

The effect of streptokinase therapy in STEMI and conventional therapy in NSTEMI patients on TIMI risk index, B-type natriuretic peptide and high-sensitive C-reactive protein

Akut STEMI’de streptokinaz tedavisi ve NSTEMI’de konvansiyonel tedavinin TIMİ risk indeksi, B-tip natriüretik peptit ve yüksek-duyarlılık C-reaktif protein üzerindeki etkisi

İbrahim Halil Kurt, Mustafa Kemal Batur¹, İlker Üna²

Department of Cardiology, Adana Numune Education and Research Hospital, Adana

¹Department of Cardiology, Faculty of Medicine, Acıbadem University, Adana

²Department of Biostatistics, Faculty of Medicine, Çukurova University, Adana-Turkey

ABSTRACT

Objective: In this study, it was aimed to investigate the effect of streptokinase therapy in ST elevation myocardial infarction (STEMI) and conventional therapy in non-ST elevation myocardial infarction (NSTEMI) patients on the thrombolysis in myocardial infarction (TIMI) risk index (TRI), B-type natriuretic peptide (BNP), and high-sensitive C-reactive protein (hs-CRP) levels.

Methods: Eighty-six STEMI (male/female ratio: 65/21, mean age 57.52±9.87 years) and eighty NSTEMI patients (male/female ratio: 50/30, mean age 57.6±1.7 years) were included in this prospective observational study. Hs-CRP and BNP were measured and TIMI risk index was calculated in all patients. Coronary angiography was performed in all patients for principally determining TIMI flow rate. Chi-square test, paired t-test or Wilcoxon signed rank test, ANOVA and Spearman correlation analysis were used for statistical analysis where appropriate.

Results: STEMI patients had higher systolic blood pressure, heart rate, BNP and hs-CRP values than NSTEMI patients at admission (p=0.04, p=0.01, p=0.001 and p=0.01, respectively). Thrombolytic therapy in STEMI patients resulted in statistically significant higher levels of BNP, hs-CRP and TRI values compared to baseline levels (p=0.001, p=0.001 and p=0.042, respectively). For NSTEMI patients conventional therapy yielded statistically significant decrease in systolic blood pressure levels and increase in TRI (p=0.001 and p=0.047, respectively). We found significantly lower BNP, hs-CRP in patients with higher TIMI flow rate (p=0.001 and p=0.001 respectively).

Conclusion: Thrombolytic therapy with streptokinase failed to decrease BNP, hs-CRP and TRI values in STEMI patients. Conventional therapy in NSTEMI patients also resulted in higher TRI values than baseline values. We reached TIMI 3 flow in only 10.5% of the study patients, which may be responsible for our findings. (*Anadolu Kardiyol Derg 2011; 11: 530-5*)

Key words: Acute myocardial infarction, thrombolytic therapy, TIMI risk index, B-type natriuretic peptide, high-sensitive C-reactive protein

ÖZET

Amaç: Bu çalışmada akut ST yükselmeli miyokart enfarktüsünde (STEMI) streptokinaz tedavisi ve ST yükselmez miyokart enfarktüsünde (NSTEMI) standart tedavinin, miyokart enfarktüsünde tromboliz risk indeksi (TRI) ve yüksek-duyarlılık C-reaktif protein (hs-CRP), B-tip natriüretik peptit (BNP) üzerindeki etkilerinin araştırılması amaçlanmıştır.

Yöntemler: Bu prospektif, gözlemsel çalışmaya 86 STEMI (erkek/kadın oranı: 65/21, ortalama yaş 57.52±9.87 yıl) ve 80 NSTEMI (erkek/kadın oranı: 50/30, ortalama yaş 57.6±1.7 yıl) hasta alındı. Tüm hastaların hs-CRP, BNP, TRI ölçüldü ve koroner anjiyografileri çekilerek TIM akımları tespit edildi. İstatistiksel analiz için Ki-kare, eşleştirilmiş t, Wilcoxon işaret sıralama, ANOVA ve Spearman korelasyon testleri kullanıldı.

Bulgular: Çalışmamızda STEMI hastalarda yatış sırasındaki sistolik kan basıncı, nabız, BNP ve hs-CRP düzeyi NSTEMI hastalara oranla daha yüksekti (p=0.04, p= 0.01, p=0.001 ve p=0.01 sırasıyla). Trombolitik tedavi sonrası STEMI hastalarda yatıştaki BNP, hs-CRP ve TRI değerleri ile karşılaştırıldığında daha yüksek bulduk (p=0.001, p=0.001 ve p=0.042 sırasıyla). Standart tedavi alan NSTEMI hastalarda ise sistolik kan basıncı ve TRI istatistiksel olarak anlamlı yükselme tespit ettik (p=0.001 ve p=0.047 sırasıyla). Ayrıca çalışmamızda anjiyografik TIMI akım değeri derecesi arttıkça BNP ve hs-CRP değerleri azalmaktadır (p=0.001 ve p=0.001 sırasıyla).

Address for Correspondence/Yazışma Adresi: Dr. İbrahim Halil Kurt, Department of Cardiology, Adana Numune Education and Research Hospital, 01330 Adana-Turkey Phone: +90 322 458 32 52 Fax: + 90 322 459 51 63 E-mail: ibrahimhalilkurt@gmail.com

Accepted Date/Kabul Tarihi: 14.03.2011 **Available Online Date/Çevrimiçi Yayın Tarihi:** 08.08.2011

©Telif Hakkı 2011 AVES Yayıncılık Ltd. Şti. - Makale metnine www.anakarder.com web sayfasından ulaşılabilir.

©Copyright 2011 by AVES Yayıncılık Ltd. - Available on-line at www.anakarder.com

doi:10.5152/akd.2011.138

Sonuç: Çalışmamızda STEMI olgularında trombolitik tedavi için verilen streptokinaz; BNP, hs-CRP düzeyini ve TRI'yi düşürmede yetersiz kaldı. Standart tedavi verilen NSTEMI da ise TRI değeri başlangıca oranla daha yüksek bulundu. Bizim bulgularımıza göre hastaların yalnızca %10.5'inde TIMI 3 sağlanmış olması, bu sonuçtan sorumlu olabilir. (*Anadolu Kardiyol Derg 2011; 11: 530-5*)

Anahtar kelimeler: Akut miyokart enfarktüsü, trombolitik tedavi, TIMI risk indeksi, B-tip natriüretik peptit, yüksek-duyarlıklı C-reaktif protein

Introduction

Acute myocardial infarction (MI) is still one of the leading causes of death despite new therapeutic options. Therefore, risk assessment has a paramount importance in decision-making process. Currently, many risk scores are being used for this purpose such as TIMI risk score, which requires multiple variables to be entered (1, 2). However, TIMI risk index (TRI) as a new risk assessment tool in both STEMI and NSTEMI patients has been used for this purpose because of its simplicity. It has been tested in 150.000 STEMI (3) and 5430 NSTEMI patients (4) and was revealed as a strong predictor of 30-day mortality in both patient's groups.

Brain natriuretic peptide (BNP) and high-sensitive C-reactive protein (hs-CRP) are also markers of increased cardiovascular mortality in acute coronary syndrome patients (5-9). However, prognostic significance of these biomarkers has been evaluated especially in both NSTEMI patients and STEMI patients treated with primary coronary intervention approach.

The aim of the present study was to determine levels of all these three markers in NSTEMI and STEMI patients treated thrombolytic therapy. We also tried to evaluate the effects of conventional and reperfusion therapy on TIMI risk index, BNP, hs-CRP levels in both NSTEMI and STEMI patients.

Methods

Study population

This single-center, prospective, observational study enrolled one hundred and sixty-six patients (115 males, 51 females, mean age 57.7 ± 10.8 years, median 57 years) who were admitted to the emergency department of Adana Numune Education and Research Hospital between May 2007 and April 2008 with the diagnosis acute myocardial infarction. Eighty-six of these patients (52%) were STEMI cases (65 males, 21 females; mean age 57.52 ± 9.87 years, median 58 years) and 80 of them (48%) were NSTEMI cases (50 males, 30 females, mean age 57.6 ± 1.7 years, median 57 years).

Exclusion criteria

Patients were excluded from the study based on following criteria: patients undergoing rescue percutaneous coronary intervention (PCI) due to failed thrombolysis determined as the absence of $\geq 50\%$ ST segment elevation resolution at 90th minutes; patients admitted to emergency service after 12 hours of onset of symptoms; patients with pericarditis, aortic dissection, chronic inflammation, renal failure (serum creatinine >1.5 mg/dl), active infection (determined as hs-CRP level >10 mg/dl), and presence of any malignancy.

The study was executed upon the consent received from the patients as per the protocol followed by the approval of the Ethics Committee of our hospital.

Study protocol

Age, gender, blood pressure, heart rate, presence of diabetes or hypertension, smoking status, alcohol use and chest pain duration was determined in all patients at admission. Blood samples for biochemistry analysis including lipid panel and electrocardiographic (ECG) recordings were undertaken. Patients had STEMI diagnosis in the presence of two of three following criteria (10):

- Chest pain and/or discomfort for at least 30 minutes;
- ST-segment elevation of >0.1 mm in at least two adjacent leads in the extremity leads and ST-segment elevation of >0.2 mm in the precordial leads in a standard 12-lead ECG;
- A more than two-fold increase in CK-MB value compared to normal.

NSTEMI patients had at least 10 minutes of typical chest pain and on one of the following: elevated biomarkers of myonecrosis and ST-depression ≥ 0.1 mV (8).

Treatment modalities

All patients were given non-enteric 300 mg acetylsalicylic acid chewable tablets. Those patients with aspirin intolerance or allergy were given clopidogrel 300 mg by oral route. In STEMI patients 1.5 million IU streptokinase was administered by I.V. infusion over 1 hour if there was no contraindication for thrombolytic therapy. Beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, Low-molecular-weight heparin (LMWH), IV nitrates and statins were also used at the discretion of responsible physician. In NSTEMI patients, we used conventional therapy including beta-blockers, ACE inhibitors, IV nitrates and statins, clopidogrel, LMWH (enoxaparine 1 mg/kg).

Angiographic study

Patients had undergone coronary angiography after the thrombolytic therapy by using standard Judkins technique before discharge (median time for coronary angiography was 5 days). The coronary angiographic procedure was performed by Shimadzu device (AUD 150 G-Digitex, Kyoto, Japan). Coronary angiograms were interpreted by two independent, experienced interventional cardiologists who were uninformed about the clinical and laboratory data of patients. Angiographic TIMI flow rates of the culprit vessel were determined after thrombolytic therapy by previously established grading system (11): TIMI 0: no flow or perfusion at the distal of stenosis; TIMI 1: penetration at the distal of stenosis but no perfusion; TIMI 2: partial perfusion; TIMI 3: complete perfusion).

TIMI risk index calculation

The thrombolysis in myocardial infarction risk index was calculated by using the following formula in all patients at admission and at the day of discharge: Heart rate*(age/10)²/SBP, where SBP is systolic blood pressure (12).

Biomarker analysis

Peripheral blood samples for plasma BNP and hs CRP determination were obtained at admission by direct venipuncture of an antecubital vein after the patient had been in the supine position for 30 minutes. Blood samples were immediately centrifuged. High sensitive-CRP levels were measured by using immune nephelometric method (IMMAGE Immunochemistry Systems; Beckman Coulter, California, USA). BNP measurements were done using Triage Meter Plus equipment (Willich, Germany).

Statistical analysis

The SPSS 16.0 software package (SPSS Inc., Chicago, Ill, USA) was used for statistical analysis of the data. Categorical analyses were expressed as numbers (n) and percentages (%), whereas continuous analyses were reported as mean and standard deviation and as median and minimum-maximum where appropriate. Chi-square test was used to compare categorical variables between the treatment groups. For comparison of continuous variables in time (before and after the treatment) within groups, the paired t-test or Wilcoxon signed rank test was used depending on whether the statistical hypotheses were fulfilled or not; and the Student's t-test or Mann-Whitney U test was used for comparisons between groups. The analysis of variance (ANOVA) or Kruskal-Wallis Test were used for comparisons between TIMI values. The correlation between certain variables of the treatment groups was performed using the Spearman correlation analysis. The statistical level of significance for all tests was considered to be 0.05.

Results

Baseline characteristics

Six patients (3.2%) undergoing rescue PCI for persistent chest pain following thrombolytic therapy and 8 patients who died (4.2%) were excluded from the study. In STEMI patients 41 (47.7%) had anterior and 45 (52.3%) had non-anterior MI localization. Chest pain duration at admission in STEMI was less than 1 hour in 28 patients (32.6%), 1-6 hours in 36 subjects (41.8%) and 6-12 hours in 22 patients (25.6%).

Patient characteristics including medication used at admission and affected coronary artery presented in Table 1 which revealed higher SBP and heart rate in STEMI patients (p=0.04 and 0.01, respectively). Moreover, BNP and hs-CRP were also significantly higher in STEMI patients compared to NSTEMI patients (p=0.001 and p=0.01) (Table 1). With thrombolytic therapy in STEMI patients we found statistically significant decrease in systolic-diastolic blood pressure levels and heart rate (p=0.001, p=0.001 and p=0.004, respectively) (Table 2).

In contrast, we detected higher BNP, hs-CRP and TRI values in STEMI patients with reperfusion therapy which reached statistical significance (p=0.001, p=0.001 and p=0.042, respectively) (Table 2). For NSTEMI patients conventional therapy yielded statistically significant decrease in systolic-diastolic blood pressure levels and increase in TRI (p=0.001, p=0.004 and p=0.047, respectively) (Table 2).

TRI, BNP and hs-CRP levels according to TIMI flow rate, and MI localization

Coronary angiographic evaluation performed after the thrombolytic therapy yielded the following TIMI grading: TIMI 0 in 12 patients (14.0%); TIMI 1 in 20 patients (23.3%); TIMI 2 in 45 patients (52.3%); TIMI 3 in 9 patients (10.5%). We found signifi-

Table 1. Demographic characteristics, clinical, laboratory and angiographic findings

Variables	STEMI (n=86)	NSTEMI (n=80)	p*
Age, years	57.52±9.87	57.6±11.7	0.987
Gender, m/f, n	65/21	50/30	0.092
Diabetes, n (%)	14 (16.3)	14 (17.5)	0.43
Hypertension, n (%)	24 (27.9)	34 (42.5)	0.053
Smoking, n (%)	28 (32.6)	35 (43.8)	0.152
Alcohol consumption, n (%)	7 (8.1)	10 (12.5)	0.445
Systolic BP, mmHg	131.10±26.44	124.5±14.0	0.044
Diastolic BP, mmHg	78.12±16.04	75.4±9.8	0.193
Pulse, bpm	80.00±16.21	74.0±14.4	0.013
Total cholesterol, mg/dl	189.16±4.86	187.4±37.7	0.784
HDL, mg/dl	38.86±0.92	40.5±10.7	0.273
TG, mg/dl	170.10±13.65	160.1±78.2	0.538
LDL, mg/dl	116.55±3.88	113.4±27.7	0.527
BUN, mg/dl	33.4±1.0	35.3±13.2	0.631
Creatinine, mg/dl	1.03±0.03	1.04±0.27	0.882
Medications			
ACEI, n (%)	37 (43.0)	35 (43.8)	0.999
ASA, n (%)	83 (96.5)	78 (97.5)	0.999
Beta-blockers, n (%)	66 (76.7)	61 (76.3)	0.999
Nitrates, n (%)	26 (30.2)	31 (38.8)	0.258
Statins, n (%)	43 (50.0)	44 (55.0)	0.538
Affected coronary artery			
LAD, n (%)	60 (69.8)	58 (72.5)	0.734
CX, n (%)	53 (61.6)	45 (56.3)	0.529
RCA, n (%)	55 (64.0)	45 (56.3)	0.343

Data are presented as mean±SD and number (percentages)

*Chi-square, unpaired t, and Mann-Whitney U tests

ACEI - angiotensin-converting enzyme, ASA - acetyl salicylic acid, BP - blood pressure, BUN - blood urine nitrogen, CX - circumflex, DBP - diastolic blood pressure, HDL - high-density lipoprotein, LAD - left anterior descending artery, LDL - low-density lipoprotein, NSTEMI - non-ST-elevation myocardial infarction, RCA - right coronary artery, STEMI-ST-elevation myocardial infarction, TG - triglyceride

cantly lower BNP, hs-CRP levels in patients with higher TIMI flow rate (p=0.001, and p=0.001 respectively) (Table 3).

We also determined that pre-treatment BNP (p=0.001) and post-treatment BNP, hs-CRP values were significantly higher in STEMI patients having non-anterior MI localization (p=0.001 and p=0.001 respectively) (Table 4).

Relationship between TIMI risk score and BNP and hs-CRP levels

According to correlation analysis we detected a weak but statistically significant correlation coefficient between TRI and BNP levels in patients with STEMI only after reperfusion therapy (p=0.030) (Table 5).

Discussion

In our study, we found that STEMI patients had higher BNP and hs-CRP values both before and after reperfusion therapy. Likewise, higher TRI values were determined in STEMI and NSTEMI patients even in the presence of appropriate treatment. BNP and hs-CRP were increased in STEMI patients having non-

anterior localization but had a tendency to decrease with increasing TIMI flow rate. Moreover, we also found a correlation between TRI and BNP levels in STEMI patients only after reperfusion therapy.

TIMI risk index is relatively strong and independent predictor of mortality in STEMI and NSTEMI patients (3, 4, 13). TIMI risk index scores can be divided into low risk (<12.5), intermediate risk (12.5-30) and high risk groups (>30) (14) and every 5 percentage points increase in TIMI risk index results in a 43% increase in 30-day mortality (14). Predictive power of TIMI risk index is decreased in patients older 65 years (12, 15), which was not the case in our study because median was 57 years in our patients.

TIMI risk index calculation is directly related to heart rate/SBP ratio, which was higher in STEMI patients (0.61) compared to NSTEMI patients (0.59) at admission in our study. Although SBP and heart rate decreased after reperfusion therapy in STEMI and conventional therapy in NSTEMI patients, heart rate/SBP ratio was still higher in STEMI patients than NSTEMI patients (0.66 vs 0.63), which explains higher TRI values in this patients group. Therefore we can assume that reperfusion or conventional therapy in our acute coronary syndrome patients

Table 2. Pre- and post-treatment vital signs and laboratory findings in STEMI and NSTEMI patients

Variables	STEMI (n=86)			NSTEMI (n=80)		
	Pre-treatment	Post-treatment	p*	Pre-treatment	Post-treatment	p*
SBP, mmHg	131.10±26.44	114.22±19.09	0.001	124.5±14.0	118.4±18.6	0.001
DBP, mmHg	78.12±16.04	69.23±10.96	0.001	75.4±9.8	72.1±9.4	0.004
Pulse, bpm	80.00±16.21	75.14±13.32	0.004	74.0±14.4	74.1±11.3	0.930
BNP, pg/ml	104.8±24.3 32.9 (1-1794.1)	248.2±32.7 163.5 (18.6-2389)	0.001	2.21±1.95 1.65 (0.1-9.8)	2.11±1.58 1.62 (0.1-6.8)	0.526
hs-CRP, mg/dl	0.86±0.09 0.56 (0-3.5)	1.65±0.16 1.125 (0.1-9.5)	0.001	0.52±0.50 0.45 (0-2.6)	0.58±0.86 0.35 (0-6.6)	0.944
TRI	21.19±9.14 19.7 (2.95-46.21)	22.78±9.28 21.6 (8.08-67.34)	0.042	20.64±9.18 19.8 (4.64-57.76)	21.80±10.03 21.2 (5.83-68.14)	0.047

Data are presented as mean±SD and median (range) values

*Paired samples t-test and Wilcoxon signed rank test

BNP- brain natriuretic peptide, DBP - diastolic blood pressure, hs-CRP - high-sensitivity C - reactive protein, NSTEMI - non-ST-elevation myocardial infarction, SBP - systolic blood pressure, STEMI-ST - elevation myocardial infarction, TRI - TIMI risk index

Table 3. Relation between post-treatment angiographic TIMI flow and TRI, BNP, and hs-CRP values

Post-treatment	Angiographic TIMI flow				p*	Chi-square (df)*
	0	1	2	3		
TRI	23.49±6.75 21.25 (14.34-39.1)	20.94±5.02 21.21 (12.91-29.77)	24.14±11.23 22.72 (8.08-67.34)	21.53±9.85 21.13 (5.83-68.14)	0.451	2.635 (3)
BNP, pg/ml [‡]	549.3±632.9 324.5 (90.2-2389.0)	221.4±184.5 206.8 (18.6-759.9)	205.1±178.3 159.7 (25.5-878.8)	14.3±39.7 1.9 (0.1-205.0)	<0.001	109.1 (3)
Hs-CRP, mg/dl [‡]	3.0±2.4 2.5(0.6-9.5)	1.6±1.5 1.1(0.1-5.6)	1.4±1.0 1.0(0.3-5.1)	0.7±1.0 0.4(0.0-6.6)	<0.001	56.9 (3)

Data are presented as mean±SD and median (range) values

* Kruskal-Wallis test and Bonferroni adjusted Mann-Whitney U test for pairwise comparison:

[‡]p<0.05 for the comparing the groups as 0 and 2, 0 and 3, 1 and 3, 2 and 3

BNP - brain natriuretic peptide, hs-CRP - high-sensitivity C - reactive protein, TRI - TIMI risk index

Table 4. Pretreatment and post-treatment measurements of TRI BNP and hs-CRP according to the STEMI localization

		STEMI		p*
		Anterior	Non-anterior	
pre-treatment	TRI	20.30±8.79 19.98 (2.95-46.21)	22.52±10.00 19.74 (7.71-57.76)	0.347
	BNP	62.47±97.28 20.50 (0.10-430.05)	84.60±249.41 12.55 (0.23-1794.06)	<0.001
	hs-CRP	0.66±0.65 0.43 (0.03-3.00)	0.79±0.80 0.52 (0.00-3.50)	0.463
post-treatment	TRI	21.43±9.79 20.45 (8.08-67.34)	24.05±9.87 22.75(9.99-68.14)	0.132
	BNP	164.28±187.04 132.25 (0.20-878.82)	185.11±337.54 82.30 (0.20-2388.99)	<0.001
	hs-CRP	1.23±1.23 0.79 (0.00-6.60)	1.48±1.65 0.94 (0.00-9.46)	<0.001

Data are presented as mean±SD and median (range) values
*Mann-Whitney U test
BNP - brain natriuretic peptide, hs-CRP-high-sensitivity C - reactive protein, STEMI-ST elevation myocardial infarction, TRI - TIMI risk index

Table 5. Correlation of TIMI risk index with BNP and hs-CRP levels

	Treatment	Pairs	Correlation coefficient*	p*
NSTEMI	Before	TRI - BNP	-0.026	0.821
		TRI - hs-CRP	0.070	0.538
	After	TRI - BNP	-0.071	0.530
		TRI - hs-CRP	0.067	0.552
STEMI	Before	TRI - BNP	0.147	0.176
		TRI - hs-CRP	0.034	0.757
	After	TRI - BNP	0.234	0.030
		TRI - hs-CRP	-0.082	0.450

*Spearman rank correlation analysis
BNP - brain natriuretic peptide, hs-CRP - high-sensitivity C - reactive protein, NSTEMI - non-ST-elevation myocardial infarction, STEMI - ST-elevation myocardial infarction, TRI-TIMI risk index

did not decrease TIMI risk score and hence patient's mortality risk. Underlying reasons for this finding in spite of early presentation of patients (74.4% of them within 6 hours) is not clear but we thought streptokinase was the cause in STEMI patients for low TIMI flow rates (only in 10.5% of the patients having TIMI 3 flow rate) and lower SBP levels. This lack of satisfactory TIMI flow rate in our study groups may also be responsible for higher TRI values in NSTEMI patients at discharge than at admission.

Brain natriuretic peptide is released in acute MI due to increased wall stress (5). It begins to rise during first 24 hours of MI but is generally more useful for prognostic purpose when measured in 2 to 5 days of admission (5, 16-18). BNP levels were higher in our STEMI patients than NSTEMI patients, which reflect greater ischemia burden and more severe left ventricular impairment in our opinion. Even higher BNP levels in STEMI patients after reperfusion therapy can be explained by our failure to provide satisfactory TIMI flow rate, and hence, to salvage myocardium at risk with streptokinase. Mega et al. (19) previously showed that patients with BNP >80 pg/ml were at significantly

higher risk of death and were also more likely to have impaired coronary flow. Indeed, we found gradual increase in BNP levels with decreasing TIMI flow rates.

CRP has an active role in MI because it reflects inflammatory reaction, which has prominent role in plaque rupture-thrombosis and infarct expansion (20, 21). Serum hs-CRP increases within the first few days of acute MI in response to myocardial necrosis (22). It has been reported that addition of hs-CRP level to TIMI risk score allowed risk stratification and provided additional prognostic information in patients with acute coronary syndromes (23). Moreover, plasma hs-CRP level at admission was suggested as a predictor for short-term and long-term reperfusion failure in AMI (24, 25). We showed higher hs-CRP levels in STEMI patients than in NSTEMI patients. In addition, we also determined even higher hs-CRP levels in STEMI patients after reperfusion therapy but not in NSTEMI patients. Possible explanations for this finding can be more powerful inflammatory response due to larger myocardial necrotic area and ensuing infarct expansion.

We showed a weak but statistically significant correlation between TRI and BNP in STEMI patients only after reperfusion therapy. If we look at this result from different perspective, we cannot use a clinical variable (TIMI risk index) and a biomarker BNP levels interchangeably. Indeed, Kuklinska et al. (8) previously postulated that only BNP and hs-CRP but not TRI could provide independent and incremental prognostic information.

Study limitations

In addition to small number of subjects recruited, our study has other major limitations to be mentioned. We did not provide mortality data because our primary aim was to determine BNP, hs-CRP and TRI values. Mortality data and its relation to BNP, hs-CRP and TRI should be investigated in other trials. We also did not measure infarct area with which we can reach to further conclusions.

Conclusion

Ineffective reperfusion achieved with streptokinase can be used to explain persistently increased biomarker's levels and TIMI risk index in our STEMI patients. For, NSTEMI patients, conventional treatment strategy did not affect BNP or hs-CRP levels but caused a possible adverse result: an increase in TRI. Therefore, we need further trials for both confirming our study results and finding answers for other important questions: Are our findings also valid for other thrombolytics in STEMI patients and early invasive strategy in NSTEMI patients?

Conflict of interest: None declared.

References

- Ryan TJ. The Thrombolysis In Myocardial Infarction risk index: a formula with a future. *J Am Coll Cardiol* 2004; 44: 790-2.

- Jacobs DR Jr, Kroenke C, Crow R, Deshpande M, Gu DF, Gatewood L, et al. PREDICT: a simple risk score for clinical severity and long-term prognosis after hospitalization for acute myocardial infarction or unstable angina: the Minnesota heart survey. *Circulation* 1999; 100: 599-607.
- Wiviott SD, Morrow DA, Frederick PD, Giugliano RP, Gibson CM, McCabe CH, et al. Performance of the thrombolysis in myocardial infarction risk index in the National Registry of Myocardial Infarction-3 and -4: a simple index that predicts mortality in ST-segment elevation myocardial infarction. *J Am Coll Cardiol* 2004; 44: 783-9.
- Bradshaw PJ, Ko DT, Newman AM, Donovan LR, Tu JV. Validation of the Thrombolysis In Myocardial Infarction (TIMI) risk index for predicting early mortality in a population-based cohort of STEMI and non-STEMI patients. *Can J Cardiol* 2007; 23: 51-6.
- de Lemos JA, Morrow DA, Bentley JH, Omland T, Sabatine MS, McCabe CH, et al. The prognostic value of B-type natriuretic peptide in patients with acute coronary syndromes. *N Engl J Med* 2001; 345: 1014-21.
- Morrow DA, de Lemos JA, Sabatine MS, Murphy SA, Demopoulos LA, DiBattiste PM, et al. Evaluation of B-type natriuretic peptide for risk assessment in unstable angina/non-ST-elevation myocardial infarction: B-type natriuretic peptide and prognosis in TACTICS-TIMI 18. *J Am Coll Cardiol* 2003; 41: 1264-72.
- Morrow DA, Rifai N, Antman EM, Weiner DL, McCabe CH, Cannon CP, et al. C-reactive protein is a potent predictor of mortality independently of and in combination with troponin T in acute coronary syndromes: a TIMI 11A substudy. *Thrombolysis in Myocardial Infarction. J Am Coll Cardiol* 1998; 31: 1460-5.
- Kuklinska AM, Sobkowicz B, Mroczko B, Sawicki R, Musial WJ, Knapp M, et al. Prognostic significance of the admission plasma B-type natriuretic peptide measurement in patients with first ST-elevation myocardial infarction in comparison with C-reactive protein and TIMI risk score. *Clin Chim Acta* 2007; 382: 106-11.
- Scirica BM, Sabatine MS, Jarolim P, Murphy SA, de Lemos JL, Braunwald E, et al. A. Assessment of multiple cardiac biomarkers in non-ST-segment elevation acute coronary syndromes: observations from the MERLIN-TIMI 36 Trial. *Eur Heart J* 2011; 32: 697-705.
- Canadian Cardiovascular Society; American Academy of Family Physicians; American College of Cardiology; American Heart Association, Antman EM, Hand M, Armstrong PW, Bates ER, Green LA, Halasyamani LK, et al. 2007 focused update of the ACC/AHA 2004 guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2008 15; 51: 210-47.
- Gibson CM, Cannon CP, Daley WL, Dodeg JT Jr, Alexander B Jr, Marble SJ, et al. TIMI frame count: a quantitative method of assessing coronary artery flow. *Circulation* 1996; 93: 879-88.
- Rathore SS, Weinfurt KP, Gross CP, Krumholz HM. Validity of a simple ST-elevation acute myocardial infarction risk index: Are randomized trial prognostic estimates generalizable to elderly patients? *Circulation* 2003; 107: 811-6.
- InTIME-II Investigators. Intravenous NPA for the treatment of infarcting myocardium early; InTIME-II, a double-blind comparison of single-bolus lanoteplase vs accelerated alteplase for the treatment of patients with acute myocardial infarction. *Eur Heart J* 2000; 21: 2005-13.
- Morrow DA, Antman EM, Giugliano RP, Cairns R, Charlesworth A, Murphy SA, et al. A simple risk index for rapid initial triage of patients with ST-elevation myocardial infarction: an InTIME II substudy. *Lancet* 2001; 358: 1571-5.
- Tu JV, Donovan LR, Lee DS, Wang JT, Austin PC, Alter DA, et al. Effectiveness of public report cards for improving the quality of cardiac care: the EFFECT study: a randomized trial. *JAMA* 2009; 302: 2330-7.
- Morita E, Yasue H, Yoshimura M, Ogawa H, Jougasaki M, Matsumura T, et al. Increased plasma levels of brain natriuretic peptide in patients with acute myocardial infarction. *Circulation* 1993; 88: 82-91.
- Richards AM, Nicholls MG, Yandle TG, Frampton C, Espiner EA, Turner JG, et al. Plasma N-terminal probrain natriuretic peptide and adrenomedullin: new neurohormonal predictors of left ventricular function and prognosis after myocardial infarction. *Circulation* 1998; 97: 1921-9.
- Talwar S, Squire IB, Downie PF, Mccullough AM, Campton MC, Davies JE, et al. Profile of plasma N-terminal proBNP following acute myocardial infarction; correlation with left ventricular systolic dysfunction. *Eur Heart J* 2000; 21: 1514-21.
- Mega JL, Morrow DA, De Lemos JA, Sabatine MS, Murphy SA, Rifai N, et al. B-type natriuretic peptide at presentation and prognosis in patients with ST-segment elevation myocardial infarction: an ENTIRE-TIMI-23 substudy. *Am Coll Cardiol* 2004; 44: 335-9.
- Libby P, Ridker PM. Inflammation and atherosclerosis: role of C-reactive protein in risk assessment. *Am J Med* 2004; 116: 9-16.
- Anzai T, Yoshikawa T, Shiraki H, Asakura Y, Akaishi M, Mitamura H, et al. C-reactive protein as a predictor of infarct expansion and cardiac rupture after a first Q-wave acute myocardial infarction. *Circulation* 1997; 96: 778-84.
- Pietilä K, Harmoinen A, Pöyhönen L, Koskinen M, Heikkilä J, Ruosteenoja R. Intravenous streptokinase treatment and plasma C-reactive protein in patients with acute myocardial infarction. *Br Heart J* 1987; 58: 225-9.
- Foussas SG, Zairis MN, Lyras AG, Patsourakos NG, Tsirimpis VG, Katsaros K, et al. Early prognostic usefulness of C-reactive protein added to the Thrombolysis In Myocardial Infarction risk score in acute coronary syndromes. *Am J Cardiol* 2005; 15: 96:533-7.
- Zairis MN, Manousakis SJ, Stefanidis AS, Papadaki OA, Andrikopoulos GK, Olympios CD, et al. C-reactive protein levels on admission are associated with response to thrombolysis and prognosis after ST-segment elevation acute myocardial infarction. *Am Heart J* 2002; 144: 782-9.
- Dibra A, Mehili J, Schwaiger M, Schühlen H, Bollwein H, Braun S, et al. Predictive value of basal C-reactive protein levels for myocardial salvage in patients with acute myocardial infarction is dependent on the type of reperfusion treatment. *Eur Heart J* 2003; 24: 1128-33.