CLINICAL IMPLICATIONS OF NT PROBNP LEVEL IN PATIENTS WITH MYOCARDIAL INFARCTION COMPLICATED BY ATRIAL FIBRILLATION

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Abstract: Our aim was to study the predictive value of NT proBNP regarding the risk of AF and clinical features in acute phase of ST-segment elevation MI (STEMI).

Methods. We examined 56 patients with STEMI and AF who did undergo the primary PCI. 35 (62.5 %) of patients had the new-onset AF (group 1), 21 (37.5 %) had pre-existing AF (group 2). Control group consisted of 60 patients with STEMI without AF (group 3).

Results. Group 3 patients were more likely to be smokers than patients in group 2. They had lower admission heart rate and glycemia, lower NT proBNP, higher hemoglobin and ejection fraction. Patients in group 1 were more likely to have anterior MI, left anterior descending artery as an infarction-related artery (IRA) and adverse cardiac events (MACEs). Patients in group 2 had higher left atrium end-systolic diameter and were more likely to have three-vessel injury. NT proBNP correlated positively with age, admission glycemia, mean PA pressure and negatively – with GFR.

ROC analysis had shown the cut-off point of NT proBNP level for prediction of AF was >1050 pg/ml. Cut-off point for prediction of the risk of MACE in STEMI complicated with AF was >2189 pg/ml.

Discussion. It was shown that NT proBNP is higher in STEMI patients who have AF. Increased NT proBNP is associated with the risk of adverse events in acute STEMI phase. NT proBNP level can be utilized as AF predictor in STEMI patients and as predictor of MACEs in patients with STEMI and AF.

Keywords: myocardial infarction, primary percutaneous intervention, NT proBNP, prognosis, atrial fibrillation, pre-existing, new-onset, MACEs, complications, predictors.

1. Introduction

Despite the significant success in treatment of patients with myocardial infarction (MI) achieved during last decades, it remains one of the most significant causes of death worldwide. Course of the acute phase and long-time prognosis of MI patients depend on the grade of coronary artery (CA) atherothrombotic injury, time to reperfusion and utilized method [1], and also on comorbidities such as diabetes mellitus (DM), chronic renal disease, atrial fibrillation (AF) [2]. AF is the most common arrhythmia worldwide. It burdens 15.5 % of MI cases [3] and is associated with 40–50 % mortality increase [4], rises the risk of complications in an acute period, hospital readmissions, major adverse cardiac events (MACEs) [5].

The rise of left ventricular (LV) pressure in response to ischemia and necrosis of LV wall during MI leads to acute left atrium pressure increase, stretching, structural and electrical remodeling of its wall which predisposes to AF. In turn, high heart rate during AF and loss of atrial contribution to cardiac output decreases left ventricular pump function and coronary perfusion, burdening the course of the MI [5]. One of the mechanisms to compensate the increase of pressure in cardiac chambers is activation of natriuretic peptides synthesis. Physiologic roles of these molecules are increase of diuresis, sodium excretion, vasodilatation. Brain natriuretic peptide (BNP) or its inactive fragment (NT proBNP) are markers of left ventricular dysfunction available for use in clinical practice [6].

Our aim was to study the predictive value of NT proBNP regarding the risk of AF and clinical presentation features in acute phase of ST-segment elevation MI (STEMI).

2. Methods

We examined 56 patients with STEMI and AF who were consequentially admitted to the Communal non-profit enterprise of the Kharkiv Regional Council "Regional Clinical Hospital" in 2017–2018 and did undergo the primary percutaneous coronary intervention (PCI). STEMI was diagnosed according to the ECS Guidelines (2017) [7]. Presence of AF was evaluated according to ESC/EHRA Guidelines (2016) [8]. Study design was approved by Ethics committee of Kharkiv medical academy of postgraduate education. According to Helsinki declaration, all the patients were informed regarding aim and methods of the current study and had provided the written informed consent.

35 (62.5 %) patients had the new-onset AF (group 1), 21 (37.5 %) patients had pre-existind AF (group 2). Inclusion criterions were age over 18 years, hospitalization during the first 12 hours of STEMI, pre-existing or new-onset AF. Non-inclusion criteria were previous MI, severe comorbidities, inability to understand and/or sign the informed consent. Control group consisted of 60 patients with STEMI who had no AF (group 3). Age and gender of patients in group 3 were statistically comparable with parameters of the entire population.

Patients were treated according to ECS Guidelines (2017) [7]. Blood samples were drawn immediately before PCI. Coronary angiography and cardiac ultrasound were performed according to the routine local protocols.

The primary endpoint was combined event (major adverse cardiac events – MACEs) that occurred during index STEMI hospitalization. MACEs were defined as the composite of CV death, acute LV heart failure, reinfarction, stroke/TIA, ventricular fibrillation.

As for statistical data analysis, continuous variables were presented as mean ± standard deviation when they were normally distributed, or median and interquartile range if otherwise. Categorical variables were presented as frequencies and percentages. Mann-Whitney and Wald-Wolfowitz criteria were used for intergroup differences and quantitative values. The qualitative variables were expressed as percentages, and were analyzed by the χ^2 test and exact Fisher test. Receiver operating characteristic (ROC) curve analysis was performed for detection of well-balanced cut-off points. All differences were considered statistically significant with $p<0.05$.

3. Results

Patients with AF had the following characteristics. There were 53.6 % of males and 46.4 % of females, mean age was 68.26±12.39 years. 92.9 % of patients had a history of hyperten-

sion, 39.3 % had DM, 32.1 % had obesity, 21.4 % were smokers, 12.3 % had angina before index STEMI.

Group 3 patients were more likely to be smokers than patients in group 2 (p_{2-3}=0.037). They had significantly lower mean heart rate at admission (p_{1-3}=0.013, p_{2-3}=0.015) and lower admission glycaemia (p_{2-3}=0.020), higher admission hemoglobin (p_{1-3}=0.004). Group 1 patients were more likely to have anterior STEMI compared to the group 3 (p_{1-3}=0.035). Patients with AF were more likely to have MACEs (p_{1-3}=0.045). Only patients in groups 1 and 2 had Killip IV acute heart failure (**Table 1**). Prevalence of DM, arterial hypertension, obesity, stable angina before MI, white blood cell count at admission, peak troponin I level, glomerular filtration rate (GFR) did not differ between groups. Prescription rate of the main drug classes recommended for STEMI treatment (angiotensin converting enzyme inhibitors/angiotensin receptor blockers, beta-blockers, aspirin, clopidogrel/ticagrelor, statins) was similar in all groups. Patients in group 3 were less likely to take warfarin (p_{1-3}=0.0001, p_{2-3}=0.014) or new oral anticoagulants (p_{1-3}=0.0001, p_{2-3}=0.0001) because AF is the main indication for those drugs.

As for coronary angiography results, patients with intact CA were present only in group 1. Patients in group 2 were significantly more likely to have three-vessel injury than groups 1 and 3 (p_{1-2}=0.019, p_{2-3}=0.001). Patients in group 1 were more likely to have left anterior descending artery as an infarction-related artery (IRA) than patients in group 3 (p_{1-3}=0.049) while patients in group 2 were significantly more likely to have right coronary artery as IRA (p_{1-2}=0.042).

According to the ultrasonic data analysis, left atrium end-systolic diameter was significantly higher in group 2 than in groups 1 and 3 (p_{1-2}=0.007, p_{2-3}=0.0003). Ejection fraction was lower (p_{1-3}=0.0001, p_{2-3}=0.043) and mean pulmonary artery pressure was higher in groups 1 and 2 than in group 3 (p_{1-3}= =0.007, p_{2-3}=0.0002).

NT proBNP level in entire population was 1788.00 (610.90; 3070.0) pg/ml: 2149.00 (439.20; 3429.00) in group 1; 1305.00 (610.90–2183.00) pg/ml in group 2. In group 3 it was significantly lower: 212.80 (26.70–802.60); p_{1-3}=0.001 p_{2-3}=0.005. We revealed correlation between NT proBNP and age of patients (r=0.433; p=0.012), stable angina before STEMI (r=0.42137; p=0.015), admission glycaemia (r=0.359; p=0.019), mean pulmonary artery pressure (r=0.520; p=0.047), body mass index (r=–0.457; p=0.022), plasma potassium level (r=–0.3517; p=0.048), GFR (r=–0.520; p=0.04).

We performed ROC analysis in order to study the predictive value of NT proBNP regarding the risk of new-onset AF. Group 2 patients were excluded from this analysis. Cut-off point of NT proBNP level was >1050 pg/ml (sensitivity 63.6 %, specificity 92.3 %, area under curve 0.839 (95 % CI 0.676 to 0.941) – **Fig. 1**.

Table 1
Clinical characteristics of examined patients

Parameter	Entire population (n=56)	Group 1 (n=35)	Group 2 (n=21)	Group 3 (n=37)	p-level
Age, years	68.26±12.39	69.31±9.56	68.76±9.09	64.32±11.48	p_{1-2}=0.833 p_{1-3}=0.050 p_{2-3}=0.134
Males, n (%)	30 (53.6)	19 (54.3)	11(52.4)	24(64.9)	p_{1-2}=0.891 p_{1-3}=0.360 p_{2-3}=0.350
Smoking, n (%)	12 (21.4)	8(29.1)	4(19.0)	17(45.9)	p_{1-2}=0.507 p_{1-3}=0.070 p_{2-3}=0.037
Mean admission heart rate, beats per minute	89.05±23.33	88.54±24.41	89.91±21,97	75.16±12.56	p_{1-2}=0.856 p_{1-3}=0.013 p_{2-3}=0.015
Glycaemia, mmol/l	8.54±3.18	8.38±3.30	8.79±3.03	7.49±3.30	p_{1-2}=0.409 p_{1-3}=0.095 p_{2-3}=0.020
Hemoglobin, g/l	128.62±18.43	126.12±16.70	134.83±20.89	137.33±18.05	p_{1-2}=0.215 p_{1-3}=0.004 p_{2-3}=0.180
Anterior MI localizatio, n (%)	27(48.2)	21(60.0)	8(38.1)	13(35.1)	p_{1-2}=0.112 p_{1-3}=0.035 p_{2-3}=0.822
Killip II, n (%)	17(30.4)	12(34.3)	5(23.8)	20(54.1)	p_{1-2}=0.303 p_{1-3}=0.092 p_{2-3}=0.0002
Killip IV, n (%)	7(12.5)	4(11.4)	3(14.3)	0(0)	p_{1-2}=0.373 p_{1-3}=0.051 p_{2-3}=0.024
MACEs, n (%)	10(17.9)	9(25.7)	1(4.8)	3(8.1)	p_{1-2}=0.047 p_{1-3}=0.045 p_{2-3}=0.540

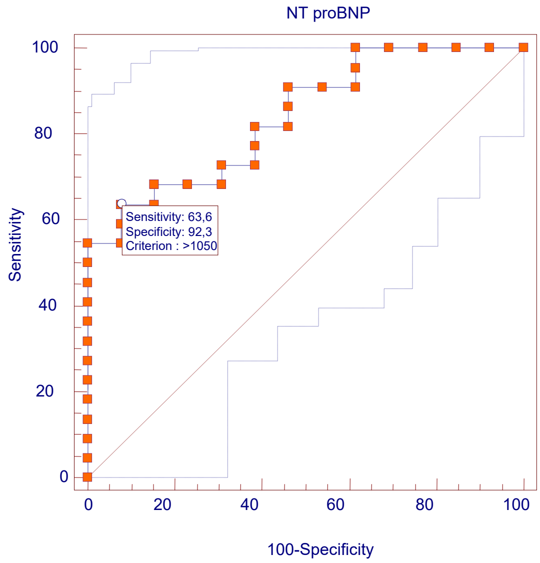

Fig. 1. ROC-curve for prediction of AF in STEMI patients using NT proBNP level

ROC analysis of predictive value of NT proBNP level regarding the risk of MACE in STEMI acute period revealed the cut-off point >2189 pg/ml (sensitivity 66.7 %, specificity 83.8 %, area under curve 0.839 (95 % CI 0.644 to 0.896) – **Fig. 2**.

4. Discussion and conclusions

It was shown in our study that NT proBNP is higher in STEMI patients who have atrial fibrillation. Increased level of NT proBNP is associated with the risk of adverse events in acute STEMI phase.

BNP or NT-proBNP is a significant predictor of prognosis in patients with MI. Admission plasma BNP and NT-proBNP concentrations are associated with all-cause mortality at long-term follow-up and with risk of hospitalizations with heart failure [9]. Plasma BNP/NT-proBNP concentration increases instantly after MI, and the grade of increase is related to the severity of ischemia [10]. Patients with smaller infarctions tend to have monophasic increase of BNP/NT-proBNP level, which peaks during the first 24 hours of MI. It was shown that in patients with high initial NT-proBNP level absence of its fast decrease after myocardial injury was associated with unfavourable short-term prognosis. Prolonged increase of this peptide level is associated with refractory ischemia and high risk of ischemic events in patients with MI without ST segment elevation [11].

Our data suggest that NT proBNP level increase can be utilized as AF predictor in STEMI patients and as predictor of adverse events in patients with STEMI and AF.

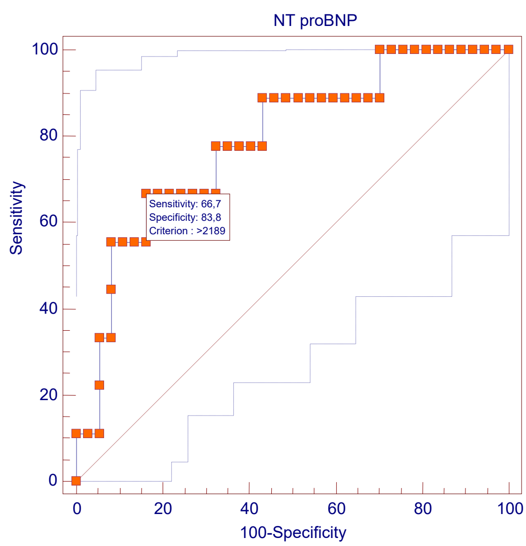

Fig. 2. ROC-curve for prediction of MACEs in STEMI patients using NT proBNP level

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