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The relationship of previously known type 2 diabetes mellitus and newly diagnosed type 2 diabetes mellitus to clinical outcomes in patients with non-ST elevation myocardial infarction

La relación de la diabetes mellitus tipo 2 previamente conocida y la diabetes mellitus tipo 2 recién diagnosticada con los resultados clínicos en pacientes con infarto de miocardio sin elevación del segmento ST

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SUMMARY

Background: *Cardiovascular disease (CVD) remains the leading global cause of morbidity and mortality, accounting for 17.9 million deaths annually (32 % of all deaths). Type 2 Diabetes Mellitus (T2DM) is a common comorbidity in CVD and significantly worsens outcomes. Over 20 % of patients treated for suspected Acute Coronary Syndrome (ACS) have T2DM, which doubles in-hospital mortality and increases the risk of Major Adverse Cardiac and Cerebrovascular Events (MACCE). This study investigates the association between diabetes status and MACCE incidence in patients with Non-ST-Elevation Myocardial Infarction (NSTEMI), along with the severity of coronary lesions.* **Methods:** *A retrospective cohort study analyzed NSTEMI patients with previously known or newly diagnosed T2DM from the Acute Coronary Syndrome Registry at Dr. Wahidin Sudirohusodo Hospital (January 2021–December 2023). Six-month follow-up assessed MACCE and coronary lesion severity via angiography.* **Results:** *Among 129 patients (mean age 61.6 ±9.3 years, 75.2 % male), those with previously known T2DM had a 2.2-fold higher MACCE risk (p=0.034) and 8.1-fold higher heart failure risk (p=0.002) compared to those with newly diagnosed T2DM. Lower LVEF (p<0.001) and lack of revascularization (p=0.047) were significant MACCE predictors. Coronary lesion severity did not significantly differ (p=0.662). A predictive algorithm showed an Area Under the Curve of 81.56 % and specificity of 76.47 %.* **Conclusion:** *Previously known*

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T2DM significantly increases the MACCE risk in NSTEMI patients. Early identification, preserved LVEF, and timely revascularization are critical for reducing adverse outcomes.

Keywords: *Non-ST elevation myocardial infarction, type 2 diabetes mellitus, major adverse cardiac and cerebrovascular events*

RESUMEN

Antecedentes: *Las enfermedades cardiovasculares (ECV) continúan siendo la principal causa de morbilidad y mortalidad a nivel mundial, con 17.9 millones de muertes anuales, lo que representa el 32 % del total. La Diabetes Mellitus tipo 2 (T2DM2) es una comorbilidad frecuente en pacientes con ECV y empeora significativamente el pronóstico. Más del 20 % de los pacientes tratados por síndrome coronario agudo (SCA) presentan T2DM2, lo que duplica la mortalidad intrahospitalaria y aumenta el riesgo de eventos cardiovasculares y cerebrovasculares mayores (MACCE, por sus siglas en inglés). Este estudio evalúa la asociación entre el estado diabético y la incidencia de MACCE en pacientes con infarto agudo de miocardio sin elevación del ST (IAMSEST), así como la severidad de las lesiones coronarias.* **Métodos:** *Estudio de cohorte retrospectivo basado en pacientes con IAMSEST y T2DM2 previamente conocida o de diagnóstico reciente, registrados en el Registro de SCA del Hospital Dr. Wahidin Sudirohusodo entre enero de 2021 y diciembre de 2023. Se realizó un seguimiento a los 6 meses para evaluar la incidencia de MACCE y la severidad de las lesiones coronarias mediante angiografía.* **Resultados:** *De 129 pacientes (edad media 61,6 ± 9,3 años; 75,2 % hombres), aquellos con T2DM2 previamente conocida presentaron un riesgo 2,2 veces mayor de MACCE (p=0,034) y 8,1 veces mayor de insuficiencia cardíaca (p=0,002), en comparación con los de diagnóstico reciente. Una fracción de eyección reducida (p<0,001) y la ausencia de revascularización (p=0,047) fueron predictores significativos. No se observaron diferencias significativas en la severidad de las lesiones coronarias (p=0,662). Se desarrolló un algoritmo predictivo con un Área Bajo la Curva de 81,56 % y una especificidad de 76,47 %.* **Conclusión:** *La T2DM2 previamente conocida se asocia significativamente con mayor riesgo de MACCE en pacientes con IAMSEST. La identificación temprana, la preservación de la función ventricular y la revascularización oportuna son fundamentales para mejorar el pronóstico.*

Palabras clave: *Infarto de miocardio sin elevación del segmento ST, diabetes mellitus tipo 2, eventos adversos cardíacos y cerebrovasculares mayores.*

INTRODUCTION

Cardiovascular disease (CVD) is the cause of the highest morbidity and mortality in the world. The increase in cardiovascular cases is increasing rapidly, with 17.9 million deaths annually, accounting for 32 % of all deaths (1). In fact, according to the World Health Organization (WHO), Ischemic Heart Disease (IHD) occupied the first position as a contributor to the death rate in 2019. In Indonesia, coronary heart disease ranked second only to stroke as the leading cause of death in 2012, with a death toll of around 128.4 thousand people (2).

Acute Coronary Syndrome (ACS) is a major cardiovascular problem because it causes high hospitalizations and mortality rates. It is known that Type 2 Diabetes Mellitus (T2DM) is a common comorbidity in patients with cardiovascular disease. Specifically, T2DM was detected in more than 20 % of patients treated for suspected ACS, providing a 2-fold increase in in-hospital mortality and a higher risk of Major Adverse Cardiac and Cerebrovascular Events (MACCE) during the follow-up period (3). Hyperglycemia is a medical condition in the form of an increase in blood glucose levels exceeding normal, which is characteristic of several diseases, especially Diabetes Mellitus, in addition to various other conditions (4).

The WHO predicts an increase in the number of type 2 diabetes mellitus (T2DM) patients in Indonesia from 8.4 million in 2000 to around 21.3 million in 2030. The International Diabetes Federation (IDF) prediction also shows that between 2019 and 2030, the number of T2DM patients is expected to increase from 10.7 million to 13.7 million. Complications that occur due to T2DM disease can be in the form of disorders in blood vessels, both macrovascular and microvascular, as well as disorders of the nervous system or neuropathy. This disorder can occur in patients with type 2 diabetes who have been suffering from the disease for a long time or in those newly diagnosed with type 2 diabetes (5).

Cardiovascular events are responsible for 80 % of all deaths in Diabetic patients. The development of Acute Ischemic Stroke in patients with Acute Myocardial Infarction (AMI) is rare but has a high risk of death. Decreased Left

Ventricle Ejection Fraction (LVEF) after AMI is associated with an increased risk of Stroke. For every 5 % decrease in the exclusion fraction point, there is an increased risk of a stroke by 18 % (6). Considering these findings, it is necessary to analyze the relationship between the clinical outcomes of MACCE of NSTEMI patients with previously known T2DM and newly diagnosed T2DM at Dr. Wahidin Sudirohusodo Hospital, Makassar. In addition, this research has never been conducted in Eastern Indonesia, so it is of novel value.

METHODS

Study design and settings

This is an observational study employing a retrospective cohort design, conducted at the Acute Coronary Syndrome Registry of the Integrated Heart Center, Dr. Wahidin Sudirohusodo Hospital, from January 2021 to December 2023, to collect data.

Populations and samples

The study population consisted of all patients recorded in the Acute Coronary Syndrome Registry at Dr. Wahidin Sudirohusodo Hospital who were diagnosed with NSTEMI and had either known type 2 diabetes mellitus (T2DM) or Newly Diagnosed T2DM.

The minimum number of samples for the study was 41 for each group. The inclusion criteria in this study were patients aged 18 years or older with NSTEMI who had previously known diabetes or were newly diagnosed with diabetes. The exclusion criteria were patients with a history of chronic heart failure, prior infarction, chronic kidney disease, sepsis, and a recent stroke.

Variables

According to medical record data, age is determined based on what is listed in *the ACS registry*. The age in this study was over 18 years. Gender is determined based on what is stated in *the ACS registry* according to medical record data, which differentiates between males and females. Obesity is determined based on a body mass index (BMI) ≥ 25 kg/m^2, listed in the *ACS registry* according to medical record data. Smoking history is determined based on what is listed in *the ACS registry,* according to medical record data. Hypertension is determined based on what is listed in the *ACS registry,* according to medical record data. Previously known Type 2 Diabetes Mellitus is a patient with a history diagnosis of T2DM, with classic symptoms of polyuria, polydipsia, and polyphagia accompanied by blood glucose levels at ≥ 200 mg/dL or fasting glucose levels ≥ 126 mg/dL, blood glucose ≥ 200 mg/dL 2 hours after an oral glucose tolerance with a glucose load of 75 grams or an HbA1C test ≥ 6.5 %, or while undergoing oral anti-diabetic drug therapy or insulin (7).

Newly diagnosed type 2 diabetes mellitus (T2DM) occurs in patients who have no previous history of diabetes mellitus, are not undergoing diabetes mellitus treatment, and exhibit classic symptoms of polyuria, polydipsia, and polyphagia, accompanied by blood glucose levels of≥ 200 mg/dL or fasting glucose levels of ≥ 126 mg/dL, or blood glucose levels of≥ 200 mg/dL or 2 hours after an oral glucose tolerance test with a glucose load of 75 grams, or an HbA1C test of≥ 6.5 %.

Acute Myocardial Infarction (AMI) is a condition characterized by an increase and/or decrease in cardiac biomarkers, and at least one of the following criteria is met, including ischemic symptoms, changes in ST segments and new T waves, or left bundle branch block (LBBB), pathological Q-waves on electrocardiography (ECG), or evidence of imaging showing decreased myocardial viability or regional heart wall abnormalities. The presence of intracoronary thrombus was found during angiography or autopsy (8).

Non-ST Elevation Myocardial Infarction (NSTEMI) is a diagnosis based on the information listed in the *ACS registry,* as per medical record data. The ejection fraction of the left ventricle is determined based on the information in the *ACS registry,* according to medical record data. The value of the LV ejection fraction calculation

is expressed in percentage units. T2DM status refers to a condition with a previously known T2DM or a newly diagnosed T2DM state at the time of diagnosis.

Dyslipidemia is a lipid metabolism disorder characterized by an increase or decrease in the level of lipid fractions in plasma, including Total Cholesterol levels ≥ 200 mg/dL, LDL ≥ 130 mg/dL, HDL < 40 mg/dL, and Triglycerides ≥ 150 mg/dL. Glucose levels are determined based on the information listed in the *ACS registry,* according to medical record data. The capillary blood glucose (CBG) calculation value is expressed in mg/dL. Fasting blood glucose (FBG) is determined based on what is listed in the *ACS registry,* according to medical record data. The value of the FBG calculation is expressed in mg/dL. Hemoglobin A1c is determined based on the information listed in the *ACS registry*, according to medical record data. The calculated value of HbA1c is expressed as a percentage.

Short-term clinical outcomes refer to clinical events that occur in NSTEMI patients within 6 months after an NSTEMI event, including cardiovascular mortality, recurrent myocardial infarction, congestive heart failure, or stroke. Cardiovascular mortality is death resulting from myocardial infarction, sudden cardiac arrest, or heart failure. Congestive heart failure is characterized by the inability of the heart to pump blood to meet the body's metabolic needs, as evidenced by symptoms of shortness of breath and/or signs of congestion, cardiomegaly on chest radiography examination, and/or echocardiography examination.

Stroke is a condition that occurs when the blood supply to the brain is disrupted or reduced due to blockage (ischemic stroke) or rupture of blood vessels (hemorrhagic stroke), characterized by neurological deficit symptoms such as severe headaches, projectile vomiting, limb weakness, and decreased consciousness. Recurrent myocardial Infarction is a condition in which recurrent myocardial infarction occurs in patients who have previously experienced an acute myocardial infarction.

Revascularization is a medical procedure that restores optimal blood perfusion through or around blocked arteries, particularly after a myocardial infarction. The procedure can be a minimally invasive endovascular procedure, such as Percutaneous Coronary Intervention (PCI), or a more invasive bypass surgery with an artery graft around the blockage (9). The severity of coronary lesions is based on what is listed in the *ACS registry*, according to medical record data showing the number of coronary arteries involved in coronary angiography.

Data Analysis

Categorical data characteristics, such as gender and smoking status, were analyzed using frequency to show the number and percentage of each category. Meanwhile, for numerical data, such as age or blood sugar levels, mean values and standard deviations are calculated to describe the data distribution. Furthermore, to assess the relationship between the status of previously and newly diagnosed diabetes mellitus and the incidence of MACCE, a Chi-Square test was performed. This test was used to determine whether there was a significant difference between the previously and newly diagnosed T2DM groups in the incidence of MACCE (yes or no).

The analysis then continued by examining the relationship between T2DM status and MACCE incidence, which included the incidence of congestive heart failure, recurrent myocardial infarction, stroke, and cardiovascular mortality. Each of these events was analyzed using the Chi-Square test to determine the relationship between T2DM status and each of these cardiovascular events. Additionally, an analysis of the relationship between T2DM status and the severity of coronary lesions was conducted using the Chi-Square test to assess whether there was a difference in CAD severity between patients with a history of previously diagnosed T2DM and those with newly diagnosed T2DM.

To evaluate the influence of confounding variables, such as hypertension or abnormal lipid profiles, on the incidence of MACCE, a Chi-Square test was performed for categorical data. For numerical data, the independent t-test was used if the data distribution was normal, and the U Mann-Whitney test was used if it was not. This

analysis aims to identify confounding variables that may affect the incidence of MACCE.

Finally, the decision tree classification method, utilizing the C5.0 algorithm, was employed to identify the variables that significantly affect the occurrence of MACCE and control for the influence of confounding variables. The C5.0 algorithm was selected due to its ability to handle large datasets with numerous variables and provide results in the form of an easy-to-interpret decision tree. The C5.0 algorithm is a machine learning algorithm used to build decision trees and rule sets for classification tasks. C5.0 utilizes information gain ratio, boosting techniques, and sophisticated pruning methods to create more accurate and robust models.

The evaluation of this model is based on *the Area Under the Curve (AUC)* value, which is used as the basis for accepting or rejecting the model. AUC is a measure that describes the model's ability to distinguish between MACCE events (yes or no). The AUC value ranges from 0.5 to 1, where the closer to 1, the better the model's ability to predict the desired event. The C5.0 model is considered acceptable if the AUC value shows a good to very good category (generally AUC ≥ 0.7), which means that the model has a strong enough ability to predict MACCE events based on the variables analyzed. As such, AUC becomes a key indicator for assessing the model's accuracy, ensuring that the model used is not only statistically complex but also relevant and useful in a clinical context. This evaluation ensures that the decision tree model used is completely reliable in understanding the risk factors for MACCE events in NSTEMI patients with previously and newly diagnosed T2DM status, so that it can help determine more appropriate treatment strategies based on the patient's characteristics.

Ethics

The research proposal has been approved by the Biomedical Research Ethics Committee in Humans at the Faculty of Medicine, Hasanuddin University, and Dr. Wahidin Sudirohusodo Hospital, Makassar, with letter number 282/UN4.6.4.5.31/PP36/2024.

RESULTS

Respondent Characteristics

Understanding these patient characteristics is crucial for determining the population's risk profile and dominant health conditions. This data analysis provides an overview of the key clinical factors commonly found, such as hypertension, dyslipidemia, heart function, and glucose control conditions.

As shown in Table 1, the characteristics of NSTEMI patient respondents indicated significant clinical differences between groups with previously known T2DM and newly diagnosed T2DM. Overall, the mean age of patients was 61.62 ± 9.3 years, with similar ages in the newly diagnosed T2DM (61.61 ± 7.85 years) and previously known T2DM (61.63 ± 9.95 years) groups. Most patients were male (75.19 %), with the proportion in the newly diagnosed T2DM (78.05 %) and previously known T2DM (73.86 %) groups. Smoking status was more commonly found in newly diagnosed T2DM patients (58.54 %) than in previously known T2DM (47.73 %), indicating higher smoking behavior in patients with newly diagnosed diabetes. Hypertension was found in both groups, with a prevalence of 60.98 % in newly diagnosed T2DM and 67.05 % in previously known T2DM. Dyslipidemia was more common in patients with newly diagnosed T2DM (82.93 %) compared to previously known T2DM (64.77 %).

Obesity was more common in patients with previously known T2DM (40.91 %) than in those with newly diagnosed T2DM (29.27 %), reflecting differences in lifestyle management between the two groups. Most patients did not undergo revascularization, with only 29.27 % in the newly diagnosed T2DM group and 22.73 % in the previously known T2DM group. Cardiac function measured by LVEF value was lower in previously known T2DM (38.72 ± 11.59 %) than in newly diagnosed T2DM (41.36 ± 11.66 %), emphasizing a more severe decline in left ventricular function in the group with previously known T2DM.

Table 1. Distribution of Respondent Characteristics.

Variable		Total (n=129) n (%) | (Mean ± SD)	Newly Diagnosed T2DM (n=41) n (%) | (Mean ± SD)	Previously Known T2DM (n=88) n (%) | (Mean ± SD)
Age (years)		(61.62 ± 9.3)	(61.61 ± 7.85)	(61.63 ± 9.95)
Gender	Man	97 (75.19)	32 (78.05)	65 (73.86)
	Woman	32 (24.81)	9 (21.95)	23 (26.14)
Smokers	No	63 (48.84)	17 (41.46)	46 (52.27)
	Yes	66 (51.16)	24 (58.54)	42 (47.73)
Hypertension	No	45 (34.88)	16 (39.02)	29 (32.95)
	Yes	84 (65.12)	25 (60.98)	59 (67.05)
Dyslipidemia	No	38 (29.46)	7 (17.07)	31 (35.23)
	Yes	91 (70.54)	34 (82.93)	57 (64.77)
Obesity	No	81 (62.79)	29 (70.73)	52 (59.09)
	Yes	48 (37.21)	12 (29.27)	36 (40.91)
Revascularization	No	97 (75.19)	29 (70.73)	68 (77.27)
	Yes	32 (24.81)	12 (29.27)	20 (22.73)
LVEF (%)		(39.56 ± 11.63)	(41.36 ± 11.66)	(38.72 ± 11.59)
HbA1c (%)		(8.25 ± 1.97)	(7.66 ± 1.49)	(8.46 ± 2.08)
	NA	27 (20.93)	14 (34.15)	13 (14.72)
AT2DMission Glucose (mg/dL)		(213.22 ± 78.72)	(217.9 ± 66.19)	(211.05 ± 84.18)
FBG (mg/dL)		(166.02 ± 61.19)	(147.25 ± 42.52)	(173.72 ± 66.07)
	NA	19 (14.73)	9 (21.95)	10 (11.36)
Hs-cTrop I (ng/L)		(6 790.45± 11 978.49)	(8 453.38 ± 14 068)	(6 047.11±10 919.71)

NA: Not available; FBG: Fasting Blood Glucose

The average HbA1c value was higher in previously known T2DM (8.46 ± 2.08 %) than in newly diagnosed T2DM (7.66 ± 1.49 %), as well as the FBG value was higher in patients with previously known T2DM (173.72 ± 66.07) compared to patients with newly diagnosed T2DM (147.25 ± 42.52), reflecting differences in long-term glucose control and worse fasting glucose levels in patients with previously known T2DM. In contrast, to the T2DM glucose value, higher outcomes were obtained in patients with newly diagnosed T2DM (217.9 ± 66.19) compared to patients with previously known T2DM (211.05 ± 84.18). Markers of cardiomyocyte necrosis, hs-cTrop I, were found to be higher in the newly diagnosed group of T2DM (8 453.38 ± 14 068 ng/L) compared with previously known T2DM (6 047.11 ± 10 919.71 ng/L). Overall, these data suggest that patients with a history of T2DM have a worse cardiovascular risk profile compared to patients newly diagnosed with T2DM. These differences highlight the importance of a holistic approach in the management of NSTEMI patients with T2DM, both in newly diagnosed patients and patients with previously known T2DM, to prevent further cardiovascular complications.

Relationship between T2DM Status and MACCE Incidence

Diabetes mellitus is a significant risk factor in the development of cardiovascular complications, including the incidence of major adverse cardiovascular events (MACCE). The duration of time a patient has T2DM is often associated with an increased risk of complications, especially in patients who have had the disease for a long time. To understand the impact of T2DM status on the risk of cardiovascular events, analyses were conducted on NSTEMI patients who had a long history of diabetes mellitus (previously known as DM) and who were newly diagnosed with T2DM. The following are the results of comparing MACCE incidence based on diabetes status in NSTEMI patients.

Table 2. Relationship of MACCE Incidence Based on T2DM Status in NSTEMI Patients.

Status T2DM	MACCE				Total		OR (95 % CI)	p-value
	No		Yes					
	n	%	n	%	n	%		
Newly Diagnosed T2DM	25	19.38	16	12.40	41	31.78	2.26 (1.06 - 4.82)	0.034
Previously Known T2DM	36	27.91	52	40.31	88	68.22		
Total	61	47.29	68	52.71	129	100.00		

Analysis using Pearson Chi-Square Test.

Based on Table 2, it was obtained that the results of the comparative analysis of MACCE incidence of NSTEMI patients showed that patients with a long history of Diabetes Mellitus (previously known DM) had a higher risk of developing MACCE than patients who were newly diagnosed with T2DM. Out of a total of 129 patients, 52.71 % of patients experienced MACCE. In the previously known T2DM group, as many as 40.31 % of patients experienced MACCE, while in the newly diagnosed T2DM group, only 12.40 % experienced similar events. The odds ratio (OR) obtained was 2.26 (95 % CI: 1.06 - 4.82) with a p-value of 0.034, which indicates that the risk of MACCE events in patients with a previously known T2DM is more than double that of patients with newly diagnosed T2DM. A p-value of less than 0.05 indicates that this difference is statistically significant. These results indicate that the duration of suffering from T2DM affects the risk of serious cardiovascular complications, so more intensive treatment is needed in patients with T2DM, especially in patients with previously known T2DM, to reduce the risk of MACCE events.

Relationship between T2DM Status and Partial MACCE Incidence

Based on previous results, cardiovascular complications often occur in patients with diabetes mellitus, particularly in those with a previous history of type 2 diabetes mellitus (T2DM). This partial event analysis is important for understanding how the duration of T2DM may affect the risk of adverse cardiovascular events. This data can also provide valuable clinical insights in determining more appropriate prevention and management strategies for patients with Diabetes Mellitus. The following is a comparison of the partial incidence of MACCE in patients with previously known T2DM and newly diagnosed T2DM.

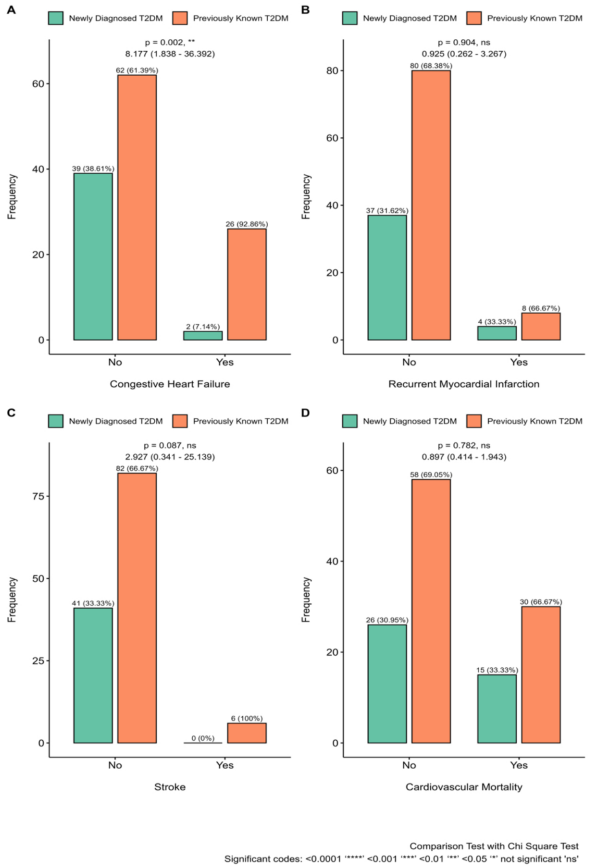

Figure 1. The Relationship between T2DM Status and the Risk of Congestive Heart Failure, Recurrent Myocardial Infarction, Stroke, and Cardiovascular Mortality in NSTEMI Patients.

Based on Figure 1, the comparative analysis of partial MACCE incidence results in NSTEMI patients reveals an interesting difference between patients with previously known T2DM and those with newly diagnosed T2DM. In the incidence of congestive heart failure (Panel A), it was seen that this event was more common in patients with a previously known T2DM (92.86 %) compared to patients with newly diagnosed T2DM (7.14 %), with a statistically significant difference ($p = 0.002$) with an OR of 8.17. This suggests that patients with a longer history of T2DM have a much higher risk of developing congestive heart failure, 8 times higher compared to patients newly diagnosed with T2DM.

In the incidence of recurrent myocardial infarction (Panel B), although it was seen more often in patients with previously known T2DM (66.67 %) than in newly diagnosed T2DM (33.33 %), this difference was not statistically significant ($p = 0.904$). The same thing was also seen in the incidence of stroke (Panel C), where the incidence of stroke was more common in patients with previously known T2DM (100 %). Still, this difference was also not statistically significant ($p = 0.087$) but had an OR value of 2.92, which means that patients with a previously known T2DM had a 2.9 times greater risk of stroke event. Mortality events (Panel D) showed a nearly balanced distribution between previously known T2DM (66.67 %) and newly diagnosed T2DM (33.33 %), with a $p = 0.782$. Overall, these results indicate that the duration of suffering from Diabetes Mellitus has a significant impact on the incidence of heart failure, but does not have a significant effect on the incidence of recurrent myocardial infarction, stroke, and cardiovascular mortality in this study. This emphasizes the importance of comprehensive management and the provision of optimal medical therapy to patients with NSTEMI accompanied by Diabetes Mellitus, especially in the history of T2DM, to reduce the risk of heart failure events.

Relationship between T2DM Status and Coronary Lesion Severity

In coronary angiography evaluation, the severity of coronary lesions ranges from involvement of one coronary artery to involvement of two or three coronary arteries. Comparative assessment of the severity of coronary lesions between patients with previously diagnosed T2DM and those with newly diagnosed T2DM provides important information regarding the higher cardiovascular risk in certain patient groups. The following presents a comparison of coronary severity in NSTEMI patients with previously diagnosed T2DM and those with newly diagnosed T2DM, related to these findings.

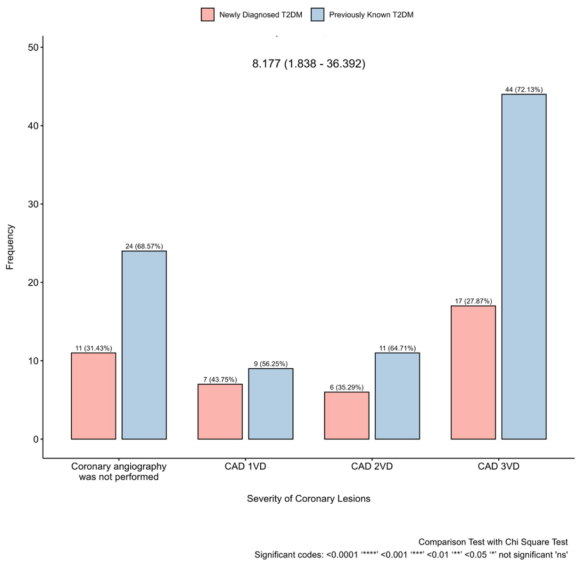

Figure 2. Relationship of T2DM Status to Coronary Lesion Severity.

Based on Figure 2, the comparative analysis of the severity of coronary lesions in patients revealed that the number of coronary arteries with stenosis did not differ significantly between patients with previously known T2DM and those with newly diagnosed T2DM, with a p-value of 0.662. Nonetheless, it was seen that most patients with previously known T2DM (72.13 %) experienced CAD3VD compared to patients with newly diagnosed T2DM (27.87 %), which indicates that patients with previously known T2DM are more likely to have more severe CAD compared to patients with newly diagnosed T2DM.

In addition, patients with previously known T2DM also did not undergo coronary angiography more often (68.57 %) compared to patients with newly diagnosed T2DM (31.43 %). This may reflect differences in treatment approaches or the possible presence of other comorbidities in patients with previously known T2DM. In the group with CAD 1VD and CAD 2VD, the distribution of newly diagnosed T2DM and previously known T2DM appeared to be relatively balanced, but not significant enough to indicate a significant difference. Overall, although there was no statistically significant difference between these two groups of patients, this study showed that patients with a previously known T2DM tended to develop more severe CAD. These results emphasize the importance of more intensive monitoring and appropriate treatment approaches in patients with a more extended history of T2DM, given the higher risk of CAD severity with a greater number of coronary artery stenoses involved.

Relationship of Confounding Variables with MACCE Incidence

Analysis of confounding variables is crucial for understanding the factors that influence the incidence of major adverse cardiovascular events (MACCE) in patients with diabetes mellitus, both those newly diagnosed and those with previously known diabetes mellitus (T2DM). This understanding can help determine a more appropriate risk management strategy. The following is a comparison of various clinical variables that affect the incidence of MACCE in non-ST-segment elevation myocardial infarction (NSTEMI) patients, along with an in-depth interpretation of these findings.

The Relationship of Confounding Variables with the Incidence of MACCE in NSTEMI Patients with Previously Known T2DM and Newly Diagnosed T2DM

Table 3. The Relationship of Confounding Variables to the Overall Incidence of MACCE in NSTEMI Patients with Previously Known T2DM and Newly Diagnosed T2DM Overall

Confounding Variables		MACCE		p-value
		No (n=61) n (%) I (Mean ± SD)	Yes (n=68) n (%) I (Mean ± SD)	
Age (years)		(60.49 ± 9.79)	(62.63 ± 8.79)	0.177 ##
Gender	Man	44 (45.36)	53 (54.64)	0.446 ###
	Woman	17 (53.13)	15 (46.88)	
Smokers	No	32 (50.79)	31 (49.21)	0.436 ###
	Yes	29 (43.94)	37 (56.06)	
Hypertension	No	20 (44.44)	25 (55.56)	0.636 ###
	Yes	41 (48.81)	43 (51.19)	
Dyslipidemia	No	14 (36.84)	24 (63.16)	0.125 ###
	Yes	47 (51.65)	44 (48.35)	
Obesity	No	43 (53.09)	38 (46.91)	0.087 ###
	Yes	18 (37.5)	30 (62.5)	
Revascularization	No	41 (42.27)	56 (57.73)	0.047 ###
	Yes	20 (62.5)	12 (37.5)	
LVEF (%)		(45.06 ± 10.56)	(34.62 ± 10.31)	<0.001 ##
HbA1c (%)		(8.41 ± 1.89)	(8.12 ± 2.04)	0.322 ##
	NA	14 (22.95)	13 (19.12)	
Glucose (mg/dL)		(207.66 ± 71.76)	(218.22 ± 84.69)	0.649 ##
FBG (mg/dL)		(169.09 ± 61.47)	(163.16 ± 61.33)	0.580 ##
	NA	8 (13.11)	11 (16.18)	
hsTrop-I (ng/L)		(4 891.08± 0086.35)	(8 494.3 ± 13 295.95)	0.470 ##

#' Independent T Test; '##' Mann Whitney Test; '###' Chi-Square Test
NA: Non-Available; FBG: Fasting Blood Glucose

Based on Table 3, comparing confounding variables in NSTEMI patients, both with previously known T2DM and newly diagnosed T2DM, revealed several important findings related to the incidence of MACCE. The mean age of patients with MACCE was higher (62.63 ± 8.79 years) compared to patients without MACCE (60.49 ± 9.79 years), but this difference was not statistically significant (p = 0.177). Gender, smoker status, and history of hypertension also did not show significant differences between the group with MACCE and those without (p > 0.05). Dyslipidemia and obesity did not differ significantly between groups with MACCE and those without MACCE. However, there was a tendency that patients with obesity experienced MACCE more often (p=0.087). Interestingly, the revascularization variable showed that patients who did not undergo this procedure had more frequent MACCE (p = 0.047), suggesting that revascularization may play a role in lowering the risk of developing MACCE.

Lower LVEF was found in patients with MACCE (34.62 ± 10.31 %) compared to patients without MACCE (45.06 ± 10.56 %), with a statistically significant difference (p < 0.001). This emphasizes the importance of LVEF as a predictor of MACCE incidence. Other variables such as HbA1c, glucose, FBG, and hs-Trop I did not show significant differences. Overall, these results suggest that decreased cardiac function and a lack of revascularization interventions are factors that have a greater influence on the incidence of MACCE, both in patients with previously known T2DM and those newly diagnosed with T2DM.

Important Variables Affecting MACCE

Based on previous analysis, several variables are known to be related to the increased risk of MACCE events in NSTEMI patients with previously known T2DM or newly diagnosed T2DM. These variables include T2DM Status, LVEF, and Revascularization. To further understand which variables are the most significant in predicting MACCE events, an analysis method is used that can capture the complexity of the interaction between these variables. The C50 algorithm is one of the decision tree methods used to create predictive models based on relevant independent variables. This algorithm excels at handling data with confounding variables, as it can perform optimal separation to improve prediction accuracy. In MACCE event prediction, C50 is particularly effective because it can control complex variables such as LVEF and revascularization actions, which often significantly affect outcomes. A study by Lundberg et al. (10) demonstrates the use of C50 algorithms, decision tree methods, and similar algorithms in medical contexts and data handling with complex variables.

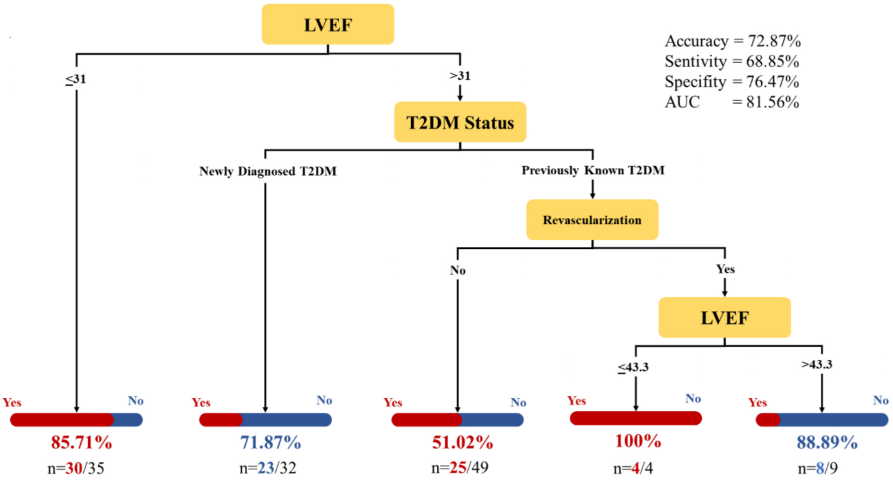

Figure 3. Model C50 MACCE Prediction.

Figure 3 shows that the classification tree using the C50 algorithm has the advantage of controlling confounding variables (11), which enables more accurate and unbiased results for the MACCE event prediction. In the context of this study, the confounding variables controlled were LVEF and revascularization actions. LVEF, which is a measure of left ventricular function, has been shown to be a highly influential factor in the risk of MACCE. By separating patients by LVEF value, this classification tree can directly identify groups with poor heart function (LVEF ≤ 31 %), who have a very high risk of developing MACCE of 85.71 % (n=30/35). Thus, this model controls the effect of LVEF, allowing the analysis of other variables, such as T2DM status, to become more precise and more focused.

Furthermore, when the LVEF >31 %, the classification tree divides patients based on T2DM status and revascularization intervention. With this separation, the model can evaluate the effect of T2DM status on the risk of MACCE without being affected by very low heart function conditions. In patients with newly diagnosed T2DM, the risk of not developing MACCE was 71.87 %. In patients with previously known T2DM, the classification tree further evaluates the impact of the revascularization action. By controlling the variable of revascularization, this model can show that patients with previously known T2DM who do not undergo revascularization have a higher risk of MACCE (51.02 %) than those who undergo revascularization, indicating the importance of this action in reducing the risk. The C50 classification tree not only identifies the primary risk factors but also systematically controls confounding variables, ensuring that the analysis results are more valid and unbiased. By setting up divisions based on key variables such as LVEF and revascularization, this algorithm ensures that the influence of T2DM status on MACCE can be measured more precisely without being interfered with by other variables that might affect the results. This makes the classification tree a powerful tool in clinical practice to help determine more appropriate prevention and intervention strategies, based on a measurable and well-controlled risk profile.

The C50 classification tree used in this study shows an *Area Under the Curve (AUC)* of 81.5 %, which indicates that this model has good predictive ability (12). AUC of more than 80 % is generally considered good in the context of predictive modeling and is often recognized as a strong indicator that a model or algorithm can serve as an effective biomarker (13). AUC above 80 % indicates that the model has a high ability to differentiate between patients at risk of MACCE events and those who do not, thereby improving the accuracy of clinical decisions.

DISCUSSION

Diabetes mellitus is one of the important and independent predictors of mortality in cardiovascular disease (14). Ischemic heart disease affects about 126 million people (1 655 per 100 000), which is about 1.72 % of the world's population. Men are more commonly affected by the disease than women, and the incidence usually begins in the fourth decade and increases with age (15). Several studies state that women with T2DM have a higher risk of developing Ischemic Heart Disease (IHD), including NSTEMI, compared to men. Some of the factors that contribute to the higher risk in women are that women with diabetes tend to have higher insulin resistance and higher visceral fat than men. This increases the risk of atherosclerosis, which is one of the leading causes of ischemic heart disease. Then, after menopause, women will lose the natural cardiovascular protection provided by the hormone estrogen. This leads to an increased risk of atherosclerosis and coronary heart disease, especially in women with Diabetes Mellitus (16). The INTERHEART study also found that diabetes was more closely associated with the risk of AMI in women than in men (OR 4.26 vs. 2.67).

Some studies have also shown that the impact of diabetes on the development of coronary heart disease (CHD) is greater in women than in men. A meta-analysis by Humphries et al. that included 858 507 individuals and 28 203 CHD events found that the relative risk (RR) for developing CHD, comparing individuals with diabetes to those without diabetes, was 44 % higher in women than in men (17). Dyslipidemia is more common in newly diagnosed T2DM (82.93 %) compared to previously known T2DM (64.77 %). Smoking, hypertension, dyslipidemia and obesity

are risk factors for the occurrence of ischemic heart disease (14).

Hypertension was found to be the most significant modifiable CV risk factor, accounting for 48 % of all strokes and 18 % of all coronary events (18). Poznyak et al. showed a positive association between increased blood pressure and the prevalence of coronary artery calcium, as well as the incidence of cardiovascular events associated with atherosclerosis. Another significant modifiable risk factor is smoking. It is known that smokers over the age of 60 have twice the risk of developing atherosclerosis and subsequent cardiovascular disease compared to those who are not smokers. For people under the age of 60, the risk is five times higher (18). Smoking can trigger myocardial infarction in individuals with minimal atherosclerosis or even with normal coronary arteries, especially in young people, causing temporary coronary vessel occlusion, as a result of the formation of thrombus, coronary artery spasm, or both (19).

We found that obesity was more common in patients with previously known T2DM (40.91 %) than in newly diagnosed T2DM (29.27 %), reflecting differences in lifestyle management between the two groups. Obesity is the most critical factor in the development of coronary heart disease (20). Obesity is currently presented as a pro-inflammatory condition with an expanded flow of inflammatory cytokines, such as interleukin-6 (IL-6) and tumor-necrosis factor-alpha (TNF-α), along with increased leptin secretion (21).

Mahabadi et al., reported that visceral adipose tissue and pericardial fat are associated with coronary heart disease (CHD) and myocardial infarction. The Framingham Heart Study highlighted the pathogenic role of obesity in the onset of heart failure, affecting 11 % of men and 14 % of women. Modification of risk factors has the potential to reduce the risk of myocardial infarction by more than 80 % to 90 % (22). Central obesity is associated with hypercholesterolemia (AOR: 5.2, 95 % CI 1.9-14.3) and elevated LDL cholesterol (AOR: 5.1, 95 % CI 1.6-15.8). High blood pressure, overweight, and abdominal obesity were significantly associated with hypertriglyceridemia ($p<0.05$) (23).

In patients with NSTEMI who have diabetes mellitus and other comorbidities, the decision to undergo revascularization should be carefully considered, taking into account the risks and benefits. An individualized approach that considers the patient's overall condition is often preferred, considering conservative medical therapies as a viable alternative if the risk is too high (24). Loss of optimal therapy time for problematic coronary artery reperfusion has been associated with adverse composite events, including extensive myocardial infarction, long duration of hospitalization, and higher mortality rates (25).

Decreased LVEF in patients with diabetes who have been suffering from diabetes for a long time tends to be worse compared to patients who have just been diagnosed, due to several pathological factors that occur due to Chronic Diabetes (26). When not well controlled, it has a cumulative and progressive impact on the heart, which can lead to Diabetic Cardiomyopathy. This is due to the increase in Advanced Glycation End Products (AGEs) and Reactive Oxygen Species (ROS) for a long time (27).

HbA1c values are higher in long-term diabetic patients compared to patients newly diagnosed with diabetes, because HbA1c reflects the average blood glucose level over the past 2-3 months. Duration of chronic hyperglycemia and more severe insulin resistance in patients with a long history of diabetes lead to glucose accumulation in hemoglobin, which will result in a higher HbA1c than in patients with newly diagnosed T2DM (28).

In patients with a longer history of T2DM, the increase in glucose production by the liver (Gluconeogenesis) is greater, resulting in higher fasting blood sugar levels because the body produces glucose excessively during the night. This is different from patients who have just been diagnosed with T2DM, where the glucose control mechanism is still relatively more effective, so fasting blood sugar levels will be lower (29). In contrast to glucose, higher results were obtained in patients with newly diagnosed T2DM (217.9 ± 66.19) compared to patients with previously known T2DM (211.05 ± 84.18). Patients newly diagnosed with T2DM often have

higher levels of glucose compared to long-time diabetic patients (30). This can be caused by late detection, unstarted treatment, and uncontrolled postprandial hyperglycemia (31).

Markers of cardiomyocyte necrosis, hs-Trop I, were found to be higher in the newly diagnosed T2DM group (8 453.38 ± 14 068 ng/L) compared with previously known T2DM (6 047.11 ± 10 919.71 ng/L). Cardiac troponins are a component of the myofibril apparatus and are released into the circulation after cardiomyocyte injury (32). In patients with newly diagnosed diabetes, hyperglycemia is generally higher and uncontrolled, especially before it is diagnosed. Uncontrolled hyperglycemia leads to more acute vascular damage and microvascular disorders that can worsen the ischemic state of the heart, causing troponin to become higher (33). These differences highlight the importance of a holistic approach in the management of NSTEMI patients with diabetes mellitus, both in newly diagnosed patients and in patients with a previous history of Diabetes Mellitus, to prevent further cardiovascular complications.

In a study conducted by Ding et al., patients with newly diagnosed T2DM were independently associated with better disease-specific health status and quality of life ($p \leq 0.04$) compared to pre-existing diabetes. No significant differences in mortality and in-hospital complications were found between newly diagnosed T2DM patients and pre-existing T2DM or non-T2DM (34).

Our study is in line with a study conducted by Li et al. (35), which found that compared to patients without diabetes, participants with longer diabetes duration and poorer glycemic control had a higher risk of fatal/non-fatal cardiovascular disease. Among participants with diabetes, the fully adjusted hazard ratios (HR) for the duration of diabetes 5 to <10 years, 10 to <15 years, and ≥15 years were 1.15 (95 % CI 0.99, 1.34), 1.50 (95 % CI 1.26, 1.79), and 2.22 (95 % CI 1.90, 2.58; P-trend <0.01), compared to patients with diabetes duration <5 years. In addition, T2DM patients with the most extended disease duration (≥15 years) and poorer glycemic control (HbA1c ≥64 mmol/mol [8 %]) had the highest risk of fatal/non-fatal cardiovascular disease (HR 3.12, 95 % CI 2.52, 3.86).

Several mechanisms may explain the relationship between the duration of diabetes and cardiovascular disease. The duration of diabetes, as a marker of cumulative exposure to chronic hyperglycemia, has been associated with atherosclerotic lesions, including the thickness of the media and intima, as well as fibroatheroma with a thin coating, which have adverse effects on both small and large blood vessels. In addition, other disorders caused by long-lasting hyperglycemia, such as endothelial dysfunction and abnormalities in fibrinogen and clotting mechanisms, can also contribute to the development of adverse effects in patients with a long history of diabetes (35).

The incidence of heart failure was more common in patients with previously known T2DM (92.86 %) compared to patients newly diagnosed with T2DM (7.14 %), with a statistically significant difference ($p = 0.002$) with an OR value of 8.17. This is in line with the research conducted by Li et al. (35). Those who had a heart failure incidence with a score (HR 3.23, 95 % CI 2.28-4.57) were identified as independent risk factors for all-cause mortality. This is also in line with the study conducted by Abdissa et al. (36), which found that T2DM was significantly associated with the incidence of HF [HR 2.04, 95 % CI: 1.32–3.14, $p = 0.001$]. Poor glycemic control is associated with an increased risk of heart failure. For every 1 % increase in HbA1c, a glycemic control indicator, the risk of heart failure increases by 8 % (36).

In the Platelet Inhibition Registry in ACS Evaluation Study (PIRAEUS), patients with T2DM had significantly higher in-hospital mortality rates due to all-cause (HR 1.66; 95 % CI 1.42-1.94), cardiovascular mortality (HR 2.33; 95 % CI 1.78-3.03), and a higher risk of recurrent infarction events. Huxley et al. (37) reported that 37 studies on type 2 diabetes and fatal coronary heart disease among a total of 447 064 patients were identified. The rate of fatal coronary heart disease was higher in patients with diabetes than in those without it (5.4 % vs. 1.6 %) (37).

In a study conducted by Rawshani et al., it was found that diabetic patients compared to the control group had a risk ratio of acute myocardial infarction of 0.84 (CI 95 %, 0.75 to 0.93).

However, if this risk factor is not controlled, it will show a linear relationship with the risk of acute myocardial infarction (38,39). In our study, although the incidence of recurrent myocardial infarction was seen more often in patients with previously known T2DM (66.67 %) than in newly diagnosed T2DM (33.33 %), this difference was not statistically significant (p = 0.904). Our study compared patients with previous and newly diagnosed T2DM, and found that when patients were diagnosed with T2DM, the incidence of recurrent myocardial infarction could still occur.

Jakobsson et al., reported that patients with T2DM after Acute Myocardial Infarction still have a higher risk of post-AMI stroke (40). Mosenzon et al. reported a higher risk of stroke in people with type 2 T2DM compared to people without diabetes (41). In the meta-analysis, the adjusted relative risk of each stroke associated with diabetes was 2.28 (95 % CI: 1.93-2.69) in women, while in men it was 1.83 (95 % CI: 1.60-2.08) when compared to individuals without diabetes. Merkler et al., found that patients with AMI, compared with those without AMI, had a nearly 3-fold risk of ischemic stroke during the first 4 weeks after the first onset of AMI (42).

Our study is in line with The Northern Manhattan Study, stating that 244 patients with ischemic stroke, 22 % had a previous history of diabetes, and 10 % were newly diagnosed with diabetes; the duration of diabetes was associated with ischemic stroke. Compared to non-diabetic patients, those who had diabetes for 0 to 5 years (adjusted HR, 1.7; 95 % CI, 1.1-2.7), 5 to 10 years (adjusted HR, 1.8; 95 % CI, 1.1-3.0), and 10 years (adjusted HR, 3.2; 95 % CI, 2.4-4.5) had a higher risk. The risk increases by 3 % each year, and triples in diabetes ≥ 10 years (43).

Several potential mechanisms may explain the relationship between diabetes and stroke duration. There is evidence of a link between the duration of diabetes and atherosclerotic lesions, including medial intima thickness and thin fibroatheroma of the hood. Carotid plaque thickness has been shown to predict ischemic stroke. In addition, hypertension is twice as common in those with diabetes as in people without diabetes, and long-term hypertension causes accelerated microvascular and macrovascular complications among those with diabetes. The risk of microalbuminuria has been shown to increase as the duration of diabetes increases, and microalbuminuria has been reported as a strong and independent risk factor for stroke among diabetic patients. Other potential mediators may be endothelial dysfunction and abnormalities in fibrinogen and clotting mechanisms (43).

The association between the achieved reduction in HbA1c and non-fatal stroke was significant and explained nearly all the relationship between major adverse cardiovascular events (MACCE) and the decrease in HbA1c. For each greater 1 % (10.93 mmol/mol) decrease in HbA1c mean risk, the risk of non-fatal stroke decreased by 41 % (44). Donahoe et al., reported that mortality on day 30 was significantly higher among patients with diabetes than without diabetes who had UA/NSTEMI (2.1 % vs. 1.1 %, P.001). Patients with diabetes, when presenting with ACS were associated with significantly higher mortality 1 year after UA/NSTEMI (HR 1.65; 95 % CI, 1.30-2.10) (45).

Our research aligns with the findings reported in the Valiant Trial, which revealed that patients with newly diagnosed diabetes were younger and had fewer comorbidities compared to patients with previously diagnosed diabetes. At 1 year, patients with pre-known and newly diagnosed diabetes had an equally increased risk of mortality (HR1.43; 95 % CI 1.29 to 1.59 and HR, 1.50; 95 % CI, 1.21 to 1.85, respectively) and cardiovascular events (HR, 1.37; 95 % CI, 1.27 to 1.48 and HR, 1.34; 95 % CI, 1.14 to 1.56) (46).

This indicates that the mortality rate between patients with previously known T2DM and those with newly diagnosed T2DM remains the same, with a high risk of death. The association between the duration of T2DM and in-hospital mortality in AMI patients can be explained by a progressive increase in microvascular and macrovascular complications that usually parallel the duration of the disease. In addition, the longer duration of T2DM was previously associated with a greater burden of coronary artery disease. Therefore, it can be concluded that the duration of T2DM reflects the patient's increasing risk of acute cardiac events (47). The risk of non-cardiac mortality in diabetic patients is equivalent to the risk of death from AMI, only in a small percentage of men aged 50 years or older, so

that with increasing age, it will be in line with the risk of MACCE incidence (48).

LVEF, reflecting left ventricular function, is associated with the incidence of MACCE in patients with NSTEMI who are previously known to have T2DM and newly diagnosed T2DM. In a study by Brezinov et al., subjects with LVEF < 30 % and LVEF 30 % to 49 % had a 4.49- and 1.83-fold greater risk of death compared to the 50 % LVEF group, which served as the reference group (HR 4.49; [95 % CI 3.57-5.61] and HR 1.83; [1.49-2.24]) (49).

Ghorashi et al., found that a very severe decrease in LVEF increased the mortality rate in hospitals, while a mild and moderate reduction in the left ventricular ejection fraction did not increase the mortality rate (50). This is in line with our study, lower LVEF was found in patients who experienced MACCE in NSTEMI patients with a previously known T2DM and newly diagnosed T2DM overall LVEF (34.62 ± 10.31 %) compared without MACCE (45.06 ± 10.56 %), with p-value < 0.001 emphasizing that decreased left ventricular function is strongly associated with an increased risk of MACCE.

In the Ram et al. study, NSTEMI patients with Diabetes Mellitus who underwent Coronary Artery Bypass Grafting (CABG) compared to Percutaneous Coronary Intervention (PCI), had a lower rate of recurrent MI at 30 days, and a lower rate of MACE defined as mortality, recurrent MI, or stroke at 30 days, with no difference in 30-day mortality or 1-year (51). The Fragmin and Fast Revascularization during Instability in Coronary artery disease II trial (FRISC II) found a more important benefit in diabetic patients than in non-diabetic patients in reducing the risk of death and relative (39 vs. 28 %) and absolute (9.3 vs. 3.1 %) MI at 1 year and an early invasive strategy (all invasive procedures within 7 days) reduced the mortality rate or MI from 29.9 % to 20.6 % in T2DM patients (52).

Although long-standing diabetes and chronic hyperglycemia lead to chronic systemic inflammation, increased insulin resistance, progressively worsening atherosclerosis, endothelial dysfunction, and loss of vascular elasticity. Diabetes is also associated with a state of hypercoagulability and increased platelet activity. Although revascularization can reopen blocked blood vessels, the risk of thrombosis remains high due to increased platelet activity (53).

Mahmud et al. (54) found that 19 % of subjects with T2DM had cardiac troponin I (CTnI) levels that increased above the 99th percentile (1.3 ng/mL). A significant increase in CTnI was observed among participants with comorbidities of T2DM and hypertension. Additionally, the diabetes group had significantly increased total levels of CK and CK-MB ($p = 0.001$) compared to healthy controls. In line with our study, Welsh et al. (55) found that the value of hs-troponin was strongly associated with cardiovascular mortality.

The mechanism of diabetes mellitus can accelerate AMI influenced by hyperglycemia and insulin resistance. Most T2DM patients have insulin resistance, hyperinsulinemia, and vascular calcification, which not only promotes the occurrence of atherosclerosis but also accelerates the development of stable plaques into unstable plaques or rupture of plaques that cause thrombosis. In addition, the effect of hyperglycemia on decreased glomerular filtration resulted in decreased troponin elimination. By affecting the microcirculation of the heart, hyperglycemia causes microvascular damage, and the consequence is ischemia, which contributes to an increase in troponin concentrations (56).

In patients with acute myocardial infarction (AMI) and diabetes mellitus, increased cardiac troponin levels are associated with increased arterial stiffness, a consequence of increased oxidative stress, endothelial dysfunction, and accelerated apoptosis. Hyperglycemia in patients with Diabetes Mellitus also causes ATP deficiency, which reduces creatine phosphate synthesis, thereby activating the creatine kinase enzyme. When the ratio of creatine phosphate to creatine kinase decreases, this leads to inhibition and leakage of enzymes into the blood circulation and an increase in creatine kinase levels in the blood (54).

In this study, we also conducted a multivariate analysis of variables known to be related using the C5.0 algorithm. This analysis method is capable of capturing the complexity of interactions between variables. In the context of MACCE event prediction, C5.0 is particularly effective because it is able to control complex variables

such as LVEF and revascularization actions, which often significantly affect outcomes. A study by Lundberg et al. (10) demonstrates that the use of the C5.0 algorithm, a decision tree method, and similar algorithms in medical contexts and data handling with complex variables enables more accurate and unbiased prediction results for MACCE events.

The C5.0 classification tree used in this study shows an Area Under the Curve (AUC) of 81.56 %, which shows that this model has good predictive ability (12). An AUC of more than 80 % is generally considered good in the context of predictive modeling and is often recognized as a strong indicator that a model or algorithm can serve as an effective biomarker (13).

Limitations of this study include its single-center, retrospective design and the inconsistency in revascularization therapy. Future research should explore the relationship between previously known and newly T2DM in non-ST-segment elevation myocardial infarction (NSTEMI) patients, with a focus on both short- and long-term clinical outcomes following acute myocardial infarction. Studies with larger sample sizes and extended follow-up periods are recommended. Additionally, future investigations should consider whether previously known T2DM is pharmacologically controlled and aim to standardize revascularization strategies in NSTEMI patients with diabetes based on established clinical guidelines

CONCLUSIONS

Our study demonstrates that diabetes status significantly influences clinical outcomes in NSTEMI patients. Patients with previously known T2DM are at a higher risk for major adverse cardiovascular and cerebrovascular events (MACCE) and heart failure within six months compared to those with newly diagnosed T2DM. Key determinants of adverse outcomes include reduced left ventricular ejection fraction and lack of revascularization. While the severity of coronary lesions did not differ significantly between the groups, the presence of diabetes, regardless of duration, was associated with multivessel disease. These findings highlight the importance of early identification, optimal glycemic control, and evidence-based revascularization strategies to improve short-term outcomes in NSTEMI patients with diabetes.

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