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# Association of Diabetes Mellitus and Its Types with In-Hospital Management and Outcomes of Patients with Acute Myocardial Infarction

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ABSTRACT

*Background:* Diabetes mellitus (DM) is an important risk factor for adverse outcomes following acute myocardial infarction (AMI), but large-scale studies investigating the differential impact of Type 1 DM (T1DM) and Type 2 DM (T2DM) on AMI outcomes are lacking.
*Methods:* All adult discharges for AMI in the National Inpatient Sample (October 2015 to December 2018) were included and stratified into T1DM, T2DM and non-DM (NDM) groups. Outcomes of interests were all-cause mortality, major adverse cardiovascular and cerebrovascular events (MACCE), major bleeding and acute ischemic stroke, as well as invasive management. Binomial hierarchical multilevel multivariable logistic regression with adjusted odds ratios (aOR) and 95 % confidence intervals (95 % CI) was used to investigate the association between DM and its subtypes with the AMI outcomes.
*Results:* Out of 2,587,615 patients, there were 29,250 (1.1 %) T1DM and 1,032,925 (39.9 %) T2DM patients. After multivariable adjustment, patients with T1DM had increased odds of MACCE (aOR 1.20, 95 % CI 1.09–1.31), all-cause mortality (aOR 1.20, 95 % CI 1.08–1.33) and major bleeding (aOR 1.28, 95 % CI 1.13–1.44), whilst T2DM patients had increased odds of MACCE (aOR 1.03, 95 % CI 1.01–1.05) and ischemic stroke (aOR 1.09, 95 % CI 1.05–1.13), compared to NDM patients. The adjusted odds of receiving percutaneous coronary intervention were lower in both T1DM and T2DM patients (aOR 0.70, 95 % CI 0.66–0.75 and aOR 0.95, 95 % CI 0.94–0.96, respectively), but T2DM patients showed higher utilization of composite percutaneous and surgical revascularization (aOR 1.03, 95 % CI 1.03–1.04) compared to NDM patients.
*Conclusions:* DM patients presenting with AMI have worse in-hospital clinical outcomes compared to NDM patients. There are important DM type-related differences with T1DM patients having overall worse outcomes and receiving less overall revascularization.


## 1. Introduction

Diabetes mellitus (DM) is the most prevalent cardiometabolic disease, with an estimated prevalence of 700 million by 2045 [1]. DM is an important risk factor for the development of coronary artery disease (CAD), a leading cause of mortality in both type 1 DM (T1DM) and type 2 DM (T2DM) [2,3]. Systemic inflammation and metabolic abnormalities predispose these patients to vascular dysfunction resulting in an increased risk of acute myocardial infarction (AMI) [4]. DM is an independent predictor of worse outcomes in AMI patients both in the short- and long-term [5,6]. Whilst numerous factors including DM itself, vascular complications [7], and more extensive CAD [8] contribute to worse outcomes, there is under-utilization of coronary

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angiography and percutaneous coronary intervention (PCI) among patients with diabetes presenting with AMI [6,9]. Furthermore, DM patients undergoing PCI with contemporary drug-eluting stents have worse angiographic and clinical outcomes compared to patients without diabetes [10].

There is limited data around the differential impact of T1DM and T2DM on revascularization strategies and outcomes following AMI. Most studies to date have investigated AMI outcomes in the overall DM population, with no distinction between T1DM and T2DM [5,11–14]. It is unknown whether management and clinical outcomes of patients

**Table 1**
Patient characteristics according to the presence of diabetes mellitus.

| Characteristics | Non-DM (59.0 %) | Type 1 DM (1.1 %) | Type 2 DM (39.9 %) | *P*-value[a] | *P*-value[b] | Standardized differences | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | Non-DM vs. type 1 DM | Non-DM vs. type 2 DM | Type 2 DM vs. type 1 DM |
| Number of discharges | 1,525,440 | 29,250 | 1,032,925 | | | | | |
| Age (years), median (IQR) | 69 (58, 81) | 59 (49, 69) | 69 (60, 78) | <0.001 | <0.001 | 0.680 | −0.034 | 0.771 |
| Female sex, % | 40.6 | 48.3 | 42.0 | <0.001 | <0.001 | −0.156 | −0.028 | −0.129 |
| Race, % | | | | <0.001 | <0.001 | | | |
| White | 78.3 | 79.9 | 68.5 | | | −0.054 | 0.182 | −0.239 |
| Black | 11.0 | 10.8 | 14.5 | | | 0.014 | −0.097 | 0.083 |
| Hispanic | 5.9 | 5.8 | 10.1 | | | 0.007 | −0.198 | 0.197 |
| Other | 4.8 | 3.5 | 6.9 | | | 0.059 | −0.082 | 0.099 |
| STEMI, % | 24.4 | 15.4 | 17.1 | <0.001 | <0.001 | 0.228 | 0.180 | 0.048 |
| Weekend admission, % | 26.8 | 26.1 | 26.2 | <0.001 | 0.549 | 0.017 | 0.014 | 0.004 |
| Primary expected payer, % | | | | <0.001 | <0.001 | | | |
| Medicare | 59.8 | 56.4 | 66.9 | | | 0.008 | −0.139 | 0.135 |
| Medicaid | 9.1 | 14.0 | 9.4 | | | −0.096 | −0.012 | −0.099 |
| Private Insurance | 23.6 | 24.0 | 17.9 | | | −0.002 | 0.036 | −0.041 |
| Self-pay | 4.4 | 3.2 | 3.1 | | | 0.013 | 0.058 | −0.002 |
| No charge | 0.4 | 0.3 | 0.3 | | | 0.001 | 0.001 | 0.001 |
| Other | 2.5 | 2.1 | 2.4 | | | 0.002 | 0.001 | 0.011 |
| Median Household Income (percentile), % | | | | <0.001 | <0.001 | 0.005 | 0.110 | −0.105 |
| 0-25th | 29.9 | 29.8 | 34.1 | | | | – | |
| 26th–50th | 27.4 | 27.4 | 27.7 | | | | – | |
| 51st-75th | 23.6 | 24.4 | 22.3 | | | – | | – |
| 76th–100th | 19.2 | 18.4 | 15.9 | | | | | – |
| Cardiogenic shock, % | 5.7 | 6.5 | 5.8 | <0.001 | <0.001 | −0.031 | −0.004 | −0.027 |
| Cardiac arrest, % | 4.0 | 4.5 | 3.7 | <0.001 | <0.001 | −0.029 | 0.015 | −0.043 |
| Ventricular tachycardia, % | 7.0 | 5.0 | 5.6 | <0.001 | <0.001 | 0.084 | 0.059 | 0.026 |
| Ventricular fibrillation, % | 3.2 | 1.8 | 2.2 | <0.001 | <0.001 | 0.090 | 0.065 | 0.024 |
| Comorbidities, % | | | | | | | | |
| Atrial fibrillation | 18.7 | 12.6 | 19.8 | <0.001 | <0.001 | 0.169 | −0.027 | 0.197 |
| Dyslipidaemia | 54.7 | 63.5 | 69.6 | <0.001 | <0.001 | −0.181 | −0.311 | 0.128 |
| Thrombocytopenia | 6.4 | 6.5 | 6.7 | <0.001 | 0.481 | −0.007 | −0.011 | 0.004 |
| Smoking | 2.0 | 1.3 | 1.4 | <0.001 | 0.202 | 0.054 | 0.047 | 0.008 |
| Previous AMI | 12.9 | 19.1 | 17.3 | <0.001 | 0.202 | −0.171 | −0.124 | −0.047 |
| History of IHD | 66.0 | 73.3 | 75.5 | <0.001 | <0.001 | −0.158 | −0.210 | 0.052 |
| Previous PCI | 13.7 | 19.2 | 19.8 | <0.001 | 0.007 | −0.147 | −0.163 | 0.016 |
| Previous CABG | 18.3 | 27.6 | 28.1 | <0.001 | 0.059 | −0.224 | −0.235 | 0.011 |
| Previous CVA | 7.3 | 9.3 | 10.1 | <0.001 | <0.001 | −0.072 | −0.101 | 0.029 |
| Anaemias | 20.4 | 37.2 | 29.5 | <0.001 | <0.001 | −0.377 | −0.211 | −0.163 |
| Heart failure | 34.5 | 43.9 | 48.3 | <0.001 | <0.001 | −0.194 | −0.283 | 0.089 |
| Valvular disease | 10.2 | 8.1 | 10.6 | <0.001 | <0.001 | 0.073 | −0.013 | 0.086 |
| Hypertension | 44.3 | 27.8 | 38.5 | <0.001 | <0.001 | 0.350 | 0.117 | 0.230 |
| Peripheral vascular disorders | 8.7 | 11.4 | 10.2 | <0.001 | <0.001 | −0.089 | −0.053 | −0.036 |
| Chronic pulmonary disease | 24.6 | 18.8 | 26.0 | <0.001 | <0.001 | 0.141 | −0.033 | 0.174 |
| Coagulopathy | 8.8 | 8.8 | 8.7 | 0.005 | 0.279 | −0.002 | 0.004 | −0.006 |
| Dementia | 8.2 | 4.3 | 7.6 | <0.001 | <0.001 | 0.158 | 0.019 | 0.139 |
| Liver disease | 3.0 | 2.8 | 3.4 | <0.001 | <0.001 | 0.010 | −0.026 | 0.036 |
| Chronic renal failure | 19.7 | 49.7 | 39.3 | <0.001 | <0.001 | −0.664 | −0.440 | −0.210 |
| Dependence on dialysis | 1.4 | 11.5 | 5.6 | <0.001 | <0.001 | −0.825 | −0.621 | −0.396 |
| Metastatic cancer | 2.0 | 0.8 | 1.3 | <0.001 | <0.001 | 0.103 | 0.054 | 0.051 |
| Bed size of hospital, % | | | | <0.001 | <0.001 | | | |
| Small | 17.3 | 16.4 | 17.2 | | | 0.046 | 0.006 | 0.040 |
| Medium | 30.0 | 28.5 | 30.0 | | | 0.014 | 0.001 | 0.012 |
| Large | 52.6 | 55.1 | 52.9 | | | −0.039 | −0.004 | −0.028 |
| Hospital Region, % | | | | <0.001 | <0.001 | | | |
| Northeast | 21.8 | 22.1 | 20.7 | | | −0.056 | 0.026 | −0.081 |
| Midwest | 23.6 | 27.8 | 23.4 | | | −0.043 | 0.004 | −0.009 |
| South | 40.5 | 36.4 | 41.6 | | | 0.086 | −0.011 | 0.018 |
| West | 14.1 | 13.6 | 14.3 | | | 0.021 | −0.005 | 0.011 |
| Location/teaching status of hospital, % | | | | <0.001 | <0.001 | | | |
| Rural | 8.4 | 7.1 | 8.2 | | | 0.088 | 0.014 | 0.073 |
| Urban non-teaching | 24.8 | 21.8 | 24.2 | | | 0.061 | 0.008 | 0.035 |
| Urban teaching | 66.8 | 71.1 | 67.6 | | | −0.044 | −0.013 | −0.086 |

Abbreviations: AMI – Acute Myocardial Infarction; CABG – Coronary Artery Bypass Graft; CVA – Cerebrovascular Accidents; DM – Diabetes Mellitus; IHD – Ischemic Heart Disease; IQR – Interquartile Range; PCI – Percutaneous Coronary Intervention; STEMI – ST-elevation Myocardial Infarction.

[a] Comparison of no diabetes mellitus vs. type 1 diabetes mellitus vs. type 2 diabetes mellitus groups.

[b] Comparison of type 1 diabetes mellitus vs. type 2 diabetes mellitus groups.

with AMI differs in relation to DM type, in line with the inherent differences in aetiology and pathophysiology [15]. Using the National Inpatient Sample (NIS), this study aimed to investigate the association of both DM types with the management strategies and in-hospital clinical outcomes among AMI population, compared to patients without DM.

## 2. Methods

The NIS contains anonymized data from >7 million discharges each year and is the largest publicly available all-payer inpatient care database in the United States (US). It is part of a family of databases developed for the Healthcare Cost and Utilization Project (HCUP) and is sponsored by the Agency for Healthcare Research and Quality (AHRQ) [16]. It includes data from community hospitals (excluding rehabilitation or long-term acute care hospitals) and is designed to produce national representative estimates of inpatient utilization, access, charges, quality, and outcomes in the US.

All adult discharges with a primary discharge diagnosis of AMI between October 2015 to December 2018 were identified and stratified by the presence of DM into 3 groups: no diabetes mellitus (NDM), T1DM and T2DM. This study period was used to achieve data granularity with the utilization of International Classification Diseases, Tenth revision (ICD-10) codes. Sensitivity analyses were conducted based on the type of AMI, stratifying the patients into ST-Elevation Myocardial Infarction (STEMI) and Non-ST Elevation Myocardial Infarction (NSTEMI). Finally, cases with primary diagnosis of unstable angina (ICD-10 codes: I20.0, I24.0, I24.9, I25.110, I25.700, I25.710, I25.720, I25.730, I25.750, I25.760, I25.790) were not included in the study.

Patient comorbidities, procedures and clinical outcomes were identified by using ICD-10 codes (Supplementary Table 1). A total of 212,465 cases were excluded due to missing data in the original dataset. In addition, elective admissions ($n = 163{,}900$) were also excluded (Supplementary Fig. 1). To allow for estimation of national averages, analyses was weighted by the discharge weights provided, as advised by HCUP [16]. The manuscript was reported according to the *Strengthening The Reporting of OBservational Studies in Epidemiology (STROBE)* guidelines (Appendix A).

Study outcomes were defined as clinical outcomes and invasive management during the in-hospital period. The main in-hospital clinical outcomes included all-cause mortality, major adverse cardiovascular and cerebrovascular events (MACCE), major bleeding, and ischemic stroke. MACCE was defined as a composite of all-cause mortality, acute ischemic stroke and reinfarction, to follow the traditional definition of 3-point MACCE. Major bleeding included subarachnoid haemorrhage, intracerebral haemorrhage, intracranial haemorrhage, gastrointestinal haemorrhage, and haemoptysis. Invasive management included the invasive management, particularly coronary angiography, PCI and coronary artery bypass grafting (CABG). Finally, an additional revascularization composite outcome that combines both PCI and CABG was reported.

Data were expressed as frequencies and percentages for categorical data and median (interquartile range) for continuous data. The Chi-squared test was used to compare categorical data across the study groups, whilst the Mann-Whitney *U* test was used to compare continuous data.

Binomial multivariable logistic regression analysis was used to generate adjusted odds ratios (aOR) with 95 % confidence intervals (CI). Hierarchical multilevel modelling was utilized to adjust for the hospital stratification (NIS_STRATUM) and hospital clustering (HOSP_NIS). Analyses were further adjusted for the following variables: bed size of hospital, region of hospital, location/teaching status of hospital, age, sex, primary expected payer, median household income, smoking status, previous AMI, previous PCI, previous CABG, previous cerebrovascular accident, dyslipidaemia, atrial fibrillation, thrombocytopenia, heart failure, dementia, chronic renal failure, arterial hypertension, chronic pulmonary disease, liver disease, metastatic cancer, peripheral vascular disease, and valvular heart disease. All regression models were full fit (non-parsimonious). As a measure of discrimination and calibration Harrell's C and Hosmer-Lemeshow coefficients were reported, respectively, in the main regression analyses. A *p*-value of <0.05 was used to define statistical significance. To account for the large sample size, standardized differences were reported together with the *p*-values in the baseline analyses. We used SPSS Statistics version 27 (IBM Corp, Armonk, NY) and Stata MP version 16.0 (StataCorp, College Station, Texas, US) for statistical analysis.

## 3. Results

Following exclusion of missing data and elective admissions, a total of 2,587,615 patients were included in analysis (Supplementary Fig. 1). This corresponded to 1,525,440 patients (59.0 %) in the NDM group, 29,250 patients (1.1 %) in the T1DM group and 1,032,925 patients (39.9 %) in the T2DM group.

Patients in the T1DM group were significantly younger in comparison to other patients (median age 59 vs. 69 in the NDM and T2DM groups, $p < 0.001$). Patients with T1DM and T2DM were more likely to present with NSTEMI compared to NDM group (84.6 % and 82.9 % vs. 75.6 %), and had a higher prevalence of comorbidities including dyslipidaemia

**Table 2**
Comparison of in-hospital invasive management and clinical outcomes according to the presence of diabetes mellitus.

| Variables | No diabetes mellitus (59.0 %) | Type 1 diabetes mellitus (1.1 %) | Type 2 diabetes mellitus (39.9 %) | *P*-value[a] | *P*-value[b] |
|---|---|---|---|---|---|
| Invasive management, % | | | | | |
| Coronary angiography | 68.7 | 65.4 | 65.3 | <0.001 | <0.001 |
| PCI | 51.3 | 43.6 | 44.7 | <0.001 | <0.001 |
| CABG | 7.0 | 10.2 | 10.0 | <0.001 | 0.006 |
| PCI/CABG | 57.5 | 53.1 | 53.8 | <0.001 | 0.042 |
| Use of IABP or assist device | 0.7 | 0.7 | 0.8 | 0.042 | 0.320 |
| Clinical outcomes, % | | | | | |
| MACCE | 5.5 | 6.2 | 6.0 | <0.001 | <0.001 |
| All-cause mortality | 4.6 | 5.0 | 4.8 | <0.001 | <0.001 |
| Major bleeding | 1.7 | 2.5 | 1.8 | <0.001 | <0.001 |
| Ischemic stroke | 0.9 | 1.2 | 1.2 | 0.545 | 0.273 |
| Cardiac complications | 0.9 | 0.7 | 0.8 | <0.001 | <0.001 |
| Coronary dissection | 0.7 | 0.2 | 0.3 | <0.001 | 0.002 |
| Hemopericardium | 0.0 | 0.1 | 0.0 | <0.001 | <0.001 |
| Reinfarction | 0.2 | 0.2 | 0.2 | 0.127 | 0.964 |
| Postprocedural haemorrhage | 0.3 | 0.2 | 0.3 | <0.001 | 0.002 |
| Length of stay (days), median (IQR) | 3 (2,6) | 5 (3,8) | 4 (2,7) | <0.001 | <0.001 |
| Total charges (USD), median (IQR) | 59,549 (31,686, 105,810) | 66,955 (35,516, 124,679) | 64,600 (33,577, 119,701) | <0.001 | <0.001 |

Abbreviations: PCI – Percutaneous Coronary Intervention; CABG – Coronary Artery Bypass Graft; IABP – Intra-Aortic Balloon Pump; IQR – Interquartile Range; MACCE – Major Adverse Cardiac and Cerebrovascular Events (composite of mortality, acute ischemic stroke and reinfarction); USD – United States Dollar.

[a] Comparison of no diabetes mellitus vs. type 1 diabetes mellitus vs. type 2 diabetes mellitus groups.

[b] Comparison of type 1 diabetes mellitus vs. type 2 diabetes mellitus groups.

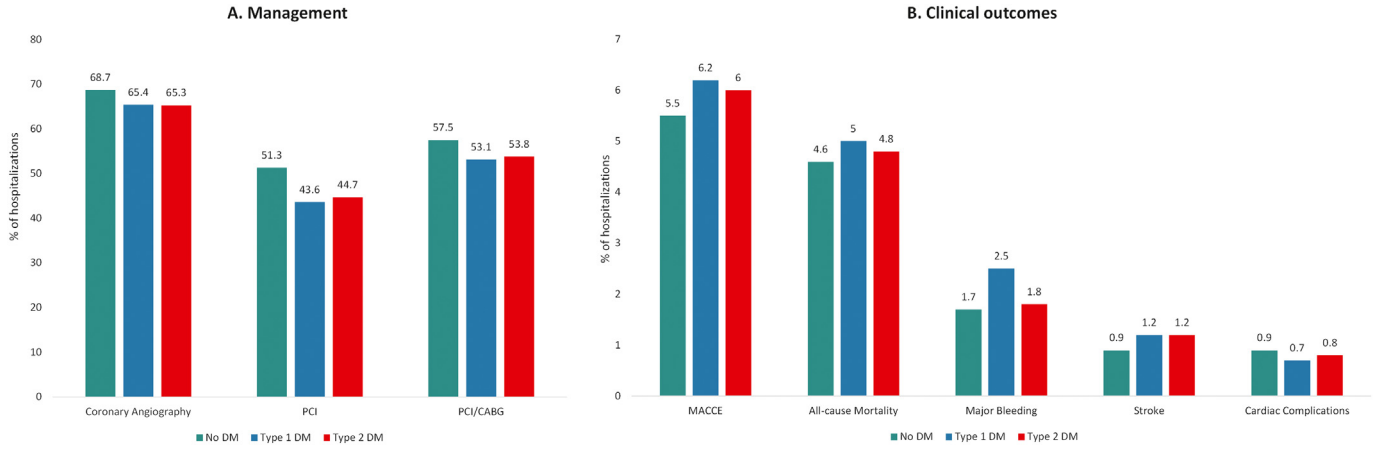


**Fig. 1.** Unadjusted rates of outcomes between the study groups: A. Management; B. Clinical outcomes.
Abbreviations: DM – diabetes mellitus; MACCE – major adverse cardiovascular and cerebrovascular events. (composite of mortality, acute ischemic stroke and reinfarction); PCI – percutaneous coronary intervention.

(63.5 % and 69.6 % vs. 54.7 %), thrombocytopenia (6.5 % and 6.7 % vs. 6.4 %), previous AMI (19.1 % and 17.3 % vs. 12.9 %), history of ischemic heart disease (73.3 % and 75.5 % vs. 66.0 %), previous percutaneous coronary intervention (19.2 % and 19.8 % vs. 13.7 %), previous coronary artery bypass graft (27.6 % and 28.1 % vs. 18.3 %), previous cerebrovascular accident (9.3 % and 10.1 % vs. 7.3 %), anaemia (37.2 % and 29.5 % vs. 20.4 %), heart failure (43.9 % and 48.3 % vs. 34.5 %), peripheral vascular disorders (11.4 % and 10.2 % vs. 8.7 %) and chronic renal failure (49.7 % and 39.3 % vs. 19.7 %, $p < 0.001$ for all) (Table 1). Substantially higher proportion of patients were dependent on dialysis in T1DM patients compared to T2DM and NDM patients (11.5 % vs. 5.6 % vs. 1.4 %, $p < 0.001$, respectively) (Table 1).

The unadjusted rates of adverse outcomes are presented in Table 2 and Fig. 1. After multivariable adjustment, patients with T1DM were more likely to develop adverse outcomes, including MACCE (aOR 1.20, 95 % CI 1.09–1.31), all-cause mortality (aOR 1.20, 95 % CI 1.08–1.33) and major bleeding (aOR 1.28, 95 % CI 1.13–1.44) compared to NDM group, while there was no difference in ischemic stroke (aOR 1.12, 95 % CI 0.95–1.32). Patients with T2DM were more likely to develop MACCE (aOR 1.03, 95 % CI 1.01–1.05) and ischemic stroke (aOR 1.09, 95 % CI 1.05–1.13), but less likely to have major bleeding (aOR 0.97, 95 % CI 0.94–1.00) compared to NDM patients (Table 3 and Fig. 2). Compared to T2DM patients, T1DM patients had increased adjusted mortality (aOR 1.19, 95 % CI 1.07–1.33, $p = 0.001$) (Table 3 and Fig. 2).

The unadjusted rates of management strategies are presented in Table 2 and Fig. 1. When accounting for the baseline characteristics, the adjusted odds of receiving coronary angiography (aOR 0.72, 95 % CI 0.67–0.76) and PCI (aOR 0.70, 95 % CI 0.66–0.75 and aOR 0.89) were lower in the T1DM group compared to NDM group. T2DM patients were less likely to receive PCI (aOR 0.95, 95 % CI 0.94–0.96) compared to NDM patients, while there was no difference in utilization of coronary angiography (Table 3 and Fig. 2). Interestingly, when looking at the composite management outcome, T1DM patients consistently had lower adjusted odds of receiving PCI/CABG compared to NDM (aOR 0.77, 95 % CI 0.75–0.79) and T2DM patients (aOR 0.67, 95 % CI 0.66–0.69). However, T2DM patients showed higher adjusted odds of receiving PCI/CABG compared to NDM patients (aOR 1.03, 95 % CI 1.03–1.04), indicating that the lower utilization of PCI was mediated by higher utilization of CABG in this patient group (Table 3 and Fig. 2).

When evaluating in-hospital clinical outcomes in the STEMI type, both diabetes subgroups showed increased odds of MACCE, all-cause mortality and ischemic stroke compared to the NDM group, while there was no statistical difference in major bleeding. In the NSTEMI type, the T1DM group displayed greater odds of MACCE, all-cause

**Table 3**
Adjusted odds ratios (aOR) of in-hospital invasive management and clinical outcomes in the groups with diabetes mellitus.

| Variables | Type 1 diabetes mellitus[a] | Type 2 diabetes mellitus[a] | Type 1 diabetes mellitus[b] | Harrell's C | Hosmer-Lemeshow |
|---|---|---|---|---|---|
| | aOR [95 % CI] | aOR [95 % CI] | aOR [95 % CI] | | |
| | *P*-value | *P*-value | *P*-value | | |
| Invasive management: | | | | | |
| Coronary angiography | 0.72 [0.67, 0.76] <0.001 | 0.99 [0.98, 1.01] 0.489 | 0.72 [0.68, 0.77] <0.001 | 0.503 | 382.3 |
| PCI | 0.70 [0.66, 0.75] <0.001 | 0.95 [0.94, 0.96] <0.001 | 0.68 [0.63, 0.72] <0.001 | 0.504 | 402.5 |
| PCI/CABG | 0.77 [0.75, 0.79] <0.001 | 1.03 [1.02, 1.04] <0.001 | 0.67 [0.66, 0.69] <0.001 | 0.503 | 404.3 |
| Clinical outcomes: | | | | | |
| MACCE | 1.20 [1.09, 1.31] <0.001 | 1.03 [1.01, 1.05] 0.001 | 1.15 [1.05,1.26] 0.002 | 0.503 | 489.2 |
| All-cause mortality | 1.20 [1.08, 1.33] <0.001 | 1.01 [0.99, 1.03] 0.410 | 1.19 [1.07, 1.33] 0.001 | 0.502 | 237.0 |
| Major bleeding | 1.28 [1.13, 1.44] <0.001 | 0.97 [0.94, 1.00] 0.034 | 1.38 [1.22, 1.56] <0.001 | 0.501 | 511.4 |
| Ischemic stroke | 1.12 [0.95, 1.32] 0.165 | 1.09 [1.05, 1.13] <0.001 | 1.02 [0.87, 1.20] 0.772 | 0.504 | 301.8 |

Multivariable logistic regression model adjusted for: bed size of hospital, region of hospital, location/teaching status of hospital, age, sex, primary expected payer, median household income, smoking status, previous myocardial infarction, previous percutaneous coronary intervention, previous coronary artery bypass graft, previous cerebrovascular accident, dyslipidemia, atrial fibrillation, thrombocytopenia, heart failure, dementia, chronic renal failure, arterial hypertension, chronic pulmonary disease, liver disease, metastatic cancer, peripheral vascular disease, and valvular heart disease.
Abbreviations: aOR – adjusted Odds Ratios; CABG – Coronary Artery Bypass Grafting; CI – Confidence Interval; PCI – Percutaneous Coronary Intervention; MACCE – Major Adverse Cardiac and Cerebrovascular Events (composite of mortality, acute ischemic stroke and reinfarction).
[a] Reference group is group without diabetes mellitus.
[b] Reference group is type 2 diabetes mellitus group.

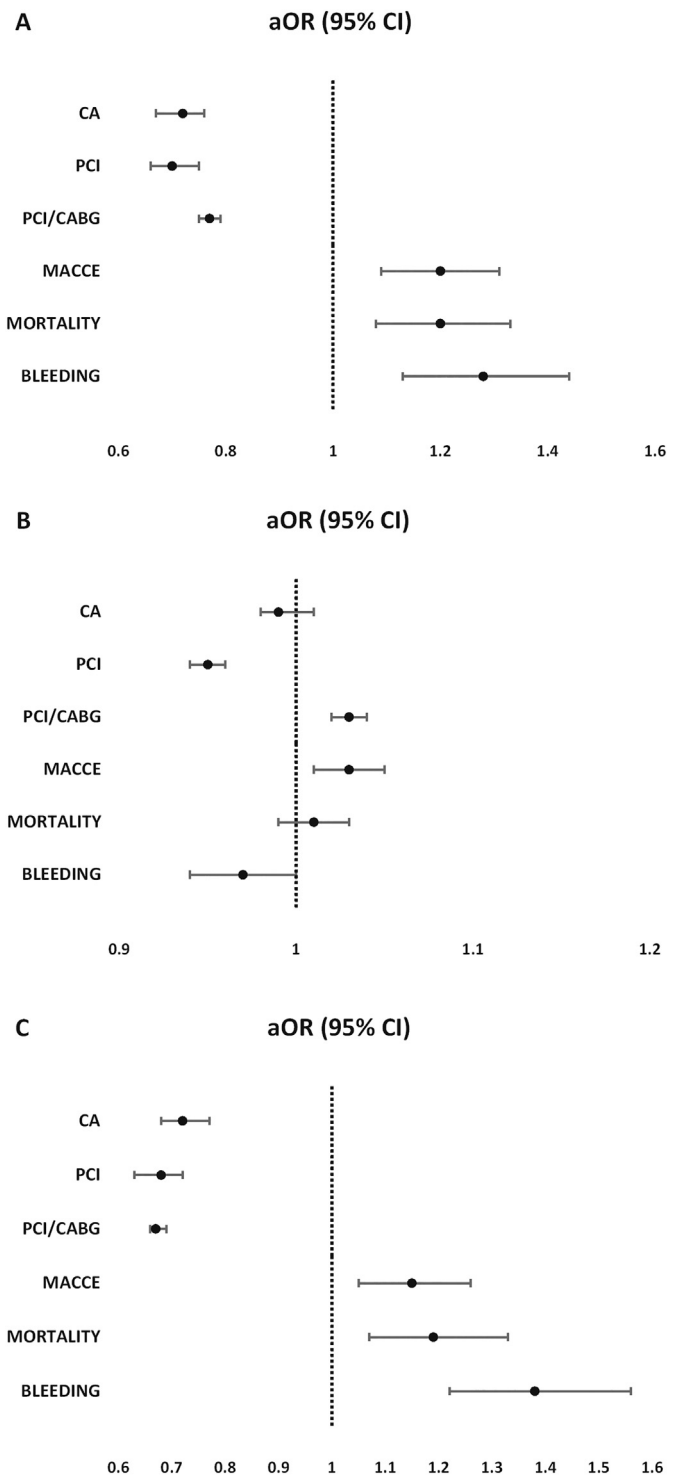


**Fig. 2.** Adjusted odds ratios (aOR) of outcomes in the diabetes mellitus groups: A. Type 1 diabetes mellitus[1]; B. Type 2 diabetes mellitus[1]; C. Type 1 diabetes mellitus[2].
[1]Reference group is group without diabetes mellitus.
[1]Reference group is type 2 diabetes mellitus group.
Multivariable logistic regression model adjusted for: bed size of hospital, region of hospital, location/teaching status of hospital, age, sex, primary expected payer, median household income, smoking status, previous myocardial infarction, previous percutaneous coronary intervention, previous coronary artery bypass graft, previous cerebrovascular accident, dyslipidemia, atrial fibrillation, thrombocytopenia, heart failure, dementia, chronic renal failure, arterial hypertension, chronic pulmonary disease, liver disease, metastatic cancer, peripheral vascular disease, and valvular heart disease.
Abbreviations: aOR – adjusted odds ratios; CA – coronary angiography; PCI – percutaneous coronary intervention; MACCE – major adverse cardiovascular and cerebrovascular events (composite of mortality, acute ischemic stroke and reinfarction).

mortality and major bleeding, while the T2DM group had only increased odds of stroke, compared to NDM group (Supplementary Table 2 and Supplementary Fig. 2).

In both STEMI and NSTEMI types, the T1DM group had consistently lower adjusted odds of receiving CA and PCI compared to NDM group ($p < 0.001$), while the T2DM group had lower adjusted odds of receiving CA (aOR 0.90, 95 % CI 0.87–0.93) and PCI (aOR 0.89, 95 % CI 0.86–0.92) in STEMI, and higher adjusted odds of receiving CA (aOR 1.04, 95 % CI 1.03–1.04) and PCI (aOR 1.04, 95 % CI 1.03–1.05) in NSTEMI (Supplementary Table 2 and Supplementary Fig. 2).

Finally, when looking at the importance of renal function in this population, it has been confirmed that renal failure was independent predictor of both all-cause mortality (aOR 1.11, 95 % CI 1.09–1.13) and lower utilization of PCI/CABG (aOR 0.67, 95 % CI 0.66–0.67). The presence of heart failure was even stronger predictor of all-cause mortality (aOR 1.64, 95 % CI 1.62–1.66) and lower utilization of PCI/CABG (aOR 0.65, 95 % CI 0.64–0.65).

## 4. Discussion

This large-scale national-level study provides data on the association of different DM types with in-hospital outcomes and invasive management among AMI population. There are several important findings of this study. Firstly, DM is present in up to 40 % of patients admitted with AMI, with T2DM accounting for 97 % of cases. Secondly, a higher comorbidity burden was seen in both T1DM and T2DM patients compared to their NDM counterparts. Thirdly, T1DM patients were less likely to receive overall revascularization, including PCI and CABG, compared to their NDM and T2DM counterparts. Fourthly, after accounting for the baseline characteristics there was significant association of DM and worse prognosis, particularly for T1DM patients that showed an increased risk of all-cause mortality, MACCE and major bleeding.

The findings of worse AMI-associated outcomes in DM patients are consistent with prior studies [5,9,11–13]. There are several possible explanations. Firstly, patients with DM have higher risk phenotype with additional comorbidities, such as renal dysfunction, heart failure and peripheral vascular disease, that are important predictors of worse outcomes [9,17,18]. This study has confirmed that renal dysfunction and heart failure are independent predictors of mortality and lower invasive management. Secondly, differences in active therapy and other unmeasured clinical data could also account for the observed differences. Thirdly, patients with DM have higher incidence of multivessel CAD and left main involvement compared to non-diabetics [9,18–20]. Prolonged hyperglycaemia in DM could lead to platelet and endothelial dysfunction, which in turn accelerates atherosclerosis [9,19]. Fourthly, DM patients are at higher risk of adverse outcomes following percutaneous [21] or surgical revascularization [22] compared to their non-DM counterparts.

The novelty of this study includes the differentiation of risk profile and AMI-associated outcomes by DM type highlighting T1DM patients that have the worst prognosis. Most prior studies have considered DM as a single entity and lack comparison between DM subtypes [5,8,9,11–14,22]. The underlying mechanisms for considerably worse outcomes of T1DM patients relative to T2DM patients are less well understood. Although they share a common endpoint of hyperglycaemia, there are obvious differences in the underlying pathophysiology. T1DM is predominantly characterised by autoimmune-mediated absolute insulin deficiency, which contrasts to T2DM, whereby hyperglycaemia results from the insulin resistance [23]. In addition, T1DM typically begins earlier in life with longer disease duration that represents a predominant risk factor for premature CAD [17]. A United Kingdom primary care study reported that 45–55-year-old patients with T1DM have an absolute cardiovascular risk equal to 10–15 years older individuals from the general population [24]. Other limited data suggest that patients with T1DM have accelerated atherosclerosis with more distal disease [25,26]. Systemic inflammation also seems to be

more prominent in T1DM patients [15,27]. Finally, patients with T1DM may present more frequently with NSTEMI, as confirmed in this study, and this has been associated with worse outcomes [28].

Interestingly, this study also demonstrates that patients with DM are less likely to receive coronary angiography and PCI, compared to NDM patients. A large study by Schmitt et al. showed a 5.3 % and 6.3 % relative reduction in the use of coronary angiography and PCI in DM patients hospitalized for AMI, compared to NDM population [9]. Likewise, data from a Swedish registry of AMI patients also revealed lower rates of revascularization among diabetic patients compared to their NDM counterparts [6]. However, these studies did not distinguish between T1DM and T2DM patients [9]. While the exact reasons for underutilization of invasive therapies among DM patients remain unclear, numerous perceived deterrents could be speculated. It is possible that physicians' perception of DM-associated complications (renal dysfunction, contrast-associated nephropathy, difficult vascular access, etc.) could mediate lower adoption of invasive management. Also, different unmeasured factors such as frailty status, abnormal laboratory findings, or concomitant medications (such as diuretics, anticoagulants, etc.) could contribute to these findings. Nevertheless, patients with DM undergoing PCI are at increased risk of MACE [6,7,29,30]. Considering that DM patients in general, and particularly T1DM patients, are more likely to present with multivessel disease, surgical rather than percutaneous revascularisation may be the preferred management. Interestingly, a composite revascularization outcome (PCI/CABG) of this study was lower in T1DM patients and higher in T2DM patients, compared to their non-diabetic counterparts. These important findings indicate that the lower utilization of PCI was mediated by higher utilization of CABG in T2DM patients, but underscore T1DM patients that received overall less revascularization.

This study has several clinical implications. First, it outlines important lacking data on the differential impact of DM subtypes. Second, it increases an awareness for T1DM patients that exhibit worse outcomes. This could improve the decision-making process by encouraging better preventive measures and advocating closer follow-up. Finally, it warrants further studies to delineate mechanisms for the observed differences among T1DM and T2DM patients.

This study has several limitations. Firstly, the utilization of the NIS dataset has inherent limitations such as missing, incomplete, or misclassified diagnoses and procedures, as well as the lack of detailed laboratory data. Secondly, important clinical data such as DM severity and duration, left ventricular ejection fraction, CAD complexity, immediate PCI result, lesion type, HbA1c, antithrombotic and hypoglycaemic medications and insulin use, are not available in the NIS. Thirdly, the NIS contains only in-hospital data, and this study was unable to analyse post-discharge events. Fourthly, due to retrospective study design, it is not possible to fully eliminate the selection bias. Finally, even though the study analyses included multivariable adjustments, residual confounding bias could not be fully eliminated.

In conclusion, diabetic patients presenting with AMI have lower utilization of invasive management and, following the adjustment for baseline characteristics, have worse in-hospital clinical outcomes compared to NDM patients. There are important DM type-related differences with T1DM patients having overall worse outcomes.

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## CRediT authorship contribution statement

PS: Data curation, Methodology, Formal analysis, Visualization, Validation, Writing- Reviewing and Editing; AM: Data curation, Methodology, Visualization, Validation, Writing- Reviewing and Editing; VB: Writing-Reviewing and Editing, Validation; PKM: Writing- Reviewing and Editing, Validation; IR: Validation, Writing- Reviewing and Editing; RB: Validation, Writing- Reviewing and Editing; CDA: Validation, Writing- Reviewing and Editing; AR: Validation, Writing- Reviewing and Editing; AB: Validation, Methodology, Writing- Reviewing and Editing; MM: Supervision, Conceptualization, Methodology, Resources, Project administration, Validation, Writing- Reviewing and Editing.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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