ACTA FACULTATIS
MEDICAE NAISSENSIS

UDC: 616.127-005.8-07-036:577.112
DOI: 10.5937/afmnai42-53487

Original article

N-Terminal Pro-Brain Natriuretic Peptide Superiority for Prognosis of Major Adverse Cardiovascular Events in Patients with Acute Myocardial Infarction without Heart Failure

Rada Vučić[1,2], Vladimir Ignjatović[1,2], Olivera Andrejić[3], Katarina Čupić[4,5], Miodrag Srećković[1,2], Jelena Vučković Filipović[1,2], Marija Sekulić[6], Milan Dobrić[7,8], Jelena Rakočević[9]

[1]*University of Kragujevac, Faculty of Medical Sciences, Department of Internal Medicine, Kragujevac, Serbia*
[2]*University Clinical Center Kragujevac, Cardiology Clinic, Kragujevac, Serbia*
[3]*Clinical Center Kragujevac, Department of Pulmonology, Kragujevac, Serbia*
[4]*University of Kragujevac, Faculty of Medical Sciences, Department of Ophthalmology, Kragujevac, Serbia*
[5]*University Clinical Center Kragujevac, Department of Ophthalmology, Kragujevac, Serbia*
[6]*University of Kragujevac, Faculty of Medical Sciences, Department of Higiene and Ecology, Kragujevac, Serbia*
[7]*Institute for Cardiovascular Diseases "Dedinje", Belgrade, Serbia*
[8]*University of Belgrade, Faculty of Medicine, Belgrade, Serbia*
[9]*University of Belgrade, Faculty of Medicine, Institute of Histology and Embryology "Aleksandar Đ. Kostić", Belgrade, Serbia*

SUMMARY

Introduction/Aim. Many markers are used to evaluate the prognosis in patients with acute myocardial infarction (AMI). Researches are focused on available markers with high sensitivity and specificity. The aim of our study was to evaluate the prognostic value of N-terminal pro brain natriuretic peptide (NT-proBNP) and its superiority compared with other prognostic markers in patients with AMI.

Patients and methods. Sixty-six patients with the diagnosis of AMI were enrolled in the study. The evaluated variables were: symptoms, cardiovascular risk factors, laboratory analyses (including NT-proBNP), GRACE risk score, electrocardiography, left ventricular ejection fraction (LVEF) and coronary angiography. One- and six-month major adverse cardiovascular events (MACE) included: reAMI, heart rhythm disorders, acute heart failure, stroke, fatal event.

Results. Patients with one-month and six-month MACE were older, had anterior AMI, higher levels of NT-proBNP, urea, creatinine, lower LVEF, creatinine clearance (CCr) and hemoglobin level. NT-proBNP is an independent predictor of short-term (p = 0.002) and long-term (p = 0.000) prognosis. Its cut point of 1,467 pg/ml is a significant independent predictor of one-month MACE and cut point of 996 pg/ml is a significant independent predictor of six-month MACE.

Conclusion. NT-proBNP is a strong short-term and long-term predictive marker in AMI patients without heart failure.

Keywords: **prognosis, acute myocardial infarction, NT–proBNP**

Corresponding author:
Rada Vučić
e-mail: rada.vucic@gmail.com

INTRODUCTION

Acute myocardial infarction (AMI) is an important cause of heart failure with preserved and reduced left ventricular ejection fraction despite improved treatment options (1). This makes the evaluation of prognostic markers in patients with AMI still relevant research. Galectin-3 (Gal-3) is a significant prognostic marker (2), however, its determination is not available in many centers. Researches are focused on available, cheap variables with high sensitivity and specificity. Biochemical analyzes continue to attract the most attention because of its availability and simple determination. N-terminal pro brain natriuretic peptide (NT-proBNP) is now used as a standard biochemical analysis in many coronary units. Our research is focused on the evaluation of prognostic significance and superiority of NT-proBNP compared with other available variables in patients with AMI without acute heart failure regarding one- and six-month major adverse cardiovascular events (MACE).

AIM

The aim of our study was to evaluate the prognostic value of NT-proBNP and its superiority compared with other prognostic markers in patients with AMI.

PATIENTS AND METHODS

Patients and study design: We enrolled 66 patients with AMI, hospitalized between January and July 2009 in the Coronary Unit, Clinical Center Kragujevac, Serbia. The local Ethics Committee approved the study and all patients signed written informed consent. We did not include the patients with end-stage chronic renal disease, acute heart failure, chronic obstructive pulmonary disease, patients under 18 years of age and patients who did not want to participate in the study. Criteria for AMI were set according to the European Society of Cardiology (ESC) guidelines (3). The evaluated variables were as follows:

1) Symptoms: chest pain, exhaustion;

2) Cardiovascular (CV) risk factors: age, gender, tabacco, dyslipidemia (HLP), diabetes mellitus (DM), arterial hypertension (HTA), obesity, known coronary artery disease (CAD), stroke, family history of CAD, emotional stress;

3) Electrocardiography on admission for AMI localization (anterior-inferior);

4) Biochemical analysis on admission: hemoglobin, glucosae, C-reactive protein (CRP), urea, creatinine, creatinine clearance (CCr), body mass index (BMI), cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, troponin, NT-proBNP (usung ELFA technique);

5) Echocardiography on admission and determination of LVEF using the Simpsons method;

6) Coronary angiography performed during hospitalization, including the identification of culprit artery and the number of diseased coronary vessels;

7) MACE after one and six months included: reAMI, heart rhythm disorders, heart failure, stroke, fatal event. Data about MACE were recorded using telephone, standard visits and medical database in case of no response to previously mentioned visists.

Statistical analysis

The prognostic values of the examined variables were evaluated using the X^2 test and Mann-Whitney U test. Plasma concentrations of continuous variables were described as the median and interquartile range (25^{th} to 75^{th} percentile). Binary logistic regression (univariate and multivariate) and

receiver-operating characteristic (ROC) curves were used to evaluate the prognostic NT-proBNP superiority compared to other markers. A p value (two-tailed) < 0.05 was considered statistically significant.

RESULTS

The study population consisted of 49 males and 17 females. Median age of patients was 64.45 ± 10.361 years, 64 ± 10.17 years for males and 65.76 ± 10.81 years for females. ECG: 33 patients had ST-elevation myocardial infarction (STEMI), and 33 patients had non-ST elevation myocardial infarction (NSTEMI); 32 (48.48%) patients had inferior AMI, 33 (50%) patients had anterior AMI and 1 (1.52%) patient did not have ECG abnormalities. Coronary angiography was performed in 61 patients: left coronary artery (LCA) was the culprit artery in 38 (57.57%) patients and right coronary artery (RCA) in 23 (34.85%) patients; 26 (39.39%) patients had one-vessel and 35 (53.03%) patients had multi-vessel disease.

One-month MACE: We verified one-month MACE in 22 (33.33%) patients: 18 males and 4 females. Patients with one-month MACE were older, had anterior AMI, higher levels of NT-proBNP, urea, creatinine, lower LVEF, CCr, and hemoglobin level (Table 1 and 2).

Table 1. *Baseline characteristics of the study's patients stratified by the presence of one-month major adverse cardiovascular events (MACE) including death*

Variable	On admission (N)	One-month MACE (N)	χ^2 (p)
Gender (male)	49	18	0.86
Exhaustion	56	17	0.25
Chest pain	63	21	1.00
Emotional stress	62	21	1.00
Family history	39	15	0.48
Arterial hypertension	44	16	0.73
Diabetes mellitus	21	10	0.18
Dyslipidemia	7	2	1.00
Previous coronary artery disease	15	8	0.13
Stroke	4	1	0.25
Smoking	44	14	0.82
Ventricular arrhythmia	39	14	0.62
STEMI/NSTEMI	33/33	12	0,79
Localization: anterior/inferior	32/33	14/8	**0.046**
Culprit artery: LCA/RCA	38/23	15/4	0.091
Multi-vessel/one vessel disease	26/35	12/8	1.00

STEMI—ST elevation myocardial infarction, NSTEMI—non-ST elevation myocardial infarction, LAD—left anterior descendent artery, RCA—right coronary artery

Table 2. *Patient characteristics according to the presence of one-month major adverse cardiovascular events (MACE) including death*

Variable	Without MACE	MACE	t* or Z** (p)
	mean ± SD	mean ± SD	
Age (years)	62.39 ± 10.429	68.59 ± 9.096	**0.021***
LDL (mmol/L)	3,681 ±1.177	3.366 ± 0.778	0.267*
Weight (kg)	81.47 ± 12.665	83.71 ± 11.529	0.495*
BMI (kg/m²)	27.53 ± 3.189	26.28 ± 3.086	0.141*
Creatine clearance	104.62 ± 36.40	72.63 ± 30.55	**0.001***
NT-proBNP (pg/ml)	658.00 (315.00-1107.00)	2424.00 (1808.00- 2557.00)	**0.000****
Hemoglobin (g/L)	141.00 (130.0-149.00)	132.00 (119.00-140.00)	**0.038****
Urea (mmol/L)	5,60 (4,10-7,00)	8.00 (6.90-10.00)	**0.000****
Creatinine (mmol/L)	78.00 (65.00-86.00)	100.00 (85.0-140.00)	**0.000****
LVEF (%)	50.00 (45.00-55.00)	45.00 (40.00-45.00)	**0.004****
Glucose (mmol/L)			0.896**
CRP (mmol/L)			0.071**
Troponin (pg/ml)			0.547**
Cholesterol (mmol/L)			0.608**
HDL cholesterol (mmol/L)			0.137**
CKMB (mmol/L)			0.427**
Heart rate (beats/min)			0.499**

Values are presented as mean ± SD or median with interquartile range (IQR). Two-tailed unpaired t-test (normalized distribution; t(p)) or Man-Whitney (non-normalized distribution; Z (p)), and χ^2 (p). BMI—body mass index, NT-proBNP—NT-pro brain natriuretic peptide, LVEF—left ventricular ejection fraction, CRP—C reactive protein, CKMB—creatine kinase isoenzime MB

Univariate binary logistic regression of MACE occurrence revealed potential predictors (Table 3). In a multivariate model, NT-proBNP was an independent predictor for one-month MACE in patients with AMI without heart failure (Table 3).

Using the ROC curve analysis (Figure 1), we found that NT-proBNP and creatinine levels had good discriminatory ability (AUC > 0.7) in selecting patients with one-month MACE occurrence; area = 0.868, p < 0.0005 and area = 0.775, p < 0.0005, respectively (Graph 1A and 1B). NT-proBNP is a better marker for one-month MACE (Z = 10.10, p < 0.0005) (Graph 1C). The optimal cut-off of NT-proBNP for predicting one-month MACE is 1,467 pg/ml with sensitivity 81.8%, specificity 86.4%, PPV 75.0%, and NPV 90.5%.

Six-month MACE: The number of patients with MACE after six months was significantly increased up to 31 patients (46.9%) (McNemar test, p = 0,0005): 22 males and 9 females. Patients with six-month MACE were older, had anterior AMI, culprit LCA, higher levels of NT-proBNP, urea, creatinine, lower LVEF, CCr, and hemoglobin level (Table 4 and 5).

Univariate binary logistic regression of MACE occurrence revealed potential predictors (Table 6). In a multivariate model, NT-proBNP was an independent predictor of six-month MACE in patients with AMI without heart failure (Table 6).

Using the ROC curve analysis (Figure 2), we found that NT-proBNP and creatinine concentrations had good discriminatory ability (AUC > 0.7) in selecting patients with six-month MACE occurrence; AUC = 0.892, p < 0.0005 and area = 0.714, p < 0.003, respectively (Figure 2A and 2B). NT-proBNP is a better marker for one-month MACE (Z = 18.69, p < 0.0005) (Figure 2C). The optimal cut-off of NT-proBNP for predicting the six-month MACE is 996 pg/ml, with sensitivity 80.6%, specificity 80.0%, PPV 78.1%, and NPV 82.3%.

Table 3. *Univariate and multivariate logistic regression for all significant univariate variables predicting major adverse cardiovascular events (MACEs) or death at one month follow-up*

Variable	Univariate		Multivariate	
	P	OR (95% CI)	p	OR (95% CI)
Age	**0.025**	1.065 (1.008–1.124)		
NT pro BNP	**0.000**	1.002 (1.001–1.003)	**0.002**	1.002 (1.001–1.003)
Hemoglobin	0.054	0.966 (0.932–1.001)		
Urea	0.665	1.000 (1.000–1.000)		
Creatinine	**0.001**	1.049 (1.020–1.079)	0.06	1.036 (0.998–1.075)
LVEF	**0.012**	0.919 (0.861–0.982)		
Triglicerides	0.065	0.557 (0.330–1.036)		
Creatinine clearance	**0.002**	0.966 (0.954–0.988)		

NT-proBNP –NT—pro brain natriuretic peptide, LVEF—left ventricular ejection fraction

ROC curve—receiver operating characteristic curve

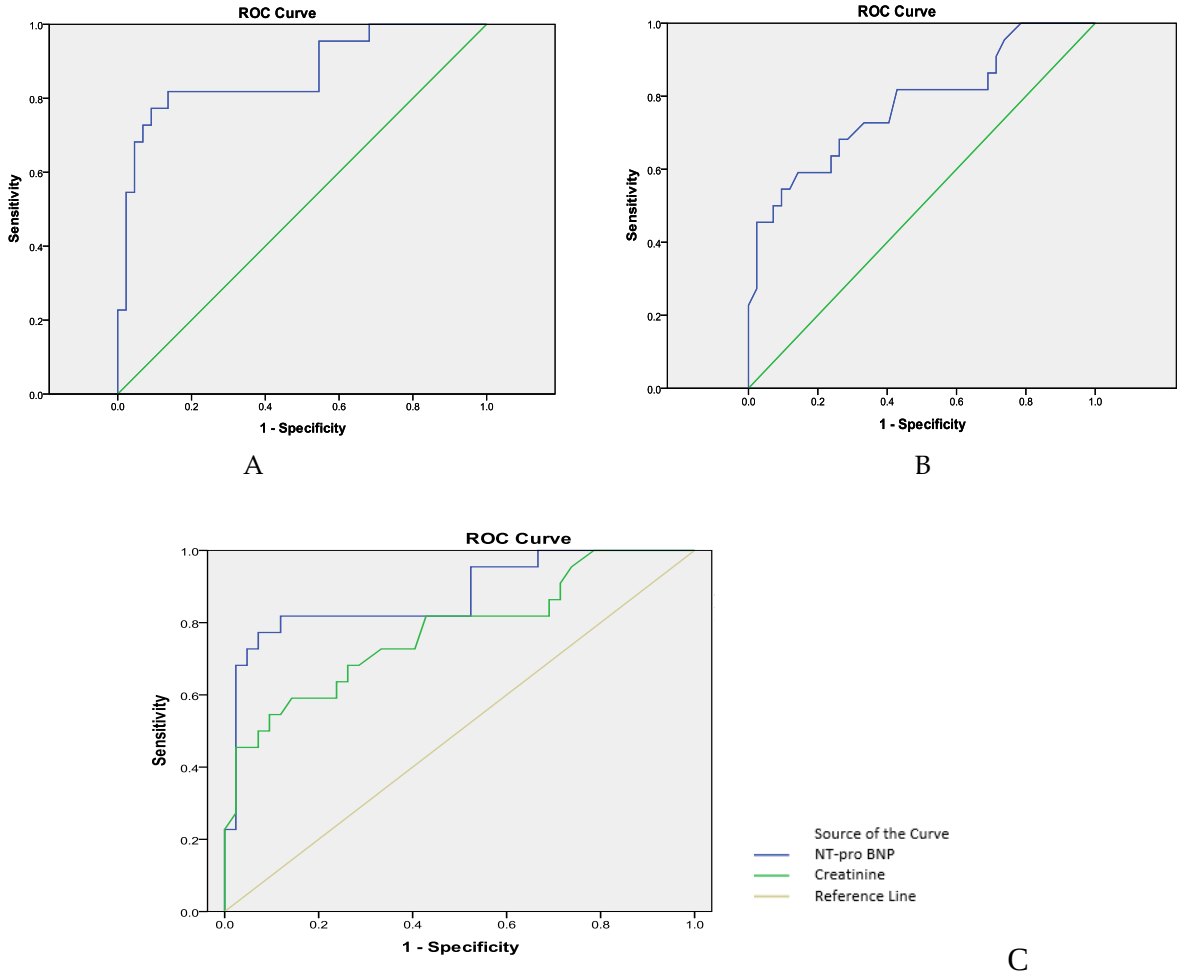


Figure 1. *The ROC curve analysis of NT-proBNP (A) and creatinine (B) in the identification of AMI patients with likelihood of one-month occurrence of MACE or death, and comparison of these two markers (C)*

Table 4. *Baseline characteristics of the study's patients stratified by the presence of six-month major*

adverse cardiovascular events (MACE) including death

Variable	On admission (N)	Six-month MACE (N)	χ^2 (p)
Gender (male)	49	22	0.77
Exhaustion	56	26	0.73
Chest pain	63	29	0.22
Emotional stress	62	30	1.00
Family history	39	20	0.68
Arterial hypertension	44	24	0.18
Diabetes mellitus	21	10	0.06
Dyslipidemia	7	4	0.70
Previous coronary artery disease	15	10	0.16
Stroke	4	2	0.44
Smoking	44	21	1.00
Ventricular arrhythmia	39	16	0.71
STEMI/NSTEMI	33/33	18	0,32
Localization: anterior/inferior/lateral	32/33	19/12	**0.012**
Culprit artery: LCA/RCA	38/23	22/5	**0.013**
Multi-vessel/one vessel disease	26/35	17/10	0.059

STEMI—ST elevation myocardial infarction, NSTEMI—non-ST elevation myocardial infarction, LAD—left anterior descendent artery, RCA—right coronary artery

Table 5. *Patient characteristics according to six-month MACE occurrence*

Variable	Without MACE	MACE	t* or Z** (p)
	mean ± SD	mean ± SD	
Age (years)	61.1±10.461	67.55±9.295	**0.021***
LDL (mmol/L)	3.624±1.2265	3.513±0.8758	0.683*
Hight (cm)	172.38±8.521	175.70±8.514	0.125*
Weight (kg)	80.88±13.126	83.70±11.225	0.363*
BMI (kg/m²)	27.14±3.248	27.093±3.170	0.94*
Creatinine clearance	107.11±39.29	78.54±39.02	**0.002***
NT-proBNP (pg/ml)	541.00 (273.00-927.00)	2034.00 (1495.00- 2503.00)	**0.000****
Hemoglobin (g/L)	141.00 (133.0-150.00)	132.00 (119.00-140.00)	**0.002****
Urea (mmol/L)	5.50 (4.10-7.00)	7.60 (6.30-9.40)	**0.003****
Creatinine (mmol/L)	75.00 (65.00-86.00)	90.00 (81.00-121.00)	**0.003****
LVEF (%)	50.00 (45.00-55.00)	45.00 (40.00-50.00)	**0.024****
Glucose (mmol/L)			0.602**
CRP(mmol/L)			0.153**
Troponin (pg/ml)			0.842**
Cholesterol (mmol/L)			0.679**
HDL cholesterol (mmol/L)			0.213**
CKMB (mmol/L)			0.451**
Hart rate (beats/min)			0.325**

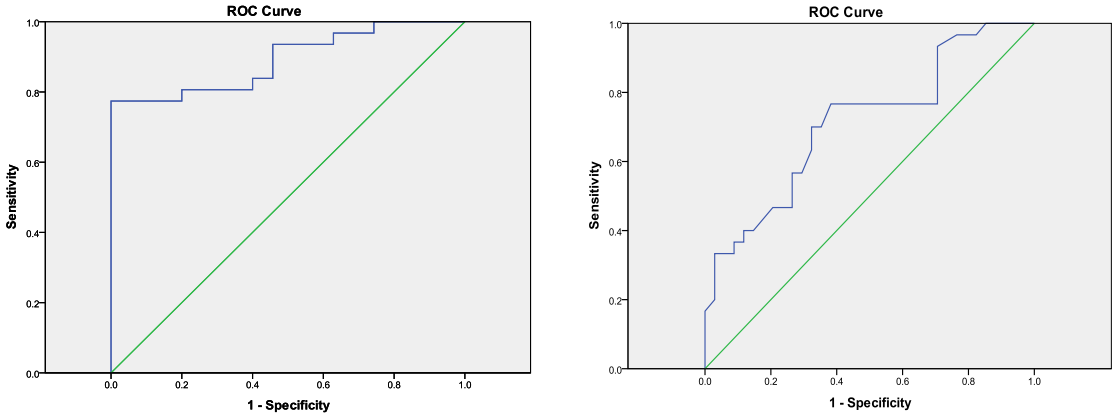
Values are presented as mean ± SD or median with interquartile range (IQR. Two-tailed unpaired t-test (normalized distribution; t(p)) or Man-Whitney (non-normalized distribution; Z (p)).
BMI—body mass index, NT-proBN—NT-pro brain natriuretic peptide, LVEF—left ventricular ejection fraction, CRP—C reactive protein, CKMB—creatine kinase isoenzime M

Table 6. *Univariate and multivariate logistic regression for all significant univariate variables predicting major adverse cardiovascular events (MACEs) or death at six months follow-up*

Variable	Univariate		Multivariate	
	p	OR (95% CI)	p	OR (95% CI)
Age	**0.025**	1.060 (1.007 – 1.115)		
NT-proBNP	**0.000**	1.002 (1.001 – 1.004)	**0.00**	1,003 (1,001 - 1,004)
Hemoglobin	0.007	0.948 (0.912 – 0.985)		
Urea	0.544	1.000 (1.000 – 1.000)		
Creatinine	**0.004**	1.020 (0.997 – 1.043)		
LVEF (%)	**0.034**	0.934 (0.877 – 0.995)		
Triglicerides	0.761	0.939 (0.624-1.411)		
Creatine clearance	**0.004**	0.973 (0.955-0.991)		
Distal LAD	0.085	1.020 (0.997-1.043)		
Culprit artery	**0.037**	0.413 (0.180/0.949)		

NT-proBNP—NT-pro brain natriuretic peptide, LVEF—left ventricular ejection fraction, LAD— left anterior descendent artery

ROC curve—receiver operating characteristic curve



A B

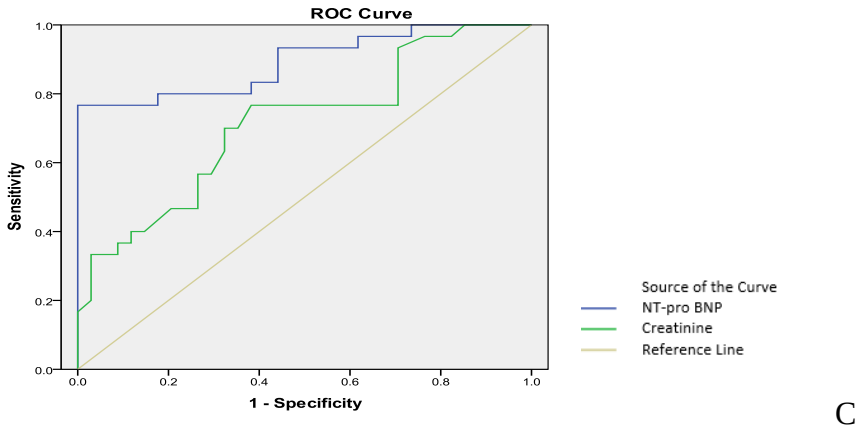


Figure 2. *The ROC curve analysis of NT-proBNP (A) and creatinine (B) in the identification of AMI patients with likelihood of six-month occurrence of MACE or death, and comparison of these two markers (C)*

DISCUSSION

NT-proBNP is the most usable marker for acute heart failure. Due to the presence of the heart failure in a wide range of diseases, the evaluation of this marker, available in almost every coronary unit, draws the attention of scientists. Our results showed higher NT-proBNP concentrations in the first hour of AMI symptoms and its level was related to infarct size (4). Worse short-term prognosis of AMI patients was detected in those with higher NT-proBNP concentrations measured in the first sample and without later rapid decline, and in those with higher NT-proBNP level three days after AMI (5) and persistently higher NT-proBNP levels in multiple measurements after AMI (6).

Our study measured the NT-proBNP level up to 24 hours of the onset of symptoms, and only patients with AMI without acute heart failure were evaluated. Patients with one-month and six-month MACE were older, with anterior AMI, culprit LCA, higher levels of NT-proBNP, urea, creatinine, lower levels of LVEF, CCr, and hemoglobin. Our results showed a connection between NT-proBNP levels and risk of re-AMI, heart failure, heart rhythm disorders, stroke and death, one and six months after AMI. A predictive value of NT-proBNP for short-term and long-term MACE in AMI patients was independent of clinical characteristics, biochemical analyses, LVEF, left ventricular wall localization or culprit artery.

The reported one-month and six-month MACE rates of 33.33% and 46.9%, respectively, in our study, were similar to the results of other reported studies. Variations in MACE rates can be explained by different length of follow-up, adverse events included in MACE, and a type of included patients (7-10).

Previously reported studies showed an impact of NT-proBNP on prognosis in patients with AMI. Wang J and colleagues made biomarker-based risk model using the baseline NT-proBNP and other biomarkers for one-year MACE. In this study, the patients with MACE were older, had higher prevalence of arterial hypertension, diabetes mellitus, congestive heart failure, history of AMI, and stroke. The best prognostic marker was NT-proBNP, the values of which were similar to our results (11). One study in Korea has developed machine learning-based model for the prediction of outcomes in AMI patients. The primary outcome was one-year all-cause death; secondary outcomes included CV deaths, one-year and three-year MACE. This study singled out the best predictors for the primary outcome: peak troponin I ($p = 0.048$), cholesterol level (0.047) and NT-proBNP level (0.039) (12). Another study with 1,105 AMI patients treated with PCI evaluated the association between NT-proBNP levels and three-year MACE. They found that patients with adverse events—all-cause death, AMI recurrence, and re-hospitalization due to heart failure had the highest concentration of NT-proBNP (13). The study of Platelet Inhibition and Patients Outcomes (PLATO

trial) showed an independent association between NT-proBNP and adverse outcomes (14). Prospective ARNI vs ACE Inhibitor Trial to Determine Superiority in Reducing Heart Failure Events After Myocardial Infarction (PARADISE-MI) found a connection of NT-proBNP with adverse events in AMI patients (15). A meta-analysis of 19 studies performed up to June 2021 confirmed a connection between higher concentration of NT-proBNP and adverse events (all cause death and MACE) (16). Compared to our study, all of them measured NT-proBNP concentration in AMI patients independently of the presence of acute heart failure which can be a contributing factor.

The evaluation of prognostic significance of NT-proBNP was performed among patients with other forms of ischemic heart disease. One study measured NT-proBNP in patients with MI with non-obstructive coronary arteries (MINOCA) and without heart failure. They showed a connection between higher NT-proBNP concentrations and risk of re-hospitalizations (17). Evaluations in patients with unstable angina and NSTEMI were evaluated in: The Fast Assessment in Thoracic Pain (FAST) study, The Global Utilization of Strategies To open Occluded arteries-IV (GUSTO IV) and Fast Revascularization during Instability in Coronary artery disease (FRISC II) trial. The FAST (755 patients; follow up 40 months) study found a connection between higher NT-proBNP concentrations and mortality (18). In the GUSTO-IV trial (7,800 patients with acute coronary syndromes without ST-segment elevations (ACS-NSTE); follow up—one year) NT-proBNP was the strongest independent predictor of mortality (19). The FRISC II trial (2,019 patients, follow up—two years) compared an early invasive to non-invasive strategy in patients with unstable angina. NT-proBNP was independently associated with mortality (20).

All of the above-mentioned studies corroborate our findings; however, the majority of these measured NT-proBNP plasma concentration in patients with ischemic heart disease independent of the presence of acute heart failure, followed up on patients over both short-term and long-term periods, and included varied adverse outcomes. The exclusion of patients with acute heart failure made our study different, being thus one step ahead of others. Our study shows the significance of NT-proBNP measurements in AMI patients, early after admission and identifies patients with high risk for adverse events. As we previously reported, Gal-3 plasma concentration in patients with AMI has a high long-term prognostic value (2). However, the availability of Gal-3 is not comparative to NT-proBNP in clinical practice. This available marker in every coronary unit can be used as a standard marker for one- and six-month prognosis for patients with AMI.

Identification of high-risk patients for MACE through simple NT-proBNP determination early after admission could be a step forward in the prognosis of AMI patients and prevention in the post-AMI period. The main limitation of our study is a small number of patients. Increasing the number of patients with different forms of ischemic heart disease and using national registries for ACS will be helpful for further research. Determination of NT-proBNP levels in different time of ACS onset and presence/absence of acute failure can determine the best time of sampling for short- and long-term prognosis.

CONCLUSION

The NT-proBNP plasma concentration measured in first 24 hours of the onset of symptoms is a strong independent short-term and long-term predictive marker in AMI patients without heart failure.

References

1. Felker GM, Shaw LK, O'Connor CM. A standardized definition of ischemic cardiomyopathy for use in clinical research. J Am Coll Cardiol 2002;39:210-8. https://doi.org/10.1016/S0735-1097(01)01738-7

2. Vucic RM, Andrejic OM, Stokanovic D, et al. Galectin-3 as a Prognostic Biomarker in Patients with First Acute Myocardial Infarction without Heart Failure. Diagnostics 2023; 13(21):3348. https://doi.org/10.3390/diagnostics13213348

3. Thygesen K, Alpert JS, Jaffe AS, ESC Scientific Document Group, Fourth universal definition of myocardial infarction. EHJ 2019; 40 (3):237-69. https://doi.org/10.1093/eurheartj/ehy462

4. Omland T. Clinical and laboratory diagnostics of cardiovascular disease: focus on natriuretic peptides and cardiac ischemia. Scand J Clin Lab Invest 2005;65 (suppl 240):18-24. https://doi.org/10.1080/00365510500236077

5. Heeschen C, Hamm CW, Mitrovic V, et al. Platelet Receptor Inhibition in Ischemic Syndrome Management (PRISM) Investigators. N-terminal pro-B-type natriuretic peptide levels for dynamic risk stratification of patients with acute coronary syndromes. Circulation 2004;110(20):3206-12. https://doi.org/10.1161/01.CIR.0000147611.92021.2B

6. O'Donoghue ML, Morrow DA, Cannon CP, et al. Multimarker Risk Stratification in Patients With Acute Myocardial Infarction. J Am Heart Assoc 2016;5(5):e002586. https://doi.org/10.1161/JAHA.115.002586

7. Cai A, Dillon C, Hillegass WB, et al. Risk of major adverse cardiovascular events and major hemorrhage among white and Black patients undergoing percutaneous coronary intervention. J Am Heart Assoc 2019;8(22):e012874. https://doi.org/10.1161/JAHA.119.012874

8. Tsai IT, Wang CP, Lu YC, et al. The burden of major adverse cardiac events in patients with coronary artery disease. BMC Cardiovasc Disord 2017;17(1):1-13. https://doi.org/10.1186/s12872-016-0436-7

9. Wang Y, Zhou J, Zhou P, et al. Prognostic significance of serial N-terminal pro-B-type natriuretic peptide levels in patients with acute myocardial infarction: A prospective study. Am Heart J 2023;262:90-9. https://doi.org/10.1016/j.ahj.2023.04.015

10. Nasution SA, Perkasa H, Ginanjar E, Rinaldi I. In-Hospital Major Adverse Cardiac Events Factor Predictors on ST-Elevation Myocardial Infarction after Primary Percutaneous Coronary Intervention at dr. Cipto Mangunkusumo General Hospital. eJKI. 2022;10(2):107-13. https://doi.org/10.23886/ejki.10.193.107-13

11. Wang J, Gao W, Chen G, et al; BIPass investigators. Biomarker-based risk model to predict cardiovascular events in patients with acute coronary syndromes - Results from BIPass registry. Lancet Reg Health West Pac 2022;25:100479. https://doi.org/10.1016/j.lanwpc.2022.100479

12. Jeong JH, Lee KS, Park SM, et al. Prediction of longitudinal clinical outcomes after acute myocardial infarction using a dynamic machine learning algorithm. Front Cardiovasc Med 2024;11:1340022. https://doi.org/10.3389/fcvm.2024.1340022

13. Li N, Chen R, Li J, et al. Prognostic significance of serial N-terminal pro-B-type natriuretic peptide levels in patients with acute myocardial infarction: A prospective study. Am Heart J 2023;262:90-9. https://doi.org/10.1016/j.ahj.2023.04.015

14. Velders MA, Wallentin L, Becker RC, et al. Biomarkers for risk stratification of patients with ST-elevation myocardial infarction treated with primary percutaneous coronary intervention: Insights from

the Platelet Inhibition and Patient Outcomes trial. Am Heart J 2015;169 (6):879-89.e7. https://doi.org/10.1016/j.ahj.2015.02.019

15. Jering KS, Claggett BL, Pfeffer MA, et al. Prognostic Importance of NT-ProBNP (N-Terminal Pro-B-Type Natriuretic Peptide) Following High-Risk Myocardial Infarction in the PARADISE-MI Trial. Circ. Heart Fail 2023, 16, e010259. https://doi.org/10.1161/CIRCHEARTFAILURE.122.010259

16. Shen S, Ye J, Wu X, Li X. Association of N-terminal pro-brain natriuretic peptide level with adverse outcomes in patients with acute myocardial infarction: A meta-analysis. Heart Lung 2021;50(6):863-9. https://doi.org/10.1016/j.hrtlng.2021.07.007

17. Sykes R, Doherty D, Morrow A, et al. NT-proBNP in patients presenting with myocardial infarction and non-obstructive coronary arteries without left ventricular systolic dysfunction. Am Heart J Plus 2023;33:100311. https://doi.org/10.1016/j.ahjo.2023.100311

18. Jernberg T, Stridsberg M, Venge P, Lindahl B. N-terminal pro brain natriuretic peptide on admission for early risk stratification of patients with chest pain and no ST-segment elevation. J Am Coll Cardiol 2002; 40: 437-45. https://doi.org/10.1016/S0735-1097(02)01986-1

19. James SK, Lindahl B, Siegbahn A, et al. N-terminal pro-brain natriuretic peptide and other risk markers for the separate prediction of mortality and subsequent myocardial infarction in patients with unstable coronary artery disease: a Global Utilization of Strategies To Open occluded arteries (GUSTO)-IV substudy. Circulation 2003; 108: 275-81. https://doi.org/10.1161/01.CIR.0000079170.10579.DC

20. Jernberg T, Lindahl B, Siegbahn A, et al. N-terminal pro brain natriuretic peptide in relation to inflammation, myocardial necrosis and the effect of an invasive strategy in unstable coronary artery disease. J Am Coll Cardiol 2003;42:1909-16. https://doi.org/10.1016/j.jacc.2003.07.015

Article info
Received: September 16, 2024
Accepted: January 26, 2025
Online first: July 9, 2025

Superiornost N-terminalnog promoždanog natriuretičkog peptida u prognozi velikih neželjenih kardiovaskularnih događaja kod bolesnika koji su doživeli akutni infarkt miokarda bez srčane dekompenzacije

Rada Vučić[1,2], Vladimir Ignjatović[1,2], Olivera Andrejić[3], Katarina Čupić[4,5], Miodrag Srećković[1,2], Jelena Vučković Filipović[1,2], Marija Sekulić[6], Milan Dobrić[7,8], Jelena Rakočević[9]

[1]*Univerzitet u Kragujevcu, Fakultet medicinskih nauka, Katedra za internu medicinu, Kragujevac, Srbija*
[2]*Univerzitetski klinički centar Kragujevac, Klinika za kardiologiju, Kragujevac, Srbija*
[3]*Univerzitetski klinički centar Kragujevac, Klinika za pulmologiju, Kragujevac, Srbija*
[4]*Univerzitet u Kragujevcu, Fakultet medicinskih nauka, Katedra za oftalmologiju, Kragujevac, Srbija*
[5]*Univerzitetski klinički centar Kragujevac, Klinika za oftalmologiju, Kragujevac, Srbija*
[6]*Univerzitet u Kragujevcu, Fakultet medicinskih nauka, Katedra za higijenu i ekologiju, Kragujevac, Srbija*
[7]*Institut za kardiovaskularne bolesti „Dedinje", Beograd, Srbija*
[8]*Univerzitet u Beogradu, Medicinski fakultet, Beograd, Srbija*
[9]*Univerzitet u Beogradu, Medicinski fakultet, Institut za histologiju i embriologiju „Aleksandar Đ. Kostić", Beograd, Srbija*

SAŽETAK

Uvod/Cilj. Kod bolesnika sa akutnim infarktom miokarda (AIM) ispituje se prognostički značaj brojnih markera. Istraživači se fokusiraju na one koji su široko dostupni i imaju visoku senzitivnost i specifičnost. Cilj ove studije bio je da utvrdi prognostički značaj N-terminalnog promoždanog peptida (NT-proBNP) i njegovu superiornost nad ostalim markerima koji se koriste kod bolesnika sa AIM-om.

Pacijenti i metode. Studija je obuhvatila 66 bolesnika sa AIM-om. Pri evaluaciji u obzir su bile uzete sledeće varijable: simptomi, kardiovaskularni faktori rizika, laboratorijske analize (uključujući NT-proBNP), elektrokardiografija, ejekciona frakcija leve komore (LVEF) i koronarna angiografija. Jednomesečni i šestomesečni veliki neželjeni kardiovaskularni događaji (engl. *major adverse cardiovascular events* – MACE) uključivali su: ponovljeni AIM, poremećaje srčanog ritma, akutnu srčanu insuficijenciju, moždani udar, smrtni ishod.

Rezultati. Bolesnici sa jednomesečnim i šestomesečnim MACE-om bili su stariji, imali su infarkte prednjeg zida, povišene nivoe NT-proBNP, uree, kreatinina, niži LVEF, CCr (engl. *creatinine clearance* – CCr) i hemoglobin. NT-proBNP je bio nezavisan prediktor kratkoročnog (p = 0,002) i dugoročnog (p = 0,000) MACE-a. Vrednost NT-proBNP koja je na prijemu iznosila 1467 pg/ml pokazala se kao nezavisan prediktor jednomesečnog MACE-a, a vrednost od 996 pg/ml kao nezavisan prediktor šestomesečnog MACE-a.

Zaključak. NT-proBNP je kod bolesnika koji su doživeli AIM bez srčane dekompenzacije snažan prediktor MACE-a, i kratkoročno i dugoročno.

Ključne reči: **prognoza, akutni infarkt miokarda, NT-proBNP**