

Non-ST segment elevation coronary syndrome: Prognostic value of the sum of the magnitude of ST segment depression

Syndrome coronarien sans sus décalage de ST: Valeur pronostique de la somme du sous décalage de ST

Héla Ben Turkia, Hanene Ghazali, Syrine Keskes, Ines Chermiti, Mouna Gamoudi, Sami Souissi

Regional hospital of Ben Arous, Medical faculty of Tunis, Tunis El Manar university

ABSTRACT

Introduction: ST segment depression is a highly predictive marker of mortality in non-ST-segment elevation acute coronary syndrome (NSTEMI). The aim of our study was to evaluate the prognostic value of the magnitude and the cumulative sum of ST depression in NSTEMI in term of major cardiovascular events (MACE) at six months.

Methods: A retrospective observational study was conducted over six years. We included NSTEMI patient with ST segment depression > 0.5 mm in at least on lead. The cumulative sum of ST-segment depression was calculated of each patient. Evaluation of MACE (Death, stroke, Myocardial infarction, Major bleeding, recurrent angina) was performed six months. logistic regression model was developed to assess the prognostic value of the magnitude and distribution of ST segment depression in predicting MACE.

Results: Inclusion of 287 patients. Mean age = 62 ± 11 years. Sex ratio = 1.7. Comorbidities (%): hypertension (59), diabetes (45), dyslipidemia (33), coronaropathy (28). Mean ST segment depression = 5 ± 4.5 mm. MACE were found in 27% of patients. Mean cumulative sum in patients how developed MACE at six months was 6.5 ± 5 mm versus 4 ± 3.3 mm in not MACE ($p < 0.001$). In multivariate analysis a cumulative sum of ST-segment depression > 7 mm (aOR = 5.34, $p < 0.001$, 95% CI [2.71; 10.51]) were independently associated with MACE at six months. Positive correlation was found between the sum of ST segment depression, the number of leads with ST segment depression and the severity of coronary artery disease with ($r = 0.352$; $p < 0.001$) and ($r = 0.361$; $p < 0.001$) respectively.

Conclusion: The cumulative sum of ST-segment depression is a strong, independent prognostic factor in NSTEMI and correlates with the angiographic severity of coronary artery disease, offering a simple tool for early risk stratification.

Keywords: Myocardial infarction; Prognosis; Emergency; Electrocardiogram (ECG).

RÉSUMÉ

Introduction: L'analyse quantitative du sous décalage du segment ST, en mesurant son amplitude, est un facteur pronostique important dans la prise en charge du syndrome coronarien aigu sans sus décalage du segment ST (SCA non-ST+).

L'objectif du travail était de Déterminer si la somme cumulée du sous décalage de segment ST permet de prédire la survenue d'évènement cardiovasculaires majeurs (MACE : décès, infarctus, récurrence angineuse, accidents vasculaires cérébraux)

Méthodes: Etude retrospective observationnelle sur six ans. Inclusion des patients avec SCA non-ST+ avec à l'ECG un sous décalage se $ST > 0,5$ mm dans au moins une dérivation Mesure de la somme cumulée du sous décalage ST, en millimètres (mm), dans toutes les dérivations montrant un sous décalage $ST > 0,5$ mm sur l'électrocardiogramme initial. Le pronostic a été évalué sur la survenue de MACE à six mois.

Résultats: Inclusion de 287 patients. Age moyen = 62 ± 11 ans. Sex ratio = 1,7. Comorbidités (%): hypertension (59), Diabète (45), dyslipidémie (33), coronaropathie (28). Moyenne de la somme cumulée été de $5 \pm 4,5$ mm. MACE ont été notés chez 27% des patients. La moyenne de la somme cumulée du sous décalage du segment ST était plus élevée chez les patients avec MACE: $6,5 \pm 5$, mm vs. $4 \pm 3,3$ mm, $p < 0,001$. La somme cumulée du sous décalage ST à l'admission était prédictive de survenue de MACE à partir d'un seuil de 7 mm avec un OR=5,34, IC 95% [2,71 ; 10,51], $p < 0,001$.

Conclusion : Une somme cumulée du sous décalage du segment ST supérieur à 7 mm est significativement associée à la survenue de MACE à six mois.

Mots clés: Infarctus du myocarde, Pronostic, Urgence, Électrocardiogramme

Correspondance

Héla Ben Turkia

Regional hospital of Ben Arous, Medical faculty of Tunis, Tunis El Manar university

Email: Hela.benturkia@fmt.utm.tn

INTRODUCTION

Coronary heart disease is a major cause of morbidity and mortality globally and it constitutes a real health problem which affects both developed and developing countries [1].

Non-ST segment elevation acute coronary syndrome (NSTEMI) accounts for approximately 2 to 2.5 million hospital admissions annually worldwide [2]. Early identification of high-risk patients is crucial for adequate management of those patients so that they can benefit from an invasive strategy on time [3].

The prognostic value of ST segment deviation has been studied since 1997 specifically in stratifying the risk of patients with coronary artery diseases and assessed by many other studies [4,5].

Kaul et al. [6] found that the quantification of the amount and distribution of ST segment depression can identify high risk patients independent of clinical and biological variables. This study also found that patients with ST segment depression of ≥ 2 mm in two contiguous leads had approximately six times the mortality risk at one year. ST segment depression and its association with the angiographic severity of coronary artery diseases have been assessed in few studies, but quantification of this electrocardiographic parameter and its correlation with early and late prognosis based on major cardiovascular events (MACE) have rarely been studied.

The aim of our study was to evaluate the prognostic value of the magnitude and the sum of ST depression in NSTEMI in terms of major cardiovascular events (MACE) at six months.

METHODS

We conducted retrospective, observational and single-center study over a six years period from June 2011 to June 2017.

Inclusion criteria

Consecutive patients aged over 18 years, who presented to the emergency department (ED) medical area for NSTEMI, with documented ST-segment depression in at least one lead on the initial electrocardiogram (ECG).

Exclusion criteria

Patients with an ST segment depression due to ventricular hypertrophy or metabolic disease (hypokalemia...) and those with another final diagnosis after investigations.

Data collection

Data collected from patients included demographic data, comorbidities, risk factors for acute coronary syndrome, symptoms that caused ED consultation, clinical presentation, ECG features and ED evaluation, ischemic risk according to the GRACE score, bleeding risk-prediction factors according to the CRUSADE score, anti-

thrombotic and anti-ischemic management, patients' outcome, final disposition (discharge, admission, or death) and prognosis at six months.

Patient follow-up was performed at six months for adverse events MACE (Death, stroke, Myocardial infarction, Major bleeding, recurrent angina) was performed during a six month period. We used telephone follow-up, in addition to record review.

The study population was divided into two cohorts: MACE+ Group: patients developed MACE and MACE – Group. A logistic regression model was developed to assess the prognostic value of the magnitude and distribution of ST segment depression in predicting six-months MACE.

Study procedure

Twelve lead ECG had been recorded in the first 10 minutes after the first medical contact. ST segment shift was measured in all leads at 80 ms after the J point for ST segment depression.

ST segment depression was measured at 1mm intervals, with every fraction rounding to the nearest whole number.

The distribution of ST segment depression was examined in four regions anterior (leads V1 to V4), inferior (leads II, III and aVF), lateral (leads I, aVL, V5 and V6) and posterior (V7,V8,V9).

The cumulative sum of ST-segment depression and the total number of leads demonstrating ST-segment depression were calculated.

Evaluation was based on Angiographic severity of coronary artery disease defined by the number of vessels with stenosis $>70\%$ and the development of MACE (Death, stroke, Myocardial infarction, Major bleeding, recurrent angina) at 6 months.

Follow up was realized by contacting patients or their relatives on phone.

Data analysis

Statistical analysis was carried out with SPSS (version 18.0) statistical software package.

Data was presented as frequency and percent for categorical variables and as mean with standard deviation for quantitative variables.

An univariate analysis comparing the two groups was performed, with the chi-square test with Yates' correction or Fisher's exact test when appropriate, odds ratio (OR) with 95% confidence intervals (CI), and the unpaired t-test.

The logistic regression analysis with MACE+ as dependent variable was there run. The analysis was performed with a binary logistic regression and "enters" method, with an entry criterion of 0.05 and removal criteria of 0.10.

Differences were considered to be statistically significant with $p < 0.05$ or when the 95% confidence interval (CI) of the odds ratio (OR) excluded the value of 1.

Correlations between magnitude of ST segment depression and angiographic severity was measured by Pearson's correlation test.

RESULTS

Characteristics of the study population

During the six years of the study, 287 patients were included. The figure 1 shows the inclusion flowchart.

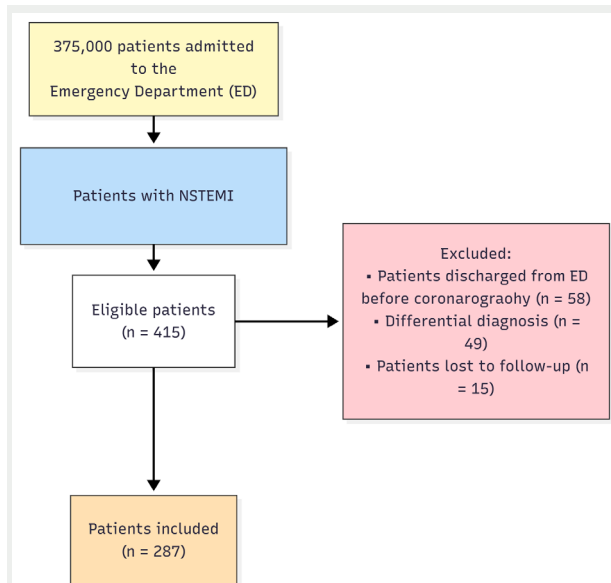


Figure 1. Inclusion flowchart

The sex-ratio was 1.7 and the mean age was 62 ± 11 years. Sixty percent of patients were aged more than 65 years old.

Cardiovascular risk factors identified were n (%): Hypertension 170(59), Diabetes 130 (45), Dyslipidemia 94 (33), Smoking 90 (32), History of coronaropathy 79(28) A total of 125 patients presented with more than three cardiovascular risk factors. Baseline clinical vital signs at admission are summarized in Table 1.

Table 1. Baseline Clinical Parameters of the Study Population

	Mean	SD	Min	Max
Systolic blood pressure (mmHg)	143	30	80	270
Diastolic blood pressure (mmHg)	80	14	50	120
Heart rate (bpm)	84	20	50	180
Respiratory rate (cpm)	16	4	12	40

SD: standard deviation; bpm: beat per minute; cpm: cycle per minute; Min: minimum; Max: Maximum

The mean number of leads with ST segment depression was 5 with extremes of 1 to 15 leads.

The ECG walls of ST segment depression were lateral for 60% of patients, inferior wall for 38 %, Posterior for 31% and 12% and 11% for the anterior and apical wall respectively.

The mean cumulative sum of magnitude of ST segment depression was 5 ± 4.5 mm.

The follow up at six months showed that 27% of patients had developed MACE: death 34 (12%), myocardial infarction 66 (24%) and two cases of stroke.

The comparative study of patients developing MACE (MACE+) versus. the other patients (MACE-) are resumed in table 2.

Table 2. Comparative study between MACE+ and MACE- groups.

Factor	MACE + n=76 26%	MACE- n=211 73%	p-value
Age (years) Mean± DS	65±10	60±11	0.004
Sex Ratio	2.45	1.5	NS
Cardio-vascular risk factors n (%):			
. Hypertension	45 (60)	125 (58)	NS
. Diabetes mellitus	38 (50)	92 (43)	NS
. Dyslipidemia	23 (30)	71 (34)	NS
. Tabagisme	25 (32)	65 (31)	NS
. Past history of coronaropathy n(%)	29 (38)	73(34)	NS
Magnitude of ST depression (mm) Mean± DS	1.4±0.7	0.7±0.4	<0.001
Sum of ST depression Mean± DS	6.5±5	4±3.30	<0.001
ECG walls n (%) :			
Anterior	11 (15)	23 (11)	NS
Inferior	21 (26)	21 (26)	NS
Lateral	50(65)	120 (55)	NS
Posterior	0	1	NS

The analysis of ROC curve identified that the cut-off a cumulative sum of ST segment as a predictive factor of MACE was >7 mm with AUC=0.68; $p<0.001$ CI 95% [0.615-0.758] (Figure 2).

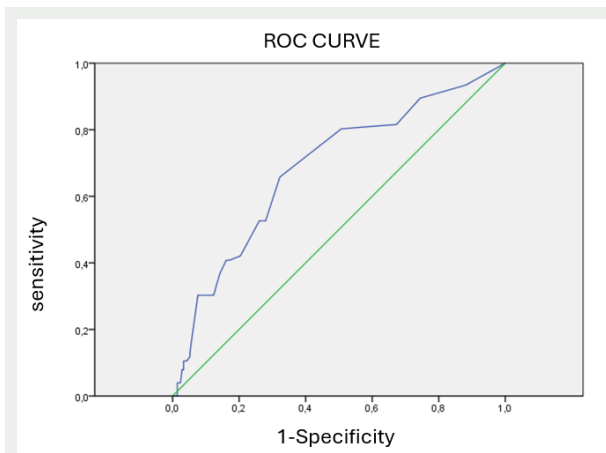


Figure 2. ROC CURVE of MACE at 6 months

Multivariate analysis identified 3 independent factors of developing MACE (table 3)

- Age >65 years
- ST segment depression > 2 mm
- Cumulative sum >7 mm

Table 3. Multivariate analysis of predictive risk factors of MACE

	Adjusted OR	CI 95%	P
Age >65 years	1,80	[1,10 ; 2 ,50]	0,03
ST segment depression > 2 mm	5,52	[3,14 ; 9,70]	< 0,001
Cumulative sum > 7 mm	5,34	[2,71 ; 10,51]	< 0,001

Patients with a cumulative sum of magnitude of ST segment depression > 7 mm had 5 times risk developing MACE than other patients.

Sensitivity, specificity, Positive predictive value and negative predictive value of the sum of ST depression >7mm were respectively 44, 85, 60 and 78 % respectively. Comparative study of patients with the sum of ST depression >7 mm versus patients with a sum < 7 mm is detailed in table 4.

Table 4. Comparative study of patients according to the sum of magnitude of ST depression.

		Sum of ST <7mm (n=220)	P
Male gender n (%)	41(61)	140(63)	NS
Age (years) mean±SD	65±9	61±11	NS
Comorbidities n(%):			
Hypertension	41(61)	129(59)	NS
Diabetes mellitus	30(45)	100(45)	NS
Dyslipidemia	18(26,9)	76(34,5)	NS
Smoking	21(32)	69(32)	NS
Coronaropathy	21(32)	81(37)	NS
Parameters at admission:			
Systolic blood pressure (mmHg) Mean ± SD	151±33	140±26	NS
Heart rate (bpm) Mean± SD	87±20	82±18	NS
SpO2 (%) Mean± SD	97±3	97±3	NS
Biology:			
Hb (g/dl) Mean± SD	13.6±2	13.6±3	NS
Creatinine(mmol/l) mean ± SD	107±80	109±90	NS
Myocardial infarction n(%)	31(51)	76(36)	0,036
Number of culprit artery mean ± SD	1.6±0.7	1.4±0.7	NS
MACE at 6 months			
Death n (%)	15 (28)	19 (10)	<0.001
Myocardial Infarction n (%)	10 (18.5)	16 (8)	<0.001
Stroke n	0	2	NS

Positive correlation was found between the cumulative sum of ST segment depression, the number of leads with ST segment depression and the severity of coronary artery disease with ($r=0.352$; $p<0.0,1$) and ($r= 0.361$; $p<0.001$) respectively.

DISCUSSION

The most important finding of this study was that higher cumulative sum of the magnitude of ST segment depression is strongly linked to poor prognosis and the severity of angiographic artery disease.

The poor prognosis in this present study was based on developing MACE at 6 months.

Predictive factors for developing MACE have been extensively studied in literature, and many clinical and demographic determinants have been identified [7]. The most important predictive factor identified was advanced age [8]. In the present study, age>65 years was a significant independent predictive factor of developing MACE with an OR=1.8 and $p<0.001$.

The risk assessment of patients with NSTEMI is based on many tools. The European society of cardiology

recommends the use of the GRACE score for ischemic risk stratification [9]. This score contains clinical, electrocardiographic and biological parameters.

In our study, the independent predictive factors of MACE, apart from age, were ST segment depression >2mm and cumulative sum >7mm.

The use of the ECG as a valuable risk assessment tool, especially regarding the ST segment depression is widely studied in the literature and was identified as a predictive factor of MACE [5,10].

Cannon et al. [11] found that the admission ECG was a very useful in risk stratifying patients with NSTEMI and ST segment deviation >0.5 mm can identify high risk patients.

Barrabés J et al.[12] found that the presence, magnitude and extent of ST segment depression were associated with an increased mortality.

Kaul et al.[6] found the powerful prognostic value of the magnitude and distribution of ST segment depression in predicting unfavorable events in both the short and long term. They also demonstrate that the extent of ST segment depression is an independent and important modulator of the risk of short- and long-term death [6]. Khan et al.[13] founded that early complications were more frequent in patient with ST segment depression ≥ 2 mm.

While most previous studies were interested primarily in the maximal magnitude of ST-segment depression as a predictive factor for MACE development, our investigation focused specifically on the cumulative sum of the magnitude of ST-segment depression across all leads.

This relatively new concept was well studied in the first time on 2005 by Savonitto et al. [14] who found that in patients with NSTEMI, the cumulative sum of ST segment depression in all ECG leads was a powerful predictor of all cases mortality at 30 days, independent of clinical variables.

In this same study, Savonitto found a positive correlation between the cumulative sum of ST segment depression and the extent and severity of coronary artery diseases. Those results are observed by Miah et al. [15] who noticed a positive correlation between the sum of the ST segment depression and Vessel score ($r=0.435$; $p<0.001$). In our study, a positive correlation was found between the sum of ST segment depression, the number of leads with ST segment depression and the severity of coronary artery disease with ($r=0.352$; $p<0.001$) and ($r= 0.361$; $p<0.001$) respectively.

The cumulative sum of magnitude of ST segment depression can predict the severity of coronary artery disease and is a strong predictive factor of developing MACE.

An important clinical observation in our study's flowchart was that 58 patients did not undergo coronary angiography and was discharged from ED due to unavailable coronarography or high risk conditions. In real-world clinical practice, several factors explain that a proportion of NSTEMI patients may not benefit from an invasive strategy. First, patients with severe comorbidities such as advanced chronic kidney disease due to contrast-

induced nephropathy risks, active malignancies, or severe cognitive impairment, frequently lead clinicians to opt for conservative management [16]. Second, high baseline bleeding risk (e.g., high CRUSADE score, recent major bleeding, or dual antiplatelet therapy contraindications) often tilts the risk-benefit ratio away from invasive procedures [17]. Third, procedural access issues, patient refusal, or death occurring rapidly after admission before cath-lab transfer represent unavoidable barriers in emergency settings [18]. Our data emphasizes that despite these clinical limitations, risk-stratifying these non-invasive patients using simple ECG criteria remains paramount.

A notable limitation of the identified > 7 mm cumulative ST-segment depression threshold is its relatively low sensitivity (44%), meaning that it would fail to identify 56% of patients who ultimately develop a 6-month MACE if utilized as a standalone screening tool. From a clinical perspective, this low sensitivity implies that a cumulative sum be used to safely "rule out" high-risk patients or justify a conservative approach and should be integrated in a new stratification risk score.

Although novel biochemical markers continue to emerge for risk stratification in NSTEMI, our study and literature findings show that common clinical variables and systematic and quantitative ECG assessment continue to offer potent tools for risk stratification.

The cumulative amount of ST-segment depression should be considered in future multivariate analyses of the incremental prognostic value of novel biomarkers.

CONCLUSION

This study shows that the magnitude and the sum of ST segment depression are an important prognostic factor in NSTEMI. We also found a positive correlation between the sum of the magnitude of ST segment depression and severity of coronary artery disease. Those findings demonstrate that the baseline ECG can offer a potent tool for risk stratification.

Developing a new risk score considering the sum of magnitude of ST segment depression can improve the care strategy of patients with NSTEMI by identifying high risk patients, early triage and more aggressive therapies. This may provide a very simple and effective base line predictor of high-risk patients and severity of coronary artery disease in the patients of non-ST segment elevation acute coronary artery syndrome.

REFERENCES

1. Chaturvedi V, Bhargava B. Health care delivery for coronary heart disease in India--Where are we headed? *Am Heart Hosp J*. 2007;5(1):32-37.
2. Cannon null. Optimizing the Treatment of Unstable Angina. *J Thromb Thrombolysis*. 1995;2(3):205-218.
3. Zaacks SM, Liebson PR, Calvin JE, Parrillo JE, Klein LW. Unstable angina and non-Q wave myocardial infarction: does the clinical diagnosis have therapeutic implications? *Journal of the American College of Cardiology*. 1999;33(1):107-118.
4. Cannon CP, McCabe CH, Stone PH, Rogers WJ, Schactman M, Thompson BW, et al. The electrocardiogram predicts one-year outcome of patients with unstable angina and non-Q wave myocardial infarction: results of the TIMI III Registry ECG Ancillary Study. *Thrombolysis in Myocardial Ischemia. J Am Coll Cardiol*. 1997;30(1):133-140.
5. Diderholm E, Andrén B, Frostfeldt G, Genberg M, Jernberg T, Lagerqvist B, et al. ST depression in ECG at entry indicates severe coronary lesions and large benefits of an early invasive treatment strategy in unstable coronary artery disease; the FRISC II ECG substudy. The Fast Revascularisation during InStability in Coronary artery disease. *Eur Heart J*. 2002;23(1):41-49.
6. Kaul P, Fu Y, Chang WC, Harrington RA, Wagner GS, Goodman SG, et al. Prognostic value of ST segment depression in acute coronary syndromes: insights from PARAGON-A applied to GUSTO-IIb. PARAGON-A and GUSTO IIb Investigators. Platelet IIb/ IIIa Antagonism for the Reduction of Acute Global Organization Network. *J Am Coll Cardiol*. 2001;38(1):64-71.
7. Ahmad I, Haris M, Javed A, Azhar* M. Assessment of risk factors and MACE rate among occluded and non-occluded NSTEMI patients undergoing coronary artery angiography: A retrospective cross-sectional study in Multan, Pakistan. *Journal of Cardiology and Cardiovascular Medicine*. 2018;3(2):023-030.
8. Faubert C, Heckman G, McKelvie R. Management of Non-ST-Elevation Myocardial Infarction in Elderly Patients: Time to Consider Frailty and Quality of Life. *Can J Cardiol*. 2018;34(3):241-243.
9. Roffi M, Patrono C, Collet J-P, Mueller C, Valgimigli M, Andreotti F, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2016;37(3):267-315.
10. Holmvang L, Clemmensen P, Wagner G, Grande P. Admission standard electrocardiogram for early risk stratification in patients with unstable coronary artery disease not eligible for acute revascularization therapy: a TRIM substudy. *Thrombolysis in Myocardial Infarction. Am Heart J*. 1999;137(1):24-33.
11. Cannon CP, McCabe CH, Stone PH, Rogers WJ, Schactman M, Thompson BW, et al. The Electrocardiogram Predicts One-Year Outcome of Patients With Unstable Angina and Non-Q Wave Myocardial Infarction: Results of the TIMI III Registry ECG Ancillary Study. The TIMI III Clinical Centers are supported by Grant R01-HL42311 and the Data Coordinating Center by Grant R01-HL42428 from the National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland. Additional support was supplied by Genentech, Inc., South San Francisco, California. *Journal of the American College of Cardiology*. 1997;30(1):133-140.
12. Barrabés JA, Figueras J, Moure C, Cortadellas J, Soler-Soler J. Prognostic significance of ST segment depression in lateral leads I, aVL, V5 and V6 on the admission electrocardiogram in patients with a first acute myocardial infarction without ST segment elevation. *J Am Coll Cardiol*. 2000;35(7):1813-1819.
13. Khan MR, Haq MA, Majumder NK, Hossain MM, Rahman Z, Rahman MT, et al. Extent of ST-Segment Depression Predicts In-Hospital Outcome in Non ST-Segment Elevation Acute Coronary Syndrome. *Cardiovascular Journal*. 2012;5(1):62-66.
14. Savonitto S, Cohen MG, Politi A, Hudson MP, Kong DF, Huang Y, et al. Extent of ST-segment depression and cardiac events in non-ST-segment elevation acute coronary syndromes. *Eur Heart J*. 2005;26(20):2106-2113.
15. Miah MEH, Chowdhury AHK, Islam KQ, Jamaluddin M, Ghafur S, Khalequzzaman M, et al. ST Segment Depression in 12 lead ECG and Severity of Coronary Artery Disease in Non-ST segment elevation Acute Coronary Syndrome. *Cardiovascular Journal*. 2017;9(2):116-121.
16. Koganti S, Rakhit RD. Management of high-risk non-ST elevation myocardial infarction in the UK: need for alternative models of care to reduce length of stay and admission to angiography times. *Clin Med (Lond)*. 2015 Dec;15(6):522-5.
17. Kakderis C, Didagelos M, Zegkos T, Theodoropoulos KC, Kouparanis A, Ioakeimidou D, et al. In-hospital prognosis of high bleeding

risk patients with an acute coronary syndrome and successful percutaneous coronary intervention: a single-center real-world registry. *Postepy Kardiol Interwencyjne*. 2025 Dec 10;21(4):512-520.

18. Felix B, Aldoohan F, Kadirage HU, Keelathara Sajeev S, Kayani M, et al. Assessment of the Impact of Comorbidities on Outcomes in Non-ST Elevation Myocardial Infarction (NSTEMI) Patients: A Narrative Review. *Cureus*. 2024 Jul 28;16(7):e65568