

Prognostic value of the CHA₂DS₂-VASc Score for cardiovascular mortality in NSTEMI patients with echocardiographic correlates

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ABSTRACT

Aim To evaluate the prognostic value of the CHA₂DS₂-VASc score in relation to major adverse cardiovascular events (MACE) and cardiovascular mortality in patients with non-ST elevation myocardial infarction (NSTEMI), and to assess its association with clinical and echocardiographic characteristics.

Methods This prospective, observational, cohort study included 311 NSTEMI patients admitted to the Internal Medicine Clinic at the University Clinical Centre Tuzla between January 2023 and April 2024. The patients were stratified into intermediate-risk (score < 4) and high-risk (score ≥ 4) groups based on the CHA₂DS₂-VASc score at admission. Demographic, clinical, and echocardiographic data were collected, including electrocardiography (ECG) and transthoracic echocardiography. All patients were followed for 3 months (90 days) to assess the occurrence of MACE and cardiovascular mortality.

Results The patients in the high-risk group were older and had significantly lower left ventricular ejection fractions and larger left atrial diameters compared with the intermediate-risk group. During the 3-month follow-up, MACE occurred in 11.9% of high-risk and 3.9% of intermediate-risk patients; cardiovascular mortality was observed exclusively in the high-risk group (2.5%). A higher CHA₂DS₂-VASc score was significantly associated with cardiovascular mortality ($p = 0.003$), but not with overall MACE ($p = 0.393$). Moderate predictive accuracy for mortality (AUC = 0.64) and shorter event-free survival in the high-risk group (log-rank $p = 0.005$) were observed.

Conclusion The CHA₂DS₂-VASc score showed potential as a simple and accessible tool for early identification of NSTEMI patients at risk of cardiovascular death. Its significant association with mortality supports its role as a supplementary risk stratification tool, although these findings require validation in larger, multicentre studies.

Keywords: CHA₂DS₂-VASc score, cardiovascular mortality, echocardiography, NSTEMI, risk stratification

INTRODUCTION

Non-ST-elevation myocardial infarction (NSTEMI) constitutes a major clinical presentation within the spectrum of acute coronary syndromes (ACS) and continues to be associated with

considerable morbidity and mortality (1). In contrast to ST-elevation myocardial infarction (STEMI), improvements in long-term survival after NSTEMI have been relatively modest over recent years (2). This persistent burden underscores the need to promptly identify patients at increased risk, optimize invasive strategies, and tailor the intensity of medical therapy (3).

Risk stratification tools such as the Global Registry of Acute Coronary Events (GRACE) score and the Thrombolysis in Myocardial Infarction (TIMI) score are widely used in clinical practice and remain the cornerstone of contemporary risk assessment (4,5). These scoring systems combine clinical variables with

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electrocardiographic (ECG) and biochemical parameters to estimate the probability of adverse outcomes (6). However, reliance on detailed laboratory results and haemodynamic measurements may reduce their practicality during early assessment, particularly in high-volume or resource-limited settings (7).

The CHA₂DS₂-VASc score incorporates common cardiovascular risk factors, including congestive heart failure, hypertension, age, diabetes mellitus, prior stroke or transient ischaemic attack, vascular disease, and female sex (8). Although initially developed for thromboembolic risk estimation in patients with atrial fibrillation (AF), many of its individual components are well-established predictors of adverse outcomes in coronary artery disease (9).

Recent studies have indicated that the CHA₂DS₂-VASc score may provide prognostic information beyond its original clinical application. Higher score values have been associated with an increased risk of major adverse cardiovascular events (MACE) and all-cause mortality after acute myocardial infarction, including among patients without atrial fibrillation (10). Taken together, these observations suggest that the score reflects a broader cardiovascular risk burden, likely related to overall systemic vulnerability rather than thromboembolic risk alone.

Despite increasing interest, the role of the CHA₂DS₂-VASc score in NSTEMI patients remains insufficiently defined (11). The current European Society of Cardiology (ESC) and American Heart Association (AHA) guidelines recognize the need for practical risk stratification tools but do not recommend this score outside its established use in AF (12–14). Given its simplicity, universal applicability, and the relevance of its components, further evaluation is warranted to determine whether the CHA₂DS₂-VASc score can provide supplementary prognostic information for predicting outcomes in NSTEMI (15).

To our knowledge, data on the predictive value of the CHA₂DS₂-VASc score specifically for short-term cardiovascular mortality in NSTEMI patients without atrial fibrillation, particularly in relation to echocardiographic correlates, remain limited. This represents a significant gap in current risk stratification strategies.

The aim of this study was to assess the prognostic value of the CHA₂DS₂-VASc score in NSTEMI patients, with emphasis on its association with MACE and cardiovascular mortality. We also investigated whether key echocardiographic parameters, including left ventricular ejection fraction (LVEF), left atrial (LA) diameter, and other structural measures derived from transthoracic echocardiography (TTE), provide additional prognostic information when combined with the score.

PATIENTS AND METHODS

Patients and study design

This prospective, observational, cohort study included 311 patients with NSTEMI and was conducted at the Internal Medicine Clinic of the University Clinical Centre Tuzla between January 2023 and April 2024. The study included consecutively admitted adult patients diagnosed with NSTEMI, based on typical clinical presentation, ischaemic ECG changes, and elevated cardiac biomarkers, according to the ESC guidelines (12).

Eligible participants were adults (≥ 18 years) admitted with a first episode of NSTEMI during their current hospitalization. To ensure cohort homogeneity and avoid confounding, several exclusion criteria were applied. Patients with a history or current diagnosis of AF or atrial flutter (AFL) were excluded, as well as

those with STEMI, unstable angina, prior myocardial infarction, or known chronic coronary artery disease requiring revascularisation or long-term therapy. Previous diagnostic coronary angiography without myocardial infarction or coronary revascularisation was not considered an exclusion criterion and was not classified as established coronary artery disease requiring long-term treatment. Additional exclusion criteria included severe comorbidities likely to affect outcomes or follow-up reliability, such as end-stage renal disease on dialysis, advanced valvular disease, cardiogenic shock, active malignancy, systemic inflammatory disorders, or cognitive impairment precluding informed consent.

All patients were assessed at admission for demographic and clinical variables, including age, sex, body mass index (BMI), cardiovascular risk profile, and pre-existing conditions. The CHA₂DS₂-VASc score was calculated for each patient (16). Based on total scores, patients were stratified into predefined risk groups for comparative analysis of outcome. The primary outcome was the occurrence of major adverse cardiovascular events (MACE) within 3 months (90 days) after index NSTEMI. Cardiovascular mortality within the same period was analysed as a secondary outcome. Follow-up data were obtained through review of hospital medical records and scheduled outpatient or telephone follow-up, with no patients lost to follow-up during the 3 months.

To minimise selection bias, patients were enrolled consecutively throughout the study period. Written informed consent was obtained from all patients after they had been informed of the study protocol and its objectives.

The study was approved by the Ethics Committee of the University Clinical Centre Tuzla and conducted in accordance with the principles of the Declaration of Helsinki.

Methods

Demographic and clinical data were collected through medical history, physical examination, and laboratory testing for all patients. Additional diagnostic procedures, including ECG and TTE, were performed within the first 24 hours of admission. All investigations followed standardized protocols and were conducted by experienced clinicians and certified sonographers.

The CHA₂DS₂-VASc score was calculated at admission according to established criteria: one point each for congestive heart failure (CHF), hypertension, diabetes mellitus (DM), vascular disease, age 65–74 years, and female sex; and two points each for age ≥ 75 years and prior stroke or transient ischaemic attack (TIA). Based on the total score, patients were stratified into two groups: intermediate risk (score < 4) and high risk (score ≥ 4), consistent with previous reports on its prognostic value outside the AF population.

The TTE examination was performed using the Vivid T8 ultrasound system (General Electric Medical Systems, Jiangsu, China). Measurements were obtained from parasternal long-axis and apical four-chamber views. Left ventricular ejection fraction (LVEF) was assessed using the modified biplane Simpson's method, in accordance with contemporary echocardiography reporting and standardization guidelines (17). Left atrial size was evaluated as an anteroposterior diameter measured in the parasternal long-axis view. Interventricular septal thickness (IVS) was measured at end-diastole. Inferior vena cava (IVC) diameter was measured in the subcostal view at end-expiration in the supine position. Key parameters included left ventricular

ejection fraction (LVEF), left atrial diameter (LA), interventricular septal thickness (IVS), and inferior vena cava diameter (IVC), with values recorded according to international echocardiography guidelines. All echocardiographic examinations were performed by experienced sonographers who were not involved in outcome assessment.

Following discharge, all patients were followed for 3 months (90 days). Major adverse cardiovascular events (MACE) were defined as non-fatal myocardial infarction, stroke, and cardiovascular death occurring within this follow-up period. Time to the first event was recorded, and events were verified through hospital records and discharge documentation. Non-fatal myocardial infarction was defined according to standard clinical, electrocardiographic, and biomarker criteria, while stroke events were confirmed by neurological assessment and imaging findings where available. Outcome ascertainment was performed by reviewing hospital medical records, and no patients were lost to follow-up during the 3-month observation period. Cardiovascular death was analysed separately as a secondary outcome. Patients without events were censored at 90 days.

All data were anonymised and stored in a dedicated research database. To ensure consistency, echocardiography was not repeated after discharge, as the primary objective was to evaluate the prognostic value of admission-based clinical and echocardiographic findings.

Statistical analysis

Categorical variables were presented as absolute frequencies (N) and corresponding percentages (%). Continuous variables were first tested for distribution normality using the Kolmogorov–Smirnov test. Because the distributions of these variables were nonparametric, results were reported as medians with interquartile ranges (IQR). A comparative analysis was performed between patients stratified into intermediate- and high-risk groups according to the CHA₂DS₂-VASc score, using appropriate non-parametric and categorical tests. Specifically, the Mann-Whitney U test was used to assess differences in continuous variables between the groups, while the Pearson χ^2 test was used to compare proportions of categorical variables.

To determine the prognostic ability of the CHA₂DS₂-VASc score in predicting major adverse cardiovascular events (MACE)

and mortality, receiver operating characteristic (ROC) curve analysis was conducted. The discriminatory performance of the score was quantified using the ROC curve (AUC), with higher values indicating greater predictive accuracy. The ROC analyses were performed for the occurrence of MACE and cardiovascular mortality within the 3-month follow-up period. Given the limited number of outcome events, particularly cardiovascular deaths, multivariable regression analyses were not performed to avoid model overfitting and unstable estimates. Event-free survival over the 3-month follow-up period was estimated using the Kaplan-Meier method. Comparisons between the intermediate- and high-risk groups were performed using the log-rank test to evaluate differences in time to first event. Time-to-event analyses were censored at 90 days. In addition to total MACE, cardiovascular mortality was analysed separately using the same statistical approach. A $p \leq 0.05$ was considered indicative of statistical significance.

RESULTS

A total of 311 NSTEMI patients were stratified into intermediate-risk (CHA₂DS₂-VASc <4; N = 152) and high-risk groups (CHA₂DS₂-VASc $\geq$ 4; N = 159). The high-risk group was significantly older, with a median age of 75 years (IQR: 70–81) compared to 60 years (IQR: 53–65) in the intermediate-risk group ($p < 0.001$). Body weight was also significantly lower in the high-risk group, with a median of 84 kg (IQR: 79–88) vs. 92 kg (IQR: 86–102) ($p < 0.001$). Active smoking was observed only in the high-risk group (2.5%), without a statistically significant difference between the groups. In comparison, congestive heart failure was more frequent in the intermediate-risk group (25.0% vs. 9.4%; $p = 0.030$). The frequency of diabetes mellitus and hyperlipoproteinemia was comparable between the groups, and no significant differences were observed for hypertension or family history of cardiovascular disease (Table 1).

Coronary angiography during the index hospitalization was performed more frequently in high-risk patients than in intermediate-risk patients (28.3% vs. 15.8%, $p < 0.001$) (Table 1).

Patients in the high-risk group had a significantly lower LVEF median than those in the intermediate-risk group, 48% (IQR: 41–54) vs. 51% (IQR: 45–56) ($p = 0.024$). In addition, left atrial

Table 1. Baseline clinical and demographic characteristics of non-ST elevation myocardial infarction (NSTEMI) patients by risk stratification*

Variable	Intermediate-risk (N = 152)	High-risk (N = 159)	<i>p</i>
Age median (IQR) (years)	60 (53–65)	75 (70–81)	<0.001
Body weight median (IQR) (kg)	92 (86–102)	84 (79–88)	<0.001
No. (%) of patients			
Active smoker	0	4 (2.5)	0.081
Congestive heart failure	38 (25.0)	15 (9.4)	0.030
Diabetes mellitus	67 (44.1)	61 (38.4)	0.211
Hypertension	45 (29.6)	38 (23.9)	0.281
Hyperlipoproteinemia	71 (46.7)	73 (45.9)	0.876
Family history of CVD	55 (36.2)	65 (40.9)	0.493
Coronary angiography performed during index hospitalization	24 (15.8)	45 (28.3)	<0.001

CVD, cardiovascular disease; IQR, interquartile range.

* Risk stratification was based on the presence of congestive heart failure, hypertension, age $\geq$ 75 years, diabetes mellitus, prior stroke or transient ischemic attack, vascular disease, age 65–74 years, and sex category, as defined by the CHA₂DS₂-VASc score.

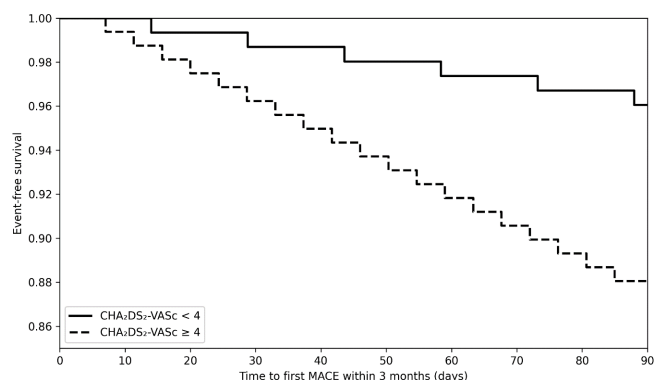
Table 2. Echocardiographic characteristics of patients at admission and 3-month clinical outcome

Variable	Intermediate-risk (N = 152)	High-risk (N = 159)	p
Median (IQR)			
Left ventricular ejection fraction (%)	51 (45–56)	48 (41–54)	0.024
Interventricular septal thickness (mm) (IQR)	12 (10–14)	12 (11–14)	0.289
Left atrial diameter (mm)	41 (38–44)	43 (41–46)	0.006
Inferior vena cava diameter	18 (16–21)	19 (17–21)	0.021
No. (%) of patients			
MACE within 3 months	6 (3.9)	19 (11.9)	0.393
Cardiovascular mortality within 3 months	0 (0.0)	4 (2.5)	0.003
Time to first MACE median (IQR) (days)	90 (14–90)	39 (7–90)	0.006

MACE, major adverse cardiovascular events; LVEF, left ventricular ejection fraction; LA, left atrium; IVC, inferior vena cava; IVS, interventricular septum; IQR, interquartile range.

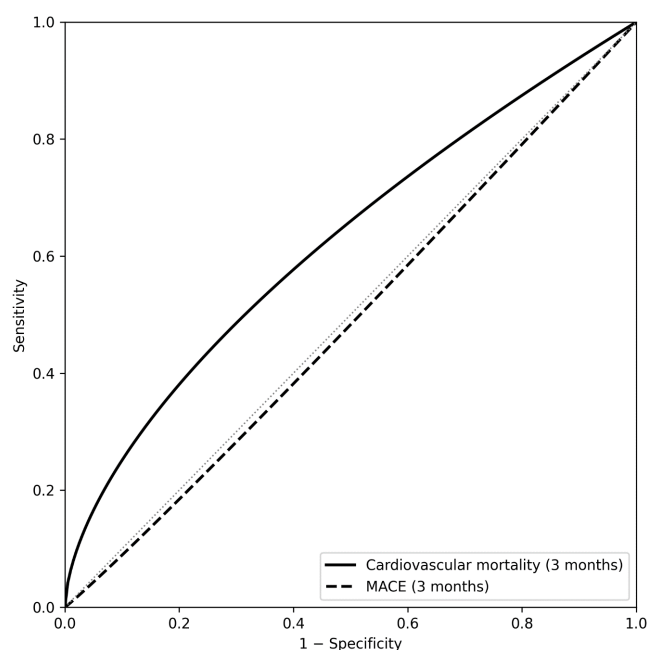
diameter was significantly greater (43 mm vs. 41 mm; $p=0.006$), and inferior vena cava diameter was slightly larger (19 mm vs. 18 mm; $p = 0.021$) in the high-risk group. Interventricular septal thickness did not differ significantly between the groups (Table 2).

During the 3-month follow-up, major adverse cardiovascular events (MACE) occurred in 19 (11.9%) patients in the high-risk group and in six (3.9%) patients in the intermediate-risk group ($p = 0.393$). Cardiovascular mortality was observed exclusively in the high-risk group, in four (2.5%) patients ($p = 0.003$). Time to first MACE was significantly shorter in high-risk patients, with a median of 39 days (IQR: 7–90) compared to 90 days (IQR: 14–90) in the intermediate-risk group ($p = 0.006$) (Table 2). Kaplan–Meier analysis demonstrated a significant separation of event-free survival curves over the 3-month follow-up period (log-rank $p = 0.005$) (Figure 1).


Figure 1. Kaplan-Meier analysis of time to first major adverse cardiovascular event (MACE) within 3 months (90 days) according to the risk groups *

* Risk groups were defined based on congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischemic attack, vascular disease, age 65–74 years, and sex category (CHA₂DS₂-VASc score).

The ROC analysis demonstrated that the CHA₂DS₂-VASc score did not discriminate overall 3-month MACE (AUC = 0.495; 95% CI: 0.404–0.586; $p = 0.915$), but showed moderate accuracy for predicting 3-month cardiovascular mortality (AUC = 0.641; 95% CI: 0.551–0.732; $p = 0.002$) (Figure 2). The score demonstrated limited discriminatory ability for non-fatal MACE at 3 months. Event-free survival was significantly shorter in the high-risk CHA₂DS₂-VASc group (Figure 1). Although the CHA₂DS₂-VASc score did not discriminate between overall MACE occur-


Figure 2. Receiver operating characteristic (ROC) curves of the CHA₂DS₂-VASc score for the prediction of cardiovascular mortality and major adverse cardiovascular events (MACE) within 3 months (90 days) in patients with non-ST elevation myocardial infarction (NSTEMI) *

* The CHA₂DS₂-VASc score comprises congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischemic attack, vascular disease, age 65–74 years, and sex category.

rence, it was associated with earlier onset of adverse events and a higher risk of cardiovascular mortality in high-risk patients. These findings indicate that the prognostic signal of the CHA₂DS₂-VASc score in NSTEMI patients is more pronounced for early cardiovascular mortality than for the overall burden of non-fatal MACE. The absence of deaths in the intermediate-risk group may be explained by the low number of events and the short-term (3-month) follow-up horizon.

DISCUSSION

Our results showed that the CHA₂DS₂-VASc score was significantly associated with cardiovascular mortality in NSTEMI patients, whereas its association with overall MACE did not reach statistical significance. Patients with higher CHA₂DS₂-

VASc scores experienced a higher risk of fatal outcomes, while differences in non-fatal events were less pronounced. Importantly, these findings suggest that the score captures aspects of mortality-related vulnerability rather than the full spectrum of adverse cardiovascular events. Although initially developed to estimate stroke risk in atrial fibrillation, the CHA₂DS₂-VASc score may reflect a broader systemic risk profile predisposing NSTEMI patients to fatal outcomes.

Patients with higher CHA₂DS₂-VASc scores in our cohort were notably older and exhibited echocardiographic markers of adverse remodelling, including reduced LVEF and LA enlargement (18). These structural abnormalities are well-established prognostic factors and correlate with the burden of comorbidities incorporated in the score, such as congestive heart failure (CHF), hypertension, DM, and vascular disease (19). This concordance supports the interpretation that the score indirectly reflects cumulative myocardial stress and reduced cardiac reserve, even outside its initial indication (20).

Nevertheless, the combination of lower LVEF and larger LA and inferior vena cava (IVC) diameters in the high-risk group supports the presence of a higher-risk structural phenotype, as reflected by elevated CHA₂DS₂-VASc scores. This finding adds mechanistic insight by linking a simple clinical score with echocardiographic markers of adverse cardiac structure and haemodynamic burden.

Our results are consistent with findings from other studies. An observational analysis of ACS patients demonstrated that higher CHA₂DS₂-VASc scores were strongly associated with increased short-term mortality (21). In addition, a large single-centre study of nearly 1,000 NSTEMI patients without atrial fibrillation showed that the score independently predicted both in-hospital mortality and angiographic complexity. In that context, the CHA₂DS₂-VASc score has been regarded as a surrogate marker of frailty, reflecting the cumulative burden of comorbidities beyond procedural or laboratory parameters (22). Collectively, these observations suggest that the score is more closely related to early cardiovascular decompensation and fatal outcomes. In contrast, non-fatal events appear to be more strongly influenced by anatomical disease severity, procedural decisions, and acute treatment strategies (23).

In our cohort, despite the significant association with mortality, the CHA₂DS₂-VASc score did not predict non-fatal MACE. This observation is not unique. In a study of ACS patients with CKD, CHA₂DS₂-VASc was an independent predictor of all-cause mortality. However, nonfatal events, such as recurrent MI or revascularization, were less consistently predicted (24). Similarly, in NSTEMI patients without atrial fibrillation, CHA₂DS₂-VASc independently predicted in-hospital mortality and angiographic complexity, whereas non-fatal MACE were not primary endpoints (25). These findings imply that while the score identifies patients at risk of death due to systemic vulnerability and cardiovascular decompensation, it does not account for anatomical or procedural factors that largely determine non-fatal events.

This distinction underscores the difference between comprehensive dynamic risk models and static clinical indices. GRACE and TIMI scores, endorsed in ACS guidelines, incorporate acute physiological, laboratory, and procedural data, thereby offering greater accuracy in the acute setting (25). In contrast, the CHA₂DS₂-VASc score relies solely on historical and demographic information, allowing immediate calculation at admission. Its simplicity may be advantageous in resource-limited or

high-volume settings, although potentially at the cost of reduced sensitivity to acute haemodynamic and biochemical changes (26). Accordingly, the CHA₂DS₂-VASc score should be viewed as a complementary rather than competitive tool, providing early risk orientation before more comprehensive assessments become available. Nevertheless, in our study, it differentiated patients at higher mortality risk, supporting its role as a simple adjunct in early triage.

From a clinical perspective, the use of this score may facilitate rapid recognition of high-risk NSTEMI patients at presentation, particularly in emergency or primary care settings where comprehensive scoring may not yet be feasible (27). Although not a replacement for GRACE or TIMI, the CHA₂DS₂-VASc score can provide an initial assessment that prompts closer monitoring or earlier intervention (28). Our findings reinforce this view, as the most apparent separation of outcomes was observed in mortality rather than non-fatal events.

Several limitations should be acknowledged. The single-centre nature and moderate sample size may limit generalisability. We did not perform a direct comparison with established scores, such as GRACE or TIMI, which could further clarify relative performance. Echocardiographic measurements were obtained only at baseline, precluding evaluation of post-discharge remodelling or functional changes (29). Although outcomes were systematically ascertained from hospital medical records and follow-up documentation, independent adjudication was not performed, which may introduce classification bias. In addition, multivariable adjustment was not undertaken, as the primary objective was to explore the prognostic signal of a simple bedside score rather than to construct a comprehensive predictive model. Finally, adherence to medical therapy and secondary prevention during follow-up was not assessed, which could have influenced the outcome.

In conclusion, the present study directly addresses the aim by demonstrating that the CHA₂DS₂-VASc score provides selective prognostic information for early cardiovascular mortality but not for overall non-fatal MACE in NSTEMI patients. Although it did not predict overall MACE, its utility as a simple, rapid, and accessible tool for early mortality risk stratification is evident. The integration of echocardiographic parameters further supports the concept that the score reflects an adverse structural and clinical phenotype. Given its ease of use in routine practice, it may serve as an initial screening instrument when applied alongside established models. Further multicentre studies with larger cohorts are needed to validate these findings and to explore the potential role of integrating the CHA₂DS₂-VASc score into standardised NSTEMI risk stratification pathways.

FUNDING

No specific funding was received for this study.

CONFLICTS OF INTEREST

None to declare.

ETHICS STATEMENT

This study is a secondary analysis of data collected as part of a prospective study. The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of the University Clinical Centre Tuzla (02-09/2-97-21).

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request and with permission of the institution.

AUTHOR CONTRIBUTIONS (CRediT)

Conceptualization: M.B., E.Beć.; **Data curation:** M.B., E.Beć., E.Beg.; **Formal analysis:** M.B., E.Beć.; **Investigation:** M.B., E.Beć., A.B., S.H., A.A., El.M., K.L., Ek.M., N.L.; **Methodology:** M.B., E.Beć., A.B.; **Project administration:** M.B., E.Beć.; **Resources:** E.Beć., El.M., Ek.M.; **Software:** M.B., E.Beć., E.Beg.; **Supervision:** M.B., E.Beć.; **Validation:** E.Beć., A.B., A.T.; **Visualization:** A.T., N.L.; **Writing – original draft:** M.B., E.Beć.; **Writing – review & editing:** M.B., E.Beć., A.B., A.A., El.M., E.Beg., K.L., Ek.M. All authors have read and agreed to the published version of the manuscript.

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