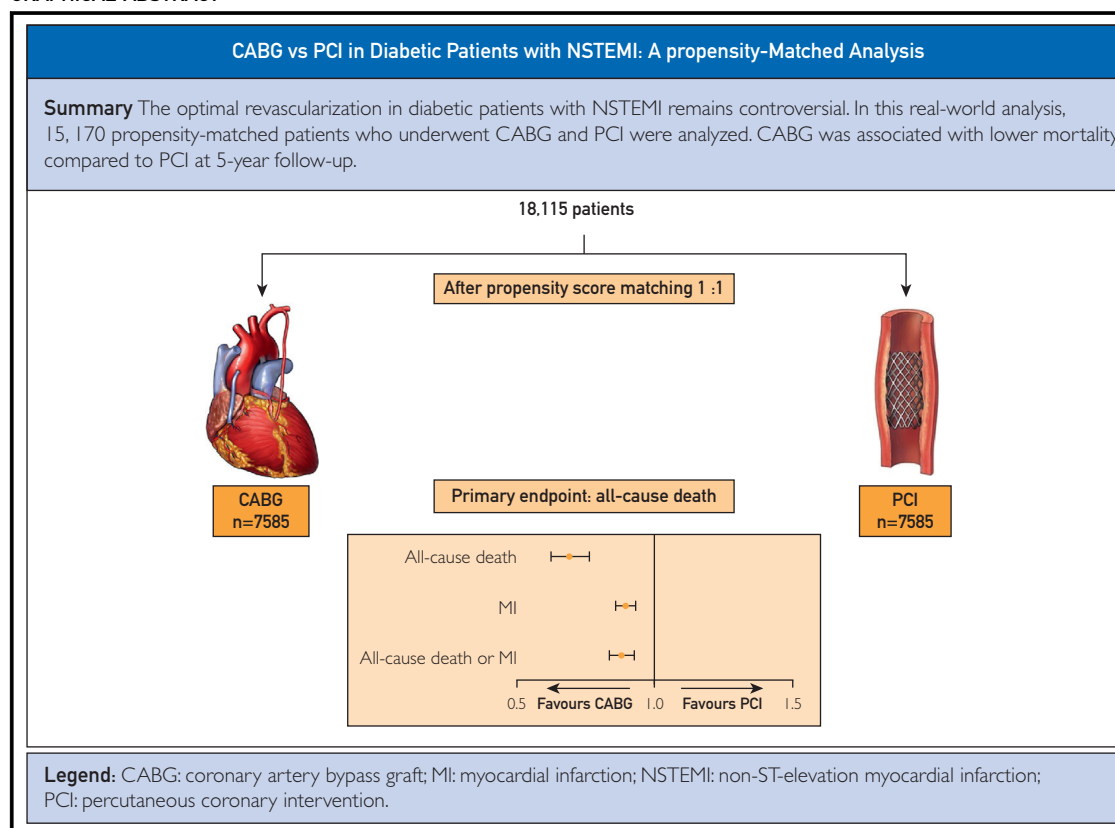


Revascularization in Diabetic Patients With Non—ST-Elevation Acute Myocardial Infarction

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GRAPHICAL ABSTRACT



Abstract

Objective: To compare the outcomes of diabetic patients hospitalized with non—ST-elevation myocardial infarction (NSTEMI) referred for coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI) in a real-world evidence population.

Patients and Methods: This study assessed major cardiovascular outcomes in diabetic patients who underwent myocardial revascularization, using data obtained on July 24, 2024, from TriNetX, a global health research network. Patients with diabetes mellitus and NSTEMI were identified using the International Classification of Diseases, Tenth Revision, diagnosis code. Main outcome measure was 5-year all-cause mortality. Proportional hazards regression and propensity score matching were used to adjust outcomes for key patients.

Results: A total of 18,115 patients with a mean age of 62.2 (SD, 8.98) years and a mean glycated hemoglobin A1c of 7.66% (SD, 2.18%) were included, of whom 8206 (45.3%) underwent CABG and 9909 (54.7%) underwent PCI. During the 5-year follow-up, 2275 (12.5%) deaths were recorded in all cohort. Propensity matching yielded a 1:1 match consisting of 7585 patients in each group (CABG vs PCI); CABG was associated with significantly lower all-cause mortality over 5 years of follow-up (10.6% vs 17.9%; hazard ratio, 0.685; 95% CI, 0.618-0.759; $P<.0001$). Myocardial infarction occurred more frequently in the PCI cohort (48.6% vs 43.3%; $P<.0001$). Additional coronary revascularization was higher for PCI patients at 5 years (14.5% vs 1.72%; $P=.0229$).

Conclusion: In this real-world study of diabetic patients with NSTEMI, CABG was associated with a lower rate of all-cause mortality at 5 years when compared with PCI.

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The global burden of diabetes mellitus (DM) has escalated sharply, affecting over 476 million people worldwide and significantly contributing to morbidity and mortality.¹ Diabetes mellitus is a well-established risk factor for coronary artery disease (CAD), with 37% of patients with acute coronary syndrome (ACS) also diagnosed with DM.² These individuals exhibit more complex atherosclerotic lesions and worse outcomes after myocardial infarction (MI) and revascularization.^{3,4} Compared with patients without diabetes, diabetic patients have higher prevalence of lipid-rich plaques (58.9% vs 44.9%) and thin-cap fibroatheroma (17.2% vs 6.3%) in nonculprit lesions, correlating with adverse cardiovascular events.^{5,6}

For revascularization, coronary artery bypass graft (CABG) is preferred over percutaneous coronary intervention (PCI) in stable CAD among diabetic patients.⁷ However, in ACS, especially in the setting of ST-segment MI, primary PCI is the treatment of choice when feasible. In non—ST-segment elevation ACS (NSTEMI-ACS), the optimal strategy remains unclear. Although observational studies suggest CABG may offer superior long-term outcomes for patients with DM and multivessel CAD (MV-CAD) and

NSTEMI-ACS,⁸⁻¹¹ large-scale randomized controlled trials (RCTs) are lacking. This study aimed to compare CABG and PCI in a real-world cohort of diabetic patients with non—ST-elevation MI (NSTEMI) and MV-CAD (graphical abstract).

PATIENTS AND METHODS

Data Source

The data used in this study were collected on July 24, 2024, from the TriNetX Network, which provided access to electronic medical records (diagnoses, procedures, medications, laboratory values, and genomic information) from approximately 130 million patients from 127 health care organizations. This network comprises aggregate deidentified data and statistical summaries from participating health care organizations worldwide. This ensures that users of the platform do not have access to any protected health information or personal data. Access to the data is available through the TriNetX research network at <https://live.trinetx.com>.

Study Population

We used the TriNetX database to identify patients aged 18 years or older with a diagnosis of DM and NSTEMI, as defined by the

International Classification of Diseases, Tenth Revision codes E08 to E14 and I21.4, respectively. Patients who had undergone either CABG or PCI within the past 5 years were selected for analysis (TriNetX code 1021150). The index date for each patient was set as the date of the CABG or PCI procedure. All comorbidity diagnoses, including DM (E08-E13) and old MI (I21.4), were considered before the procedure based on the sequence of records in the electronic medical chart and the time interval preceding the index date.

However, using administrative databases carries the risk of temporal misclassification.¹² To mitigate this risk, we carefully reviewed the coded records in relation to the timeline of clinical events, ensuring that comorbidity codes were recorded before the procedure date. Furthermore, additional clinical data, including medication prescriptions and laboratory test results, were used to corroborate diagnoses of previous MI or diabetes before revascularization.

Patients with severe heart failure, classified as New York Heart Association class III or IV, and those with a history of valve operation, malignancy, acute infections, single-vessel CAD, ST-elevation MI, or cardiogenic shock were excluded.

The primary outcome was all-cause mortality at 5 years. Secondary outcomes included MI, stroke, and repeat revascularization. Outcomes were identified using International Classification of Diseases, Tenth Revision codes: MI: I21.x (acute MI); stroke: I63.x (cerebral infarction) and I64.x (stroke, not specified as hemorrhagic or ischemic); and additional revascularization: identified through procedure codes that include both percutaneous and surgical revascularization. Mortality data were extracted directly from TriNetX. To provide a clear and clinically relevant summary of the survival data comparing CABG and PCI, we applied the restricted mean survival time method to report the effects of interventions.

COVARIATES

We captured demographic variations, comorbidities, and medication consumption as covariates from electronic medical records that could be potential confounding variables. These include age, sex, race (White or Black),

overweight or obese, hypertension, left ventricular ejection fraction, previous stroke or MI, hypercholesterolemia, diabetes, current smoking, aspirin, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, β -blockers, and lipid-lowering medication. These variables were used to model the propensity score matching analysis.

Statistical Analyses

Baseline characteristics between the 2 groups were compared using the χ^2 test of independence for categorical variables and independent samples *t* test for continuous variables, where appropriate. Propensity score matching was used to balance the cohorts. Kaplan-Meier analysis was performed to estimate the survival probability for all-cause mortality and other outcomes from 1 day up to 5 years postprocedurally. Comparisons between the CABG and PCI cohorts were made using the log-rank test. Cox proportional hazards regression was used to calculate hazard ratios (HRs) with 95% CIs for the primary and secondary outcomes. The proportional hazard assumption was tested using Schoenfeld residuals, and in cases where this assumption was violated, stratified models or time-dependent covariates were used. In all analyses, statistical significance was set at a 2-sided *P* value of $<.05$. All statistical analyses were performed using Python version 3.7 (scikit-learn package) and R version 3.6.1 (survival package for Kaplan-Meier analysis and Cox regression).

Propensity Score Estimation and Overlap Assessment

In this study, we used propensity score matching to balance the baseline characteristics between patients undergoing CABG and PCI. Propensity scores were estimated using logistic regression, where the treatment assignment (CABG vs PCI) was modeled as a function of key covariates, including age, sex, comorbidities (hypertension, diabetes, hypercholesterolemia, and chronic kidney disease), and clinical variables such as glycated hemoglobin A1c and left ventricular ejection fraction. The logistic regression was used to estimate the probability of each patient receiving either CABG or PCI based on their baseline characteristics.

To ensure the validity of the matching process, we assessed common support (or overlap)

between the propensity score distributions of the 2 groups. Overlap was evaluated by visual inspection of propensity score histograms and density plots for both groups, ensuring that the scores for CABG and PCI patients shared a significant region of overlap, thus indicating that the propensity score model adequately balanced the treatment groups. Patients falling outside the region of common support were excluded from the analysis to avoid biased comparisons between unmatched groups.

We further assessed the balance of baseline characteristics between the groups by calculating the standardized mean differences (SMDs) for each covariate. A SMD below 0.1 for each covariate was considered indicative of good balance.¹³ Postmatching diagnostics confirmed that the matching process effectively reduced the imbalance between the groups.

Ethical Considerations

This retrospective study was exempt from informed consent, using deidentified data per Health Insurance Portability and Accountability Act Privacy Rule (Section §164.514[a]).

RESULTS

Baseline Characteristics

A total of 18,115 individuals with DM, NSTEMI, and MV-CAD were included in the time-dependent analysis. After propensity score matching, the final cohorts consisted of 7585 patients in both the CABG and PCI groups, ensuring balanced comparison between the 2 revascularization strategies. Table 1 details the baseline characteristics of the cohorts, both before and after propensity score matching.

The mean age of the overall population was 62.2 years, with males comprising 66% of the participants. The prevalence of key cardiovascular risk factors was high, reflecting the complexity of the patient population. Approximately 28% of patients in the matched cohort had hypertension, whereas 5% had a history of MI, and 6% were diagnosed with chronic kidney disease. Notably, 21% of patients were on cholesterol-lowering medications, and 19% were receiving antiplatelet therapy.

Before propensity score matching, there were significant differences between the CABG and PCI groups in several key characteristics, including age, the prevalence

of hypertension, and the use of cholesterol-lowering medications ($P<.0001$). However, after matching, these variables were well-balanced across both cohorts, with SMDs <0.1 for all major covariates, indicating a high degree of comparability between the 2 groups.

Primary and Secondary Outcomes

Over the 5-year follow-up period, all-cause mortality occurred in 582 patients (10.6%) in the CABG group and in 978 patients (17.9%) in the PCI group, reflecting a significantly lower risk of mortality in the CABG group (HR, 0.68; 95% CI, 0.62-0.76; log-rank test, $P<.0001$) (Table 2 and Figure 1). Additionally, we found that the 30-day mortality rate for CABG was 1.33%, and for PCI, it was 2.24% (HR, 0.59; 95% CI, 0.46-0.76; long-rank test, $P<.0001$).

The restricted mean survival time for the CABG group was 4.45 years, whereas for the PCI group it was 4.33 years, resulting in a difference of 0.12 years, with the CABG group showing a slightly longer average survival time. These results suggest that, on average, patients in the CABG group experienced 0.12 more years of event-free survival (free from MI, stroke, or revascularization) over the 5-year period compared with those in the PCI group.

In addition to lower all-cause mortality, the incidence of MI and the need for subsequent coronary revascularization were significantly lower in the CABG group compared with that in the PCI group. The incidence of MI was 43.3% in the CABG group and 48.6% in the PCI group, corresponding to a 10.1% relative reduction in MI risk with CABG (HR, 0.89; 95% CI, 0.85-0.93; $P<.0001$). Similarly, the need for additional coronary revascularization was dramatically lower in the CABG group, occurring in only 1.72% of patients compared with 14.5% in the PCI group (HR, 0.12; 95% CI, 0.09-0.15; $P=.0036$), demonstrating an 88% reduction in repeat interventions (Table 2 and Figure 1).

Stroke rates were similar between the groups, with no significant difference observed (9.5% vs 10.9%; HR, 0.97; 95% CI, 0.86-1.11; $P=.5434$), suggesting that the higher incidence of stroke historically associated with CABG may no longer be a major differentiating factor in this population (Table 2 and Figure 1). At 30

TABLE 1. Baseline Characteristics of Study Participants Before and After Propensity Score Matching

Characteristic	Before matching			After matching		
	CABG(n=8206)	PCI(n=9909)	SMD	CABG(n=7585)	PCI(n=7585)	SMD
Race, n (%)						
White	5916 (72.1)	6480 (65.4)	0.145	5158 (68.0)	5195 (68.5)	0.010
Unknown	952 (11.6)	1258 (12.7)	0.033	872 (11.5)	880 (11.6)	0.003
Black or African American	648 (7.9)	1288 (13.0)	0.167	731 (9.64)	748 (9.87)	0.007
Others	706 (8.6)	921 (9.3)	0.024	661 (8.72)	667 (8.8)	0.002
Male, n (%)	5654 (68.9)	6312 (63.7)	0.110	5158 (68.0)	5196 (68.5)	0.010
Age (y), mean (SD)	67.3 (8.82)	68.2 (8.71)	0.102	61.8 (8.85)	61.8 (8.71)	0.000
Hypertension, n (%)	6515 (79.4)	7322 (73.9)	0.130	6265 (82.6)	6197 (81.7)	0.023
Hypercholesterolemia, n (%)	6318 (77.0)	6520 (65.8)	0.249	5802 (76.5)	5734 (75.6)	0.021
Previous MI, n (%)	1912 (23.3)	2844 (28.7)	0.123	2237 (29.5)	2192 (28.9)	0.013
CKD, n (%)	2626 (32.0)	3062 (30.9)	0.023	2715 (35.8)	2669 (35.2)	0.012
Heart failure, n (%)	2174 (26.5)	1744 (17.6)	0.216	1729 (22.8)	1790 (23.6)	0.019
AF or flutter, n (%)	2396 (29.2)	1516 (15.3)	0.339	1653 (21.8)	1646 (21.7)	0.002
PVD, n (%)	1247 (15.2)	1684 (17.0)	0.049	1418 (18.7)	1395 (18.4)	0.007
Stroke, n (%)	509 (6.2)	584 (5.9)	0.012	554 (7.3)	523 (6.9)	0.015
Overweight or obesity, n (%)	3496 (42.6)	3418 (34.5)	0.167	3178 (41.9)	3140 (41.4)	0.010
Smoking, n (%)	2174 (26.5)	2655 (26.8)	0.006	2108 (27.8)	2063 (27.2)	0.013
COPD, n (%)	1206 (14.7)	1605 (16.2)	0.041	1244 (16.4)	1259 (16.6)	0.005
Medications, n (%)						
β-blockers	7139 (87.0)	6817 (68.8)	0.449	6402 (84.4)	6364 (83.9)	0.013
Antilipemic agents	7590 (92.5)	7154 (72.2)	0.552	6804 (89.7)	6728 (88.7)	0.032
ACE inhibitors	3651 (44.5)	4191 (42.3)	0.044	3709 (48.9)	3625 (47.8)	0.022
Hypoglycemic agents	3569 (43.5)	3537 (35.7)	0.160	3307 (43.6)	3284 (43.3)	0.006
Insulin	6581 (80.2)	5281 (53.3)	0.596	5529 (72.9)	5499 (72.5)	0.009
Platelet aggregation inhibitors	7484 (91.2)	7184 (72.5)	0.500	6690 (88.2)	6652 (87.7)	0.01
BMI (kg/m ²), mean (SD)	32.0 (6.52)	31.4 (7.1)	0.088	31.2 (6.52)	31.4 (7.1)	0.029
Glucose (mg/dL), mean (SD)	154 (73.1)	143 (68.1)	0.155	153 (72.2)	145 (68.6)	0.113
Creatinine (mg/dL), mean (SD)	1.5 (2.1)	1.69 (2.04)	0.092	1.62 (2.42)	1.74 (2.06)	0.053
Total cholesterol (mg/dL), mean (SD)	184 (52.4)	178 (51.4)	0.115	182 (57.7)	180 (53.1)	0.036
LDL-C (mg/dL), mean (SD)	106 (43.9)	99.8 (42.9)	0.143	104 (46.3)	101 (42.7)	0.067
HDL-C (mg/dL), mean (SD)	38.3 (14.1)	39.3 (14.3)	0.070	38.7 (14.2)	38.8 (14.2)	0.007
Triglycerides (mg/dL), mean (SD)	195 (179)	196 (170)	0.005	195 (179)	196 (170)	0.005
Hemoglobin A1c (%), mean (SD)	7.72 (2.40)	7.49 (2.14)	0.101	7.77 (2.48)	7.55 (2.20)	0.094
LVEF (%), mean (SD)	51.3 (13.7)	51.5 (15.4)	0.013	51.3 (14.1)	51.0 (15.6)	0.020

ACE, angiotensin-converting enzyme; AF, atrial fibrillation; BMI, body mass index; CABG, coronary artery bypass graft; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; SMD, standardized mean difference.

days, however, the rate of stroke was 0.45% after PCI and 1.27% after CABG (HR, 0.41; 95% CI, 0.29-0.67; $P < .001$), indicating a higher early stroke risk with CABG.

The subgroup analysis (Figure 2) reported a consistent trend toward an increased risk of mortality with PCI across all key subgroups

analyzed, including patients with varying degrees of left ventricular function, the presence or absence of chronic kidney disease, and other comorbidities. Notably, PCI was associated with a higher mortality risk even in traditionally lower-risk subgroups, emphasizing the robustness of the findings favoring CABG.

TABLE 2. Clinical Outcomes After PCI or CABG at 5-Year Follow-up

Outcomes	CABG, n (%)	PCI, n (%)	HR (95% CI)	P
Primary end point	582 (10.6)	978 (17.9)	0.68 (0.62-0.76)	<.0001
MI	2321 (43.3)	2608 (48.6)	0.89 (0.85-0.93)	<.0001
All-cause death or MI	2702 (48.9)	3146 (56.9)	0.87 (0.83-0.92)	<.0001
Stroke	520 (9.5)	594 (10.9)	0.97 (0.86-1.09)	.5634
Additional coronary revascularization	95 (1.72)	803 (14.5)	0.12 (0.09-0.15)	.0229

CABG, coronary artery bypass graft; HR, hazard ratio; MI, myocardial infarction; PCI, percutaneous coronary intervention.

DISCUSSION

Our study provides robust evidence that, in patients with DM, MV-CAD, and NSTEMI, CABG is associated with significantly lower mortality compared with PCI over a 5-year follow-up. Our findings align with a growing body of literature that consistently shows the superiority of CABG over PCI in patients with DM and stable CAD.^{7,14-16} However, this study extends that understanding to the real-world setting of ACSs, specifically NSTEMI-ACS, demonstrating that CABG also confers a survival advantage in patients with NSTEMI, DM, and MV-CAD.

Several studies have previously highlighted the benefits of CABG in diabetic patients with stable CAD, yet few have focused on this population in the context of NSTEMI-ACS.⁸⁻¹¹ Our results are consistent with a meta-analysis of 8 trials involving 3612 patients, which reported a lower all-cause mortality rate at the 5-year follow-up for patients treated with CABG compared with that in those treated with PCI.¹⁶ Similarly, other studies suggest that CABG is associated with lower long-term mortality in patients with MV-CAD and NSTEMI-ACS.^{10,17,18} These findings are further supported by a meta-analysis of 3 RCTs, which found that CABG reduced the risk of a composite primary end point—encompassing all-cause mortality, MI, and stroke—when compared with PCI.¹⁹

Our study's inclusion of patients with more complex comorbidities, such as heart failure (20%), previous MI (30%), renal dysfunction (35%), and chronic obstructive pulmonary disease (16%), reflects the broader patient population likely to be encountered in real-world clinical settings. This diversity enhances the external validity of our findings, making them more applicable to everyday

practice, especially given the limitations of traditional RCTs, which may not always reflect the complexities of routine clinical care.

Despite strong evidence favoring CABG, current guidelines recommend an early invasive strategy for all patients with DM and ACS.^{20,21} However, real-world data indicate that diabetic patients, particularly those with NSTEMI, are less likely to receive invasive treatment, including CABG.²²⁻²⁴ Several factors contribute to this underutilization, including the presence of diffuse coronary disease, cerebrovascular conditions, and renal comorbidities, which increase surgical risk and complicate decision-making.²⁵ Nevertheless, our findings underscore the importance of considering surgical revascularization for reducing both mortality and MI in this high-risk population, even when invasive treatments may be underused.

For patients without MV-CAD, PCI remains a straightforward and effective revascularization option, particularly in single-vessel disease. However, in diabetic patients, the complexity and diffuse nature of coronary lesions often make CABG a more appropriate choice. Percutaneous coronary intervention primarily targets the most significant lesions, potentially leaving untreated plaques that could contribute to future adverse events. This is particularly concerning in the context of the heightened inflammatory state seen in ACS, which may further drive the progression of untreated plaques.²⁶ This may help explain why patients with ACS who undergo CABG experience fewer recurrent cardiovascular events.

In clinical practice, selecting the optimal revascularization strategy for diabetic patients with MV-CAD and NSTEMI involves a multifactorial approach, considering the patient's

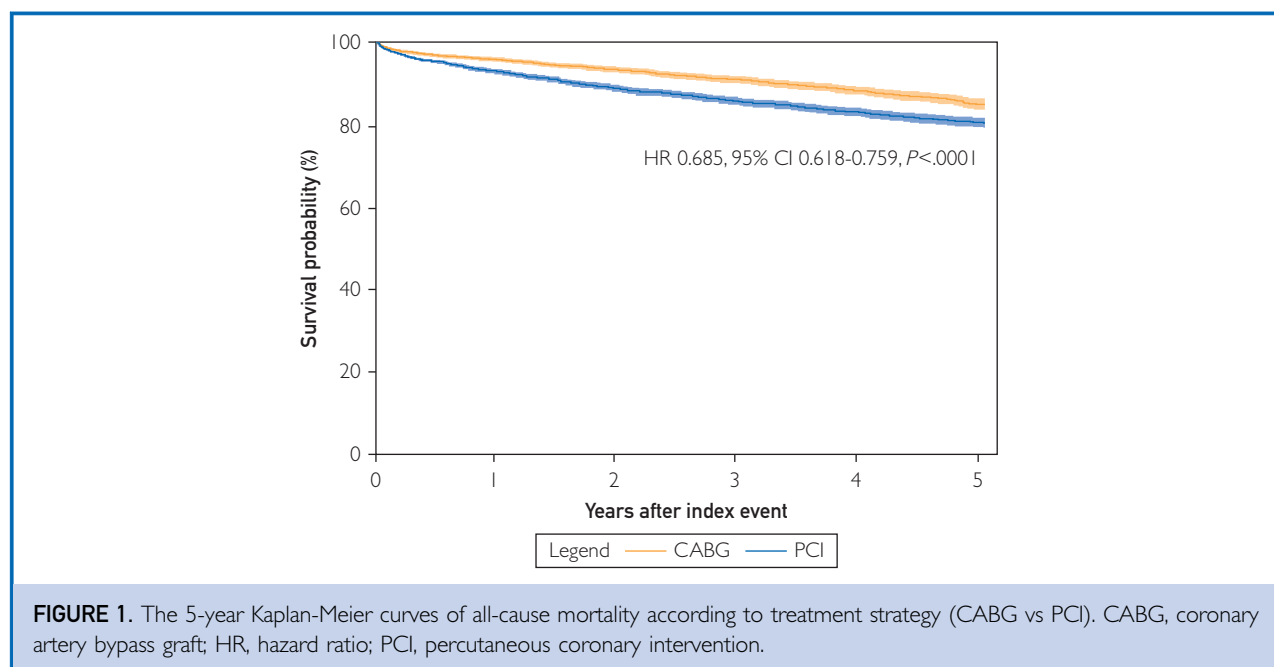


FIGURE 1. The 5-year Kaplan-Meier curves of all-cause mortality according to treatment strategy (CABG vs PCI). CABG, coronary artery bypass graft; HR, hazard ratio; PCI, percutaneous coronary intervention.

clinical status, infection risk, and the presence of comorbidities that could increase surgical risk. These variables introduce potential bias, which we sought to mitigate through propensity score matching, balancing baseline characteristics between the groups.

Interestingly, although previous studies have highlighted an increased risk of stroke after CABG in patients with MV-CAD and DM,²⁷ our findings suggest comparable stroke rates between CABG and PCI, further supporting the safety of CABG in this context. Additionally, we observed a significantly higher long-term rate of MI in the PCI group, reinforcing the role of CABG in providing more durable protection against recurrent ischemic events.

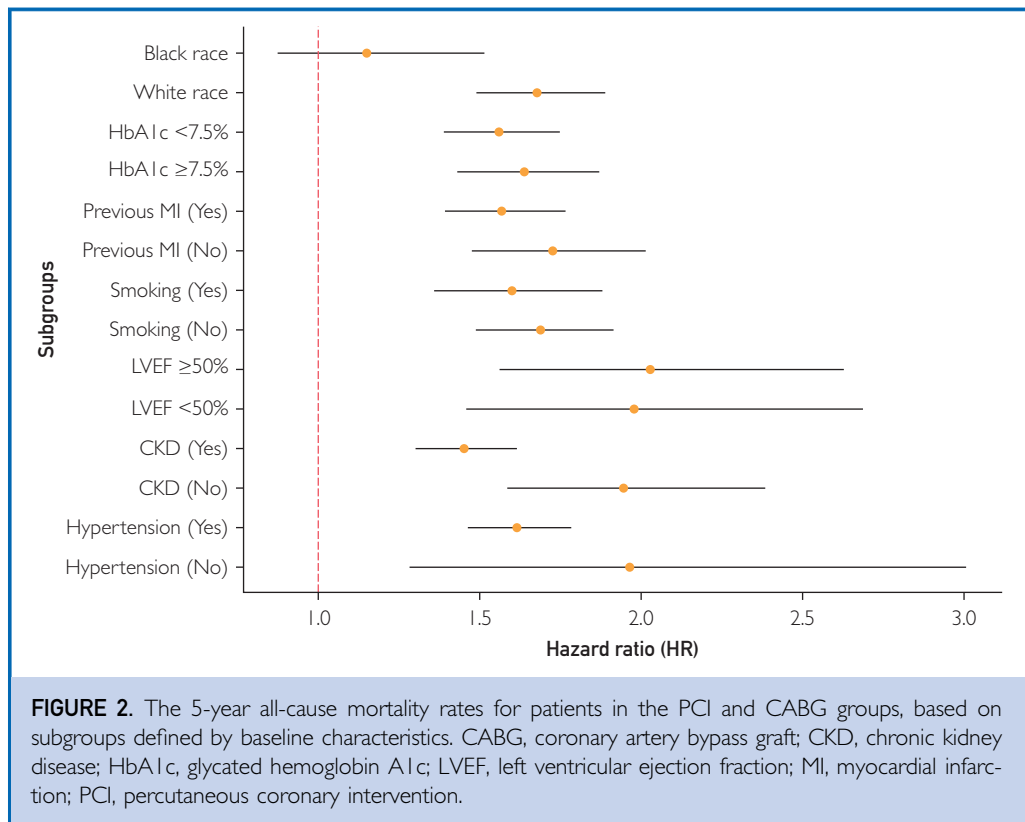
Limitations

Our study has several limitations that should be acknowledged. First, as an observational study, it cannot fully eliminate the potential for residual or unmeasured confounding, even with the use of propensity score matching. Although this method helped balance baseline characteristics between the CABG and PCI groups, it is possible that important confounders—such as the complexity of coronary anatomy or frailty—were not captured in the data set, potentially influencing the results.

This selection bias could contribute to the higher rates of long-term mortality, MI, and revascularization observed in the PCI group. Observational studies like ours have the advantage of reflecting real-world clinical practice, but they inherently cannot establish causal relationships or infer direct causality.

Second, the use of all-cause mortality as the primary outcome of the study is a point that deserves attention. Although an important outcome, all-cause mortality does not necessarily reflect the direct benefit of the intervention (CABG or PCI). Other factors, such as comorbidities and noncardiac causes of death, may have influenced mortality, making it difficult to assess the specific impact of treatments. This limitation suggests that additional end points, such as cardiovascular-specific mortality, major adverse cardiovascular events, or functional status, should be considered in future studies to better understand the impact of revascularization strategies in this population.

Third, angiographic characteristics, including detailed coronary anatomy and lesion complexity, were not consistently available for all patients. As a result, we were unable to analyze which specific coronary territories were affected or to categorize patients according to their SYNTAX scores.



This limitation is significant because SYNTAX scoring provides valuable information for risk stratification and decision-making regarding the optimal revascularization strategy, particularly in patients with MV-CAD. Furthermore, we do not have information on the number of grafts and type of conduits used in the cohort of patients undergoing CABG, nor on the number of stents placed in each patient.

Fourth, the use of International Classification of Diseases codes to identify patients and outcomes introduces the potential for misclassification bias. Although International Classification of Diseases codes are widely used for epidemiologic studies, they are not always accurate in capturing clinical diagnoses, which may have led to the inclusion of patients with varying severity of CAD or inaccurately recorded comorbidities.

Fifth, database-based events are often underreported. This means that some adverse events may not have been recorded in electronic health records, which may have affected the accuracy of the study results. Although our data set integrates information from multiple

health care institutions, limitations in event reporting could have led to an underestimation of certain clinical outcomes. This issue is particularly relevant for events occurring outside the hospital setting, such as late MI, repeat revascularization, or cause-specific mortality.

Sixth, clustered standard errors are a robust method for Cox analysis within propensity score-matched groups. However, because of the nature of the TriNetX database, which provides aggregated and anonymized data, we do not have access to individual patient identifiers or detailed pair-level information. This limitation prevented us from applying clustered standard errors because this method requires knowledge of the dependency structure between matched pairs, which was not available in our data set.

Seventh, the low initial mortality observed in our study may be explained by limitations inherent to the TriNetX database, which aggregates electronic health records from various institutions and may not fully capture fatal events occurring outside the network

hospitals, potentially underestimating early mortality. Additionally, recent advances in perioperative management and possible selection bias favoring lower-risk patients for revascularization could contribute to this finding. Compared with studies like the Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial, where higher early mortality was reported, these differences reflect variations in the studied population and procedural settings. Although this limitation should be acknowledged, it does not compromise the validity of our analysis.

Finally, our study's generalizability may be limited to the health care settings and populations represented in the data. The findings are based on patients treated in specific institutions, and practice patterns, patient characteristics, and health care resources may differ in other regions or health care systems. This could impact the applicability of our results to broader populations or settings with different levels of access to CABG or PCI.

Despite these limitations, our study contributes valuable evidence supporting CABG as the optimal revascularization strategy for patients with DM, MV-CAD, and NSTEMI. The use of real-world data enhances the relevance of our findings, particularly for clinical decision-making in everyday practice.

CONCLUSION

This study reported that CABG significantly reduces 5-year mortality compared with PCI in real-world patients with DM, NSTEMI, and MV-CAD. To refine future guidelines, further RCTs are needed.

POTENTIAL COMPETING INTERESTS

The authors report no competing interests.

ETHICS STATEMENT

This retrospective study was exempt from informed consent, using deidentified data per Health Insurance Portability and Accountability Act Privacy Rule (Section §164.514[a]).

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Abbreviations and Acronyms: ACS, acute coronary syndrome; CABG, coronary artery bypass graft; CAD, coronary artery disease; DM, diabetes mellitus; HR, hazard ratio; MI, myocardial infarction; MV-CAD, multivessel coronary artery disease; NSTEMI, non-ST-segment elevation acute coronary syndrome; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; RCT, randomized controlled trial; SMD, standardized mean difference

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REFERENCES

1. Lin X, Xu Y, Pan X, et al. Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. *Sci Rep*. 2020;10(1):14790. <https://doi.org/10.1038/s41598-020-71908-9>.
2. Zhou M, Liu J, Hao Y, et al. Prevalence and in-hospital outcomes of diabetes among patients with acute coronary syndrome in China: findings from the Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome Project. *Cardiovasc Diabetol*. 2018;17(1):147. <https://doi.org/10.1186/s12933-018-0793-x>.
3. Creager MA, Lüscher TF, Cosentino F, Beckman JA. Diabetes and vascular disease: pathophysiology, clinical consequences, and medical therapy: part I. *Circulation*. 2003;108(12):1527-1532. <https://doi.org/10.1161/01.CIR.0000091257.27563.32>.
4. Sanchís J, Bertomeu González V, Bodí V, et al. [Invasive strategy in patients with advanced diabetes and non-ST-segment elevation acute coronary syndrome. Angiographic findings and clinical follow-up. PREDICAR study results]. *Rev Esp Cardiol*. 2006; 59(4):321-328. <https://doi.org/10.1157/13087054>.
5. Bouisset F, Bataille V, Schiele F, et al. Type 2 diabetes mellitus in acute myocardial infarction: a persistent significant burden on long-term mortality. *Front Cardiovasc Med*. 2024;11:1401569. <https://doi.org/10.3389/fcvm.2024.1401569>.
6. Sugiyama T, Yamamoto E, Bryniarski K, et al. Coronary plaque characteristics in patients with diabetes mellitus who presented with acute coronary syndromes. *J Am Heart Assoc*. 2018;7(14): e009245. <https://doi.org/10.1161/JAHA.118.009245>.
7. Farkouh ME, Domanski M, Sleeper LA, et al. Strategies for multivessel revascularization in patients with diabetes. *N Engl J Med*. 2012;367(25):2375-2384. <https://doi.org/10.1056/NEJMoa1211585>.
8. Ram E, Fisman EZ, Tenenbaum A, et al. Revascularization outcomes in diabetic patients presenting with acute coronary syndrome with non-ST elevation. *Cardiovasc Diabetol*. 2022;21(1): 175. <https://doi.org/10.1186/s12933-022-01595-5>.
9. Ramanathan K, Abel JG, Park JE, et al. Surgical versus percutaneous coronary revascularization in patients with diabetes and acute coronary syndromes. *J Am Coll Cardiol*. 2017; 70(24):2995-3006. <https://doi.org/10.1016/j.jacc.2017.10.029>.
10. Jia S, Zhang C, Jiang L, et al. Comparison of percutaneous coronary intervention, coronary artery bypass grafting and medical therapy in non-ST elevation acute coronary syndrome patients

- with 3-vessel disease. *Circ J*. 2020;84(10):1718-1727. <https://doi.org/10.1253/circj.CJ-20-0300>.
11. Ben-Gal Y, Mohr R, Feit F, et al. Surgical versus percutaneous coronary revascularization for multivessel disease in diabetic patients with non-ST-segment-elevation acute coronary syndrome: analysis from the Acute Catheterization and Early Intervention Triage Strategy trial. *Circ Cardiovasc Interv*. 2015; 8(6):e002032. <https://doi.org/10.1161/CIRCINTERVENTIONS.114.002032>.
 12. Mack MJ, Herbert M, Prince S, Dewey TM, Magee MJ, Edgerton JR. Does reporting of coronary artery bypass grafting from administrative databases accurately reflect actual clinical outcomes? *J Thorac Cardiovasc Surg*. 2005;129(6):1309-1317. <https://doi.org/10.1016/j.jtcvs.2004.10.036>.
 13. Garrido MM, Kelley AS, Paris J, et al. Methods for constructing and assessing propensity scores. *Health Serv Res*. 2014;49(5):1701-1720. <https://doi.org/10.1111/1475-6773.12182>.
 14. BARI 2D Study Group, Frye RL, August P, et al. A randomized trial of therapies for type 2 diabetes and coronary artery disease. *N Engl J Med*. 2009;360(24):2503-2515. <https://doi.org/10.1056/NEJMoa0805796>.
 15. Kappetein AP, Head SJ, Morice MC, et al. Treatment of complex coronary artery disease in patients with diabetes: 5-year results comparing outcomes of bypass surgery and percutaneous coronary intervention in the SYNTAX trial. *Eur J Cardiothorac Surg*. 2013;43(5):1006-1013. <https://doi.org/10.1093/ejcts/ezt017>.
 16. Verma S, Farkouh ME, Yanagawa B, et al. Comparison of coronary artery bypass surgery and percutaneous coronary intervention in patients with diabetes: a meta-analysis of randomised controlled trials. *Lancet Diabetes Endocrinol*. 2013;1(4):317-328. [https://doi.org/10.1016/S2213-8587\(13\)70089-5](https://doi.org/10.1016/S2213-8587(13)70089-5).
 17. Widmer RJ, Hammonds K, Mixon T, et al. Acute coronary syndrome revascularization strategies with multivessel coronary artery disease. *Am J Cardiol*. 2024;220:33-38. <https://doi.org/10.1016/j.amjcard.2024.04.003>.
 18. Ram E, Sternik L, Klempfner R, et al. Outcomes of different revascularization strategies among patients presenting with acute coronary syndromes without ST elevation. *J Thorac Cardiovasc Surg*. 2020;160(4):926-935.e6. <https://doi.org/10.1016/j.jtcvs.2019.08.130>.
 19. Chang M, Lee CW, Ahn JM, et al. Comparison of outcome of coronary artery bypass grafting versus drug-eluting stent implantation for non-ST-elevation acute coronary syndrome. *Am J Cardiol*. 2017;120(3):380-386. <https://doi.org/10.1016/j.amjcard.2017.04.038>.
 20. Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur Heart J*. 2023;44(38):3720-3826. <https://doi.org/10.1093/eurheartj/ehad191>.
 21. Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI guideline for coronary artery revascularization: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145(3):e4-e17. <https://doi.org/10.1161/CIR.0000000000001039>.
 22. Mahmoud AN, Elgendy IY, Mansoor H, et al. Early invasive strategy and in-hospital survival among diabetics with non-ST-elevation acute coronary syndromes: a contemporary national insight. *J Am Heart Assoc*. 2017;6(3):e005369. <https://doi.org/10.1161/JAHA.116.005369>.
 23. Elbarouni B, Ismael N, Yan RT, et al. Temporal changes in the management and outcome of Canadian diabetic patients hospitalized for non-ST-elevation acute coronary syndromes. *Am Heart J*. 2011;162(2):347-355.e1. <https://doi.org/10.1016/j.ahj.2011.05.020>.
 24. Gustafsson I, Hvelplund A, Hansen KW, et al. Underuse of an invasive strategy for patients with diabetes with acute coronary syndrome: a nationwide study. *Open Heart*. 2015;2(1):e000165. <https://doi.org/10.1136/openhrt-2014-000165>.
 25. Pandey A, McGuire DK, de Lemos JA, et al. Revascularization trends in patients with diabetes mellitus and multivessel coronary artery disease presenting with non-ST elevation myocardial infarction: insights from the National Cardiovascular Data Registry Acute Coronary Treatment and Intervention Outcomes Network Registry-Get with the Guidelines (NCDR ACTION Registry-GWTG). *Circ Cardiovasc Qual Outcomes*. 2016;9(3):197-205. <https://doi.org/10.1161/CIRCOUTCOMES.115.002084>.
 26. Godoy LC, Rao V, Farkouh ME. Coronary revascularization of patients with diabetes mellitus in the setting of acute coronary syndromes. *Circulation*. 2019;140(15):1233-1235. <https://doi.org/10.1161/CIRCULATIONAHA.119.040683>.
 27. Head SJ, Milojevic M, Daemen J, et al. Stroke rates following surgical versus percutaneous coronary revascularization. *J Am Coll Cardiol*. 2018;72(4):386-398. <https://doi.org/10.1016/j.jacc.2018.04.071>.