes control, and it is a marker for the average blood glucose level over a three-to-four-month period prior to the measurement [10].

CABG procedures have traditionally been completed with the aid of cardiopulmonary bypass (CPB), a method also known as on-pump CABG (ONCAB) [11]. Off-pump CABG (OPCAB) may be used in an effort to reduce the number of side effects related to CPB [12]. Advances in the field have to lead to a better understanding of how CABG outcomes are affected by various pre-operative variables, with one of the most important variables being pre-operative diabetes control. Despite there being significant information in the literature regarding CABG outcomes in the diabetic population, there are still further relationships to elucidate. More specifically, there is a paucity of information regarding potential differences in outcomes between both surgical techniques with rising HbA1c levels. The aim of this study is to evaluate the effects of elevated HbA1c levels on the outcomes of ONCAB versus OPCAB for our patient population.

## Methods

### Study design

In this retrospective cohort study, patient data from our institutional Society of Thoracic Surgeons (STS) database was reviewed to find datapoints on patient demographics, pre-operative risk factors, history of cardiac interventions and cardiac status, operative details, and post-operative outcomes. We received institutional review board (IRB) approval for this retrospective study, and informed consent was waived due to the nature of the study. Our cohort consisted of patients who underwent either ONCAB or OPCAB surgery at our institution from January of 2014 through December of 2020. Patients who had concomitant surgery, patients who were converted from OPCAB to ONCAB, patients with an unknown pre-operative HbA1c, or patients less than 18 years of age were excluded. The cohort was divided into groups based on if they underwent ONCAB or OPCAB surgery. They were also stratified into four subgroups based on their pre-operative levels of HbA1c. The parameters for the HbA1c groups are as follows:

1. HbA1c $\leq$ 6.0
2. 6.0 < HbA1c $\leq$ 7.0
3. 7.0 < HbA1c $\leq$ 8.5
4. HbA1c > 8.5

### Study endpoints

The primary endpoints for the study are operative mortality and stroke. Secondary endpoints will include post-operative renal failure, new-onset post-operative dialysis, sternal wound infection, reoperation due to bleeding, post-operative transfusion, readmission rate, and length of stay. Definitions for these terms are based on the categorization of outcomes found in the STS Adult Cardiac Surgery Database (ACSD).

### Statistical analysis

Descriptive statistics and summary statistics were generated to describe pre-operative, operative, and post-operative data elements in the overall, OPCAB, and ONCAB patient groups. Furthermore, we evaluated the differences in pre-operative characteristics and post-operative outcomes in OPCAB vs. ONCAB patients by pre-operative HbA1c levels. One-way ANOVA analyses were conducted to detect differences by OPCAB vs. ONCAB in the outcomes and covariates across the pre-operative HbA1c levels. Multivariable analyses were conducted to identify optimal pre-operative HbA1c cut-offs for predicting composite adverse events (post-op renal failure, dialysis, operative mortality, ≥75th percentile length of stay, readmission, sternal wound infection). All the analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

## Results

Of the 9695 patients that underwent cardiac surgery at our institution from 2014 to 2020, 4209 individuals underwent CABG surgery. We excluded 1649 CABG patients with concomitant procedure(s). Our final study cohort consisted of 2560 patients undergoing isolated

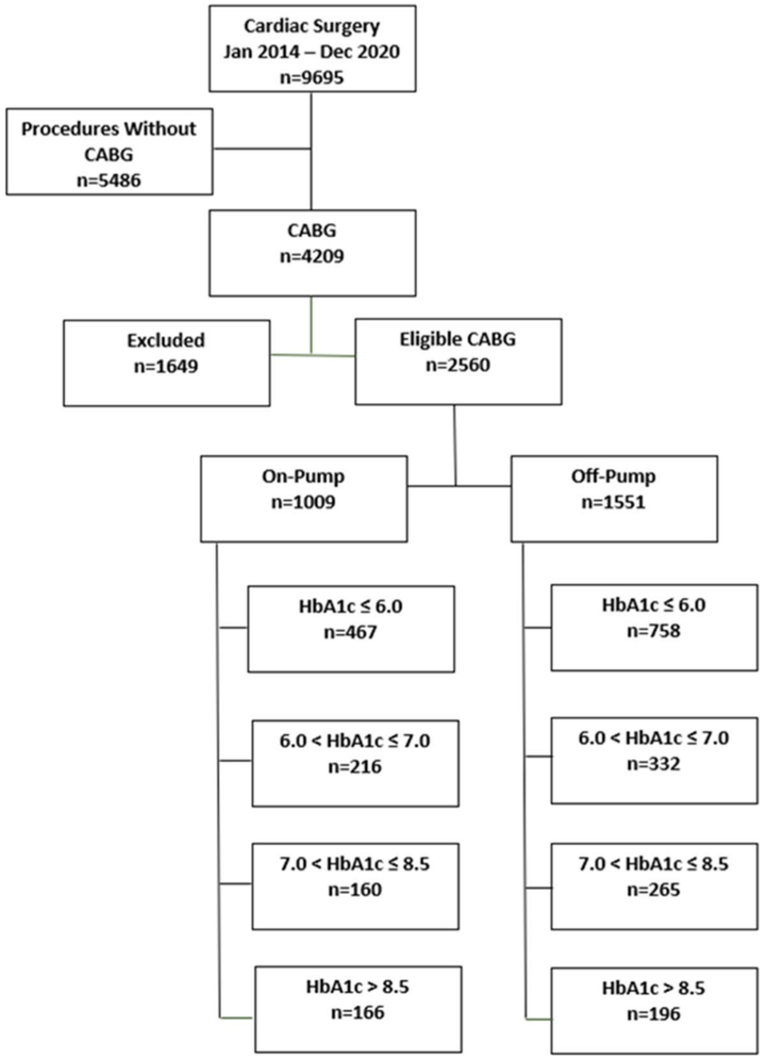


**Fig. 1** Patient selection and stratification. CABG, coronary artery bypass grafting; HbA1c, hemoglobin A1c

**Table 1** Patient distribution based on pre-operative HbA1c and surgical technique

| HbA1c | ONCAB | OPCAB | *p*-value |
|---|---|---|---|
| **≤ 6.0** | 467 (46.28%) | 758 (48.87%) | 0.2002 |
| **(6.0, 7.0]** | 216 (21.41%) | 332 (21.41%) | 0.9991 |
| **(7.0, 8.5]** | 160 (15.86%) | 265 (17.09%) | 0.4143 |
| **>8.5** | 166 (16.45%) | 196 (12.64%) | 0.0068 |
| **Total** | 1009 (100%) | 1551 (100%) | 0.0500 |

Data displayed as n (%)

*HbA1c* hemoglobin A1c, *ONCAB* on-pump coronary artery bypass grafting, *OPCAB* off-pump coronary artery bypass grafting

CABG, with 1009 ONCAB and 1551 OPCAB (Fig. 1). The distribution of pre-operative HbA1c in the study group is listed in Table 1.

Descriptive statistics and results of univariable analyses for demographics and pre-operative factors are listed in Table 2. There was a significant relationship between increasing BMI and elevated HbA1c for both ONCAB and OPCAB groups. There were also significant increases in rates of hypertension as HbA1c levels rose for both surgical techniques. Smoking was more prevalent among ONCAB patients than OPCAB (Table 2).

For each HbA1c grouping, patients who underwent ONCAB surgery had histories with higher rates (mean: 62.8%) of myocardial infarctions when compared to the OPCAB group (mean: 46.4%) For each HbA1c grouping, patients who underwent OPCAB surgery had histories with higher rates (mean: 86.6%) of heart failure when compared to the ONCAB group (mean:

**Table 2** Demographics and pre-operative risk factors

| | ONCAB | | | | | OPCAB | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **≤6.0** | **(6.0, 7.0]** | **(7.0, 8.5]** | **>8.5** | ***p*-value** | **≤6.0** | **(6.0, 7.0]** | **(7.0, 8.5]** | **>8.5** | ***p*-value** |
| | ***n*=467** | ***n*=216** | ***n*=160** | ***n*=166** | | ***n*=758** | ***n*=332** | ***n*=265** | ***n*=196** | |
| **Female** | 104 (22.3%) | 54 (25.0%) | 35 (21.9%) | 58 (34.9%) | 0.0095 | 190 (25.1%) | 94 (28.3%) | 73 (27.5%) | 69 (35.2%) | 0.042 |
| **Age (year)** | 61.6 ± 10.6 | 64.9 ± 9.7 | 63.0 ± 9.2 | 57.6 ± 9.5 | <.0001 | 64.7 ± 10.8 | 64.9 ± 10.5 | 65.0 ± 9.9 | 58.8 ± 9.5 | <.0001 |
| **White** | 352 (77.2%) | 157 (75.1%) | 110 (74.3%) | 105 (66.5%) | 0.0665 | 624 (84.4%) | 250 (78.1%) | 207 (81.5%) | 141 (74.6%) | 0.0058 |
| **Black** | 94 (20.6%) | 47 (22.5%) | 32 (21.6%) | 49 (31.0%) | 0.0601 | 106 (14.3%) | 66 (20.6%) | 39 (15.4%) | 45 (23.8%) | 0.0039 |
| **BMI** | 28.9 ± 5.9 | 31.4 ± 6.5 | 31.9 ± 6.1 | 32.4 ± 8.4 | <.0001 | 28.6 ± 5.6 | 31.3 ± 6.1 | 32.2 ± 6.1 | 32.7 ± 7.1 | <.0001 |
| **History of HTN** | 407 (87.7%) | 202 (93.5%) | 157 (98.1%) | 159 (95.8%) | <.0001 | 659 (86.9%) | 310 (93.4%) | 248 (93.6%) | 186 (94.9%) | <.0001 |
| **History of DM** | 61 (13.1%) | 150 (69.4%) | 159 (99.4%) | 166 (100%) | <.0001 | 101 (13.3%) | 242 (72.9%) | 265 (100%) | 196 (100%) | <.0001 |
| **Current Smoker** | 178 (38.9%) | 58 (27.6%) | 31 (19.7%) | 58 (35.4%) | <.0001 | 179 (25.8%) | 63 (20.2%) | 44 (17.7%) | 41 (22.2%) | 0.0364 |
| **Chronic Lung Disease** | 95 (20.6%) | 37 (17.1%) | 27 (16.9%) | 30 (18.1%) | 0.6195 | 129 (17.1%) | 61 (18.7%) | 45 (17.1%) | 31 (15.8%) | 0.8611 |
| **Pre-Op Cr (mg/dL)** | 1.5 ± 1.9 | 1.3 ± 1.2 | 1.8 ± 2.2 | 1.2 ± 1.0 | 0.0204 | 1.4 ± 1.8 | 1.4 ± 1.5 | 1.3 ± 1.1 | 1.3 ± 1.4 | 0.7675 |
| **History of Dialysis** | 31 (6.6%) | 10 (4.6%) | 10 (6.3%) | 7 (4.2%) | 0.5778 | 33 (4.4%) | 20 (6.0%) | 10 (3.8%) | 10 (5.1%) | 0.5602 |
| **Beta Blocker Use** | 434 (92.9%) | 208 (96.3%) | 158 (98.8%) | 162 (97.6%) | 0.0055 | 708 (93.4%) | 319 (96.1%) | 254 (95.8%) | 192 (98.0%) | 0.0313 |
| **ACEi or ARB Use** | 137 (29.7%) | 62 (29.8%) | 65 (41.7%) | 67 (41.1%) | 0.0044 | 277 (37.1%) | 146 (45.3%) | 117 (45.9%) | 84 (43.5%) | 0.0176 |

Data displayed as n (%) and n ± standard deviation

*BMI* body mass index, *HTN* Hypertension, *DM* Diabetes Mellitus, *Cr* Creatinine, *Pre-op* pre-operative, *ACE* angiotensin converting enzyme inhibitor, *ARB* angiotensin receptor blocker, *ONCAB* on-pump coronary artery bypass grafting, *OPCAB* off-pump coronary artery bypass grafting

71.7%) (Table 3). The ONCAB group had more vessels bypassed than the OPCAB group. Our study reported over 80% of patients in the ONCAB group had three or more vessels bypassed, and the average number of vessels bypassed was 3.2 ± 0.9. On the other hand, only 69% of patients in the OPCAB group had 3 or more vessels bypassed, and the average number of vessels bypassed was 2.7 ± 0.8 (Table 4).

When patients were stratified into four HbA1c subgroups, neither group showed a significant relationship between HbA1c and primary outcomes of operative mortality (ONCAB, $p$=0.76; OPCAB, $p$=0.073) and stroke (ONCAB, $p$=0.79; OPCAB, $p$=0.34). The ONCAB group showed a statistically significant positive relationship between HbA1c levels and rates of readmission ($p$=0.0032) and greater lengths of stay ($p$=0.0021). For OPCAB surgery, there was a statistically significant relationship between rising HbA1c levels and increasing rates of post-operative renal failure ($p$=0.0001), new post-operative dialysis ($p$=0.0001), sternal wound infection ($p$=0.015), and greater lengths of stay ($p$=0.029). A trend was present that showed higher rates of post-operative transfusion, readmission, and longer lengths of stay in the ONCAB group when compared to the OPCAB group as HbA1c levels increased (Table 5).

In addition to examining our outcomes by stratifying patients into four HbA1c subgroups, post-operative outcomes were also analyzed as a subgroup analysis using a HbA1c level of 7.0% as a cutoff point. For ONCAB surgery, a HbA1c >7.0 was significantly associated with increasing rates of new post-operative dialysis ($p$=0.01), readmission rate ($p$=0.0002), and length of stay ($p$=0.002). For OPCAB surgery, a HbA1c >7.0 was associated with increasing rates of operative mortality ($p$=0.04), post-operative renal failure ($p$<0.0001), new post-operative dialysis ($p$<0.0001), sternal wound infection ($p$=0.003), and length of stay ($p$=0.003) (Table 6) (Fig. 2).

Multivariate analysis of outcomes data was also performed to evaluate the effect of HbA1c level on composite adverse events (post-operative renal failure, dialysis, operative mortality, ≥75th percentile length of stay, readmission, sternal wound infection). For the overall study population undergoing either ONCAB or OPCAB surgery, a HbA1c level of 6.851 ($p$=0.0334) was found to be the cutoff point associated with composite adverse events following CABG. For the OPCAB group, a HbA1c level of 5.995 ($p$=0.0277) was found to be the cutoff point associated with composite adverse events. Multivariate analysis for ONCAB surgery revealed no significant relationship between HbA1c level and composite adverse events following surgery.

## Discussion

The goal of this study was to characterize the relationship between increasing HbA1c levels and post-operative outcomes among patients receiving ONCAB versus OPCAB surgery. There have been numerous studies that examined CABG outcomes in the diabetic population. For example, there have been systematic reviews examining the association between HbA1c and outcomes in those undergoing cardiac surgery [10, 13, 14]. Additional studies have also examined this relationship [15, 16]. While these studies did provide valuable insight, they did not examine differences between ONCAB and OPCAB surgical techniques. In other studies such as the systematic review by Wang et al, ONCAB and OPCAB outcomes in the diabetic population were compared, but the effects of elevated HbA1c between the two techniques were not examined (Wang et al, 2017) [17]. To our knowledge, there have not been any studies to date that sought to examine if elevated pre-operative HbA1c levels were associated with differing postoperative outcomes in ONCAB vs OPCAB surgery. Our study explores this relationship, and this may contribute to some of the differences noted between our data and previous research.

When initially examining the primary outcomes of operative mortality and stroke, there was no significant relationship found with increasing levels of HbA1c for either group. However, a positive trend was noted between increasing HbA1c levels and increasing operative mortality in the OPCAB group. Surprisingly, rates of operative mortality decreased as HbA1c levels rose for the ONCAB group. In diabetic patients, there is decreased expression of elastin fibers, arterial stiffening, and increased inflammatory signaling [18, 19]. Unlike ONCAB surgery, OPCAB maintains pulsatile flow through all arteries during the stress of operation. The continuous flow seen in ONCAB surgery has been associated with worse outcomes. For example, in patients with a left ventricular assist device, continuous flow has been shown to lead to microvascular and macrovascular complications secondary to vessel stiffening [20]. Knowing these relationships, we may expect to see worse outcomes in the ONCAB group secondary to high vascular stress. However, our operative mortality results do not support this rationale. We believe this finding may likely reflect that surgeons treating less controlled diabetic patients pursued a longer and more thorough pre-operative optimization to minimize the risk for post-operative complications. Also, it might reflect that there were more patients with moderately increased HbA1c levels who presented in need of urgent or expedited operation, and as such, had an increased profile risk. Similar to cardiovascular disease, we expect uncontrolled diabetes to predispose patients to higher risk of stroke. However,

**Table 3** History of cardiac interventions and cardiac status

| | ONCAB | | | | | OPCAB | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **≤6.0** | **(6.0, 7.0]** | **(7.0, 8.5]** | **>8.5** | ***p*-value** | **≤6.0** | **(6.0, 7.0]** | **(7.0, 8.5]** | **>8.5** | ***p*-value** |
| | ***n*=467** | ***n*=216** | ***n*=160** | ***n*=166** | | ***n*=758** | ***n*=332** | ***n*=265** | ***n*=196** | |
| **History of CVA** | 44 (9.5%) | 22 (10.2%) | 19 (11.9%) | 23 (13.9%) | 0.4301 | 55 (7.3%) | 34 (10.2%) | 24 (9.1%) | 25 (12.8%) | 0.0763 |
| **History of PCI** | 174 (37.3%) | 75 (34.7%) | 62 (38.8%) | 71 (42.8%) | 0.4349 | 216 (28.5%) | 111 (33.4%) | 84 (31.7%) | 69 (35.2%) | 0.1852 |
| **History of MI** | 300 (64.5%) | 125 (58.4%) | 88 (55.0%) | 121 (73.3%) | 0.0025 | 330 (43.7%) | 140 (42.4%) | 116 (43.8%) | 109 (55.6%) | 0.0146 |
| **History of Heart Failure** | 221 (70.2%) | 122 (72.2%) | 87 (73.7%) | 84 (70.6%) | 0.8883 | 327 (85.6%) | 173 (84.8%) | 136 (89.5%) | 101 (86.3%) | 0.6106 |
| **Number of Diseased Vessels: 1** | 17 (3.6%) | 4 (1.9%) | 4 (2.5%) | 2 (1.2%) | 0.3066 | 43 (5.7%) | 18 (5.4%) | 7 (2.7%) | 9 (4.6%) | 0.2613 |
| **Number of Diseased Vessels: 2** | 90 (19.3%) | 36 (16.7%) | 20 (12.5%) | 32 (19.3%) | 0.242 | 158 (20.8%) | 59 (17.8%) | 50 (18.9%) | 25 (12.8%) | 0.0723 |
| **Number of Diseased Vessels: 3** | 360 (77.1%) | 175 (81.4%) | 136 (85.0%) | 132 (79.5%) | 0.1629 | 555 (73.2%) | 255 (76.8%) | 207 (78.4%) | 161 (82.1%) | 0.0415 |
| **LM Stenosis ≥ 50%** | 149 (53.2%) | 81 (57.9%) | 45 (51.1%) | 42 (47.7%) | 0.4883 | 237 (53.5%) | 110 (58.8%) | 81 (54.7%) | 41 (40.2%) | 0.0238 |
| **Ejection Fraction (%)** | 51.4 ± 12.1 | 52.1 ± 11.8 | 50.3 ± 12.4 | 50.3 ± 13.2 | 0.37 | 52.5 ± 12.3 | 50.8 ± 13.1 | 51.4 ± 12.6 | 48.7 ± 14.0 | 0.0024 |
| **STS Risk Score for Mortality** | 2.0 ± 2.5 | 2.8 ± 4.1 | 2.7 ± 3.8 | 2.1 ± 3.0 | 0.0048 | 1.8 ± 2.1 | 2.2 ± 3.0 | 2.0 ± 2.7 | 2.0 ± 2.6 | 0.0916 |

Data displayed as n (%) and n ± standard deviation

*CVA* cerebrovascular accident, *PCI* percutaneous coronary intervention, *MI* myocardial infarction, *LM* left main, *STS* Society of Thoracic Surgeons, *ONCAB* on-pump coronary artery bypass grafting, *OPCAB* off-pump coronary artery bypass grafting

**Table 4** Operative details

| | ONCAB | | | | | OPCAB | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **≤6.0** | **(6.0, 7.0]** | **(7.0, 8.5]** | **>8.5** | ***p*-value** | **≤6.0** | **(6.0, 7.0]** | **(7.0, 8.5]** | **>8.5** | ***p*-value** |
| | ***n*=467** | ***n*=216** | ***n*=160** | ***n*=166** | | ***n*=758** | ***n*=332** | ***n*=265** | ***n*=196** | |
| **Number of CAB Vessels** | 3.1 ± 0.9 | 3.1 ± 0.8 | 3.3 ± 0.8 | 3.3 ± 0.9 | 0.0062 | 2.7 ± 0.8 | 2.7 ± 0.8 | 2.8 ± 0.7 | 2.8 ± 0.7 | 0.4839 |
| **Cardiopulmonary Bypass Time (minutes)** | 87.6 ± 29.9 | 87.7 ± 27.1 | 91.4 ± 32.3 | 92.0 ± 25.6 | 0.2288 | NA | NA | NA | NA | NA |
| **Cross Clamp Time (minutes)** | 58.8 ± 21.9 | 60.2 ± 21.2 | 62.5 ± 23.6 | 64.5 ± 20.9 | 0.0217 | NA | NA | NA | NA | NA |
| **Lowest Intra-Op Hematocrit** | 25.0 ± 4.4 | 24.6 ± 4.7 | 24.4 ± 4.9 | 24.7 ± 4.5 | 0.3986 | 30.4 ± 5.8 | 29.6 ± 5.7 | 29.9 ± 5.9 | 29.9 ± 5.9 | 0.2093 |
| **Intraoperative Transfusion** | 172 (36.9%) | 90 (41.9%) | 66 (41.3%) | 82 (49.4%) | 0.0437 | 110 (14.6%) | 69 (20.8%) | 37 (14.2%) | 21 (10.9%) | 0.0113 |
| **Intraoperative Use of IABP** | 106 (24.3%) | 43 (21.9%) | 41 (27.7%) | 48 (30.4%) | 0.2586 | 123 (17.4%) | 56 (18.9%) | 41 (16.5%) | 31 (16.7%) | 0.8842 |

Data displayed as n (%) and n ± standard deviation

*CAB* coronary artery bypass, *intra-op* intra-operative, *IABP* intra-aortic balloon pump, *ONCAB* on-pump coronary artery bypass grafting, *OPCAB* off-pump coronary artery bypass grafting

**Table 5** Post-operative outcomes in ONCAB and OPCAB surgery

| | **ONCAB** | | | | | **OPCAB** | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **≤6.0** | **(6.0, 7.0]** | **(7.0, 8.5]** | **>8.5** | ***p*-value** | **≤6.0** | **(6.0, 7.0]** | **(7.0, 8.5]** | **>8.5** | ***p*-value** |
| | ***n*=467** | ***n*=216** | ***n*=160** | ***n*=166** | | ***n*=758** | ***n*=332** | ***n*=265** | ***n*=196** | |
| **Primary Outcomes** | | | | | | | | | | |
| **Operative Mortality** | 6 (1.3%) | 4 (1.9%) | 2 (1.3%) | 1 (0.6%) | 0.7613 | 6 (0.8%) | 7 (2.1%) | 6 (2.3%) | 6 (3.1%) | 0.0726 |
| **Stroke** | 3 (0.6%) | 1 (0.5%) | 0 (0.0%) | 1 (0.6%) | 0.7906 | 7 (0.9%) | 3 (0.9%) | 1 (0.4%) | 4 (2.0%) | 0.3407 |
| **Secondary Outcomes** | | | | | | | | | | |
| **Post-Op Renal Failure** | 4 (0.9%) | 6 (2.8%) | 4 (2.5%) | 4 (2.4%) | 0.2261 | 10 (1.3%) | 2 (0.6%) | 13 (4.9%) | 9 (4.6%) | 0.0001 |
| **New Post-Op Dialysis** | 1 (0.2%) | 2 (0.9%) | 4 (2.5%) | 3 (1.8%) | 0.0521 | 5 (0.7%) | 1 (0.3%) | 10 (3.8%) | 6 (3.1%) | 0.0001 |
| **Sternal Wound Inf.** | 8 (1.9%) | 4 (2.1%) | 3 (2.1%) | 7 (4.5%) | 0.3265 | 7 (1.0%) | 6 (2.1%) | 8 (3.3%) | 8 (4.4%) | 0.0145 |
| **Reop Due to Bleeding** | 6 (1.3%) | 5 (2.3%) | 0 (0.0%) | 3 (1.8%) | 0.2772 | 14 (1.8%) | 3 (0.9%) | 4 (1.5%) | 1 (0.5%) | 0.424 |
| **Post-Op Transfusion** | 172 (36.8%) | 89 (41.2%) | 74 (46.3%) | 59 (35.5%) | 0.1255 | 244 (32.2%) | 111 (33.4%) | 84 (31.7%) | 55 (28.1%) | 0.6318 |
| **Readmission Rate** | 48 (10.7%) | 21 (10.0%) | 30 (19.5%) | 30 (18.6%) | 0.0032 | 74 (10.1%) | 40 (12.8%) | 26 (10.2%) | 29 (15.9%) | 0.1231 |
| **Length of Stay (days)** | 6.3 ± 3.6 | 6.9 ± 4.1 | 7.0 ± 4.3 | 8.3 ± 11.1 | 0.0021 | 5.7 ± 3.4 | 5.9 ± 3.4 | 6.7 ± 9.3 | 6.8 ± 9.8 | 0.0293 |

Data displayed as n (%) and n ± standard deviation

*Post-op* post-operative, *Inf* infection, *Reop* reoperation, *ONCAB* on-pump coronary artery bypass grafting, *OPCAB* off-pump coronary artery bypass grafting

strokes in CABG patients can be multifactorial and may result from various sources such as emboli, thrombosis, or hypoperfusion [21]. In our patient population, there was no significant association between stroke and rising HbA1c, and this may be secondary to this multifactorial nature.

The data showed a statistically significant relationship between increasing HbA1c levels and the secondary outcomes of higher readmission rates and greater lengths of stay for the ONCAB group. For OPCAB surgery, there was a statistically significant relationship between increasing HbA1c and post-operative renal failure, new post-operative dialysis, sternal wound infection, and greater lengths of stay. When we ran our analysis using the HbA1c cutoff of 7.0%, a commonly used cutoff in the literature, we found additional significant relationships between HbA1c level and post-operative outcomes. For ONCAB surgery, we found there to be a significant relationship between higher HbA1c level and new post-operative dialysis. For OPCAB surgery, we found there to be a significant relationship between higher HbA1c level and operative mortality. A trend was seen for both variables when stratifying patients into four HbA1c groups, but the analysis was not sufficiently powered in these cases. In regard to new post-operative renal failure and dialysis, it is well known that diabetic patients are at increased risk of developing renal dysfunction [22]. In addition, patients undergoing CABG procedures have previously been shown to be at risk for acute kidney injury and failure [23]. Diabetic patients also have impaired wound healing, which increases their risk for sternal wound infection [24]. Overall, data shown in this study suggests that increasing levels of preoperative HbA1c are positively correlated with the prevalence of multiple adverse outcomes, particularly in OPCAB (5 of 9) compared to ONCAB (3 of 9). The specific adverse outcomes that showed positive relationship with HbA1c differed between the two groups. This variance shows that the two surgical approaches are not equally impacted by increasing HbA1c levels.

There have been conflicting reports in the literature as to what outcomes are significantly impacted by high HbA1c levels. A systematic review by Zheng et al examining the clinical implications of HbA1c in diabetic patients undergoing CABG found that elevated HbA1c levels were significantly associated with increased all-cause mortality, stroke, and MI [13]. They also found no significant relationship between elevated HbA1c levels and renal failure in this population [13]. Our results contrast these data. Our data show no significant relationship between increased HbA1c and stroke in both ONCAB and OPCAB groups. We did find that there was a statistically significant increase in operative mortality as HbA1c levels rose in the OPCAB group, but this relationship was not seen for ONCAB surgery. We also found there to be a significant relationship between increasing HbA1c levels and post-operative renal failure in the OPCAB group and new-post operative dialysis for both groups. A separate systematic review by Wang et al observed that higher pre-operative HbA1c levels in diabetic patients were associated with increased risk of surgical site infections, renal failure, myocardial infarction, and increase lengths of stay in diabetic patients, but they found no

**Table 6** Post-Operative Outcomes in ONCAB and OPCAB Surgery

| | ONCAB | | | OPCAB | | |
|---|---|---|---|---|---|---|
| | ≤ 7.0 | >7.0 | *p*-value | ≤ 7.0 | >7.0 | *p*-value |
| | *n*=683 | *n*=326 | | *n*=1090 | *n*=461 | |
| **Primary Outcomes** | | | | | | |
| **Operative Mortality** | 10 (1.5%) | 3 (0.9%) | 0.4683 | 13 (1.2%) | 12 (2.6%) | 0.0435 |
| **Stroke** | 4 (0.6%) | 1 (0.3%) | 0.5552 | 10 (0.9%) | 5 (1.1%) | 0.7585 |
| **Secondary Outcomes** | | | | | | |
| **Post-Op Renal Failure** | 10 (1.5%) | 8 (2.5%) | 0.2666 | 12 (1.1%) | 22 (4.8%) | <0.0001 |
| **New Post-Op Dialysis** | 3 (0.4%) | 7 (2.1%) | 0.0104 | 6 (0.6%) | 16 (3.5%) | <0.0001 |
| **Sternal Wound Inf.** | 12 (1.9%) | 10 (3.3%) | 0.1945 | 13 (1.3%) | 16 (3.7%) | 0.0031 |
| **Reop Due to Bleeding** | 11 (1.6%) | 3 (0.9%) | 0.3807 | 17 (1.6%) | 5 (1.1%) | 0.4696 |
| **Post-Op Transfusion** | 261 (38.2%) | 133 (40.8%) | 0.4314 | 355 (32.6%) | 139 (30.2%) | 0.3504 |
| **Readmission Rate** | 69 (10.5%) | 60 (19.0%) | 0.0002 | 114 (10.9%) | 55 (12.6%) | 0.3531 |
| **Length of Stay (days)** | 6.5 ± 3.8 | 7.7 ± 8.5 | 0.002 | 5.8 ± 3.4 | 6.7 ± 9.5 | 0.003 |

Data displayed as n (%) and n ± standard deviation

*Post-op* post-operative, *Inf* infection, *Reop* reoperation, *ONCAB* on-pump coronary artery bypass grafting, *OPCAB* off-pump coronary artery bypass grafting

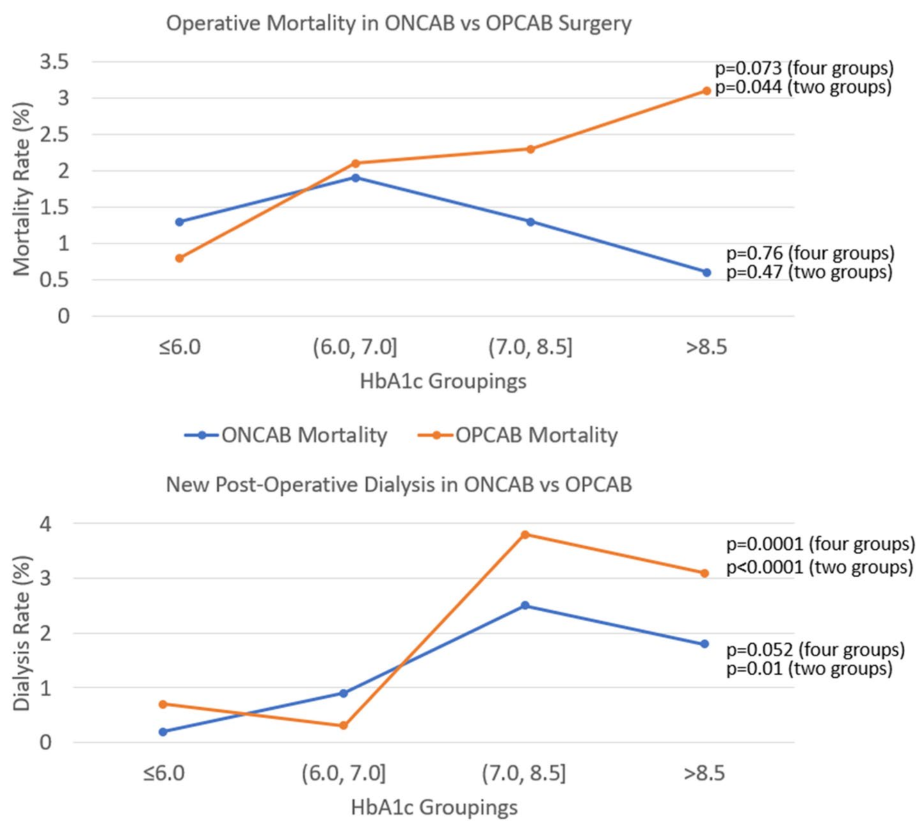


**Fig. 2** Post-operative outcomes when stratifying by two and four HbA1c groupings. HbA1c, hemoglobin A1c; ONCAB, on-pump coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass grafting. The top graphic represents operative mortality for both surgical techniques. The bottom graphic represents new post-operative dialysis for both surgical techniques. For these outcomes, *p*-values are present from the analysis of each using both four HbA1c groups (Table 5) and two HbA1c groups (Table 6). For operative mortality, OPCAB surgery showed a positive trend that was shown to be significant when using two HbA1c groups for analysis. For new post-operative dialysis, ONCAB surgery showed a positive trend that was shown to be significant when using two HbA1c groups for analysis

significant association between elevated HbA1c levels in diabetic patients and increased risk of mortality or stroke [10]. Our study shows a similar relationship between increasing HbA1c levels and rates of sternal wound infection and renal failure in the OPCAB group as well as increased lengths of stay for both surgical techniques. Despite showing a positive trend between rates of sternal wound infection and preoperative HbA1c in patients undergoing ONCAB, our study was not sufficiently powered to suggest a significant positive correlation between the two. Additional studies have also been completed that compared ONCAB vs OPCAB surgery outcomes in diabetic patient populations [12, 17]. In a systematic review by Wang et al, it was found that in a diabetic population OPCAB surgery significantly reduces the incidences of post-operative stroke and bleeding complications, but it found no differences regarding mortality, myocardial infarction, and renal failure between the two techniques [17]. Our own data showed a similar trend for decreased need for post-operative transfusion in the OPCAB group but did not find a significant decrease in incidence of post-operative stroke when compared to the ONCAB group.

In studies evaluating the effects of elevated HbA1c on CABG outcomes, a HbA1c level of 7.0% is commonly used [25–28]. This distinction is often used due to its relevance as a major diagnostic criterion for diagnosis of diabetes mellitus (DM). However, the pathological manifestations of DM are not binary. The scalar nature of HbA1c provides more granularity beyond the diagnostic cutoff for DM, and it could prove useful as part of a risk score in clinical and operative decision making. Multivariate analysis of our own data demonstrated an increased risk of composite adverse outcomes at an HbA1c cutoff of 6.85% ($p$=0.03), approximately the same as the widely used 7.0%. However, we see a markedly lower cutoff, 5.995% ($p$=0.03) in patients undergoing OPCAB surgery. Other studies have demonstrated increasing rates of sternal wound infection as well as increased severity of infection with incremental increase of HbA1c above 5.5% [29]. The EPIC-Norfolk study illustrated a continuous relationship between all cardiovascular mortality and HbA1c >5%, suggesting the cutoff for concerning HbA1c may be lower than other arbitrary cutoffs may suggest [30]. As has been discussed above, there is not uniformity in the results that have been obtained thus far on the effects of elevated HbA1c on CABG outcomes. The studies referenced above used the values of either 6.5% or 7.0% for their HbA1c cutoffs. This, along with data showing that the cutoff for elevated HbA1c and its associated adverse effects may be lower than commonly used, may contribute to discrepancies in the conclusions that have been reached thus far.

This study is not without limitations. Due to its retrospective design, this study is subject to selection and recall bias. Additionally, the patient population examined in this study may be less generalizable to the general population. Our institution is a tertiary care center that commonly sees patients with numerous comorbidities and may be sicker than those that are seen in other parts of the country or at institutions that would ordinally refer out complex patients. In both the ONCAB and OPCAB groups, around 30% of the patients had a HbA1c level over 7.0%, and half of those patients had a HbA1c over 8.5%. Confounding could have contributed to the results we found as well, and this will be addressed going forward through propensity score matching for ONCAB and OPCAB surgery. Post-discharge diabetes control data for the patients were not examined in this study, and accounting for this information in future studies will be valuable in understanding the long-term impact of HbA1c levels on outcomes.

## Conclusions

Our study demonstrates that elevated levels of HbA1c are significantly associated with increasing rates of numerous adverse patient outcomes in both ONCAB and OPCAB surgery.

For our primary outcomes of operative mortality and stroke, a significant relationship was only found between elevated HbA1c and operative mortality in the OPCAB group. We also observed differences in which secondary outcomes were most impacted by elevated HbA1c levels between the two surgical techniques. A significant relationship was noted between high HbA1c levels and new post-operative dialysis, rates of readmission, and greater lengths of stay for ONCAB surgery. For OPCAB surgery, there was a significant relationship between elevated HbA1c and post-operative renal failure, new post-operative dialysis, sternal wound infection, and greater lengths of stay. Our data suggest a threshold other than the diagnostic criterion for DM at which perioperative risk ought to be considered beyond standard precaution. Our data offer novel insight into complications to be considered in the diabetic population with discrete HbA1c cutoffs. Furthermore, by stratifying into OPCAB and ONCAB, our study offers evidence to suggest a propensity for different complications between the two. However, a multi-institutional or a randomized study would add more evidence to this hypothesis.

**Abbreviations**

| | |
|---|---|
| CAD | Coronary Artery Disease |
| CABG | Coronary Artery Bypass Graft |
| HbA1c | Hemoglobin A1c |
| CPB | Cardiopulmonary Bypass |
| ONCAB | On-Pump Coronary Artery Bypass Graft |

| | |
|---|---|
| OPCAB | Off-Pump Coronary Artery Bypass Graft |
| STS | Society of Thoracic Surgeons |
| IRB | Institutional Review Board |
| ACSD | Adult Cardiac Surgery Database |
| DM | Diabetes Mellitus |

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**Authors' contributions**
BC conducted a review of the current literature, aided in data collection, reviewed trends in data, and led manuscript writing. LW reviewed current literature, reviewed trends in data, and participated in manuscript writing. KD also reviewed current literature, reviewed trends in data, and participated in manuscript writing. RX planned and conducted data collection, data analysis, and participated in manuscript writing. KC also planned and conducted data collection, data analysis, and participated in manuscript review. JD helped formulate study design and manuscript completion. PV served as senior author and oversaw all aspects of the project.

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**Availability of data and materials**
The datasets analyzed during the current study are not publicly available due to it being gathered from our institutional Society of Thoracic Surgeons (STS) database.

## Declarations

**Ethics approval and consent to participate**
We received institutional review board (IRB) approval for this retrospective study, and informed consent was waived due to the nature of the study.

**Consent for publication**
Not applicable.

**Competing interests**
The authors have no relevant disclosures or competing interests.

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