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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA MAKALESİ

Early Prognostic Values of Cardiac Biomarkers in STEMI patients that underwent Percutaneous Coronary Intervention

Perkutanöz Girişim Yapılan STEMI hastalarındaki Kardiyak Biyomarkerların Erken Prognostik Önemi

Gökce AKGÜL[1], Elif DEĞİRMENCİ[1], Can AKTAŞ[1], Şevki Hakan EREN[2], Yoldaş DEMİRTAŞ[1]

ABSTRACT

Aim: To assess the early prognostic values of admission cardiac biomarkers (CKMB, hs-Troponin T, BNP) in patients with STEMI by determining the association of these markers with mortality, Gensini scores and LAD involvement prospectively.

Materials and Method: The current study was performed through the six-month period on 70 STEMI patients admitted to ED who had chest pain for the first time in their lives and underwent to percutaneous coronary intervention (PCI). Admission first cardiac biomarker values measured within 6 hours, patient demographics and clinical characteristics (age, gender, PCI results, LAD involvement) and Gensini scores calculated in regards to PCI results were recorded. Association of each cardiac biomarker (CKMB, hs-Troponin T, BNP) with the presence of mortality and LAD involvement was calculated. Correlation between biomarker levels and gensini scores were sought with Spearman correlation coefficients test.

Results: BNP (p=0.005) and hs-Troponin T (p=0.002) were associated with increased mortality. There was no association between mortality and the first admission value of cardiac biomarkers (BNP, CK-MB, hs-troponin T) with Gensini score (p>0.05). Higher BNP values indicated higher LAD (+) lesion probability (p<0.05) while no association between LAD(+) lesion and the other biomarkers (CKMB, hs-Troponin T) (p>0.05).

Conclusions: Acute STEMI with high BNP and hs-Troponin T levels predict increased mortality and needs more serious treatment and close follow-up. Additionally, higher BNP levels suggest a potential LAD (+) lesion which is closely related with mortality. Admission BNP and hs-Troponin T values indicate early prognostic outcome in STEMI patients, however they don't point out the severity of the lesions.

Keywords: Myocardial infarction, Biomarkers, Percutaneous Coronary Intervention, Mortality

ÖZET

Amaç: ST segment elevasyonlu miyokard infarktüsü olan hastalarda başvuru anındaki kardiyak biyomarkerların (CKMB, hs-Troponin T, BNP) prospektif olarak mortalite, Gensini skoru ve LAD lezyonun varlığını belirleyerek erken prognostik önemini değerlendirmektir.

Materyal ve Metod: Bu çalışma altı aylık bir periyotta acil servise ilk kez göğüs ağrısı ile başvurup perkutan koroner girişim (PCI) yapılan 70 hastada yapılmıştır. Başvuru anında ilk kardiyak biyomarkerlar ölçülmleri, hastaların demografik ve klinik özellikleri ve PCI sonuçlarına göre Gensini skorları hesaplanarak kaydedilmiştir. Her bir kardiyak biyomarker ile ilişkili mortalite varlığı ve LAD tutulumu hesplanmıştır. Biyomarker düzeyleri ile Gensini skoru arasındaki korelasyon Spearman korelasyon analizi ile test edilmiştir.

Bulgular: BNP (p=0.005) ve hs-Troponin T (p=0.002) artmış mortalite ile ilşkliydi. Gensini skoru ile mortalite ve ilk başvuru anındaki kardiyak biyomarkerlar arsında herhangi bir ilişki tespit edilmemiştir (p>0.05). Yüksek BNP düzeylerinde yüksek oranda LAD tutulumu tespit edilmiştir (p<0.05) ancak diğer biyomarkerlar (CKMB, hs-Troponin T) ile LAD lezyonu varlığı arasında bir ilişki tespit edilmemiştir (p>0.05).

Sonuç: Akut ST segment elevasyonu MI ile başvuran hastalarda yüksek BNP ve hs-Troponin düzeyleri artmış mortalitenin bir göstergesi olabilir bu nedenle daha ciddi bir yaklaşım ve takibe gereksinim vardır. Buna ilaveten yüksek BNP düzeyleri potansiyel olarak LAD tutulumunu gösterebilmekte olup bu da mortalite ile sıkı bir ilişki içerisindedir. Başvuru anındaki BNP ve hs-Troponin T değerleri ST segmen elevasyonu olan MI' lü hastalarda erken prognostic sonuçları gösterebilmektedir ancak lezyonun ciddiyeti hakkında bir fikir vermemektedir.

Anahtar Kelimeler: Miyokard İnfarktüsü, Perkutan koroner girişim, Mortalite

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[1]Koc University Department of Emergency Medicine Istanbul, Turkey

[2]Cumhuriyet University, Department of Emergency Medicine , Sivas, Turkey

Introduction

Coronary artery disease (CAD) is considered as the most common cause of death in the world (1). In the recent years, physicians started to use cardiac marker testing in the evaluation of cardiac events. The significance of the cardiac biomarker troponin in evaluation of acute myocardial infarction (AMI) patients has been better understood so that nowadays troponin measurement is considered as the standart test for patients with AMI (2). Cardiac biomarkers have a significant role in the risk stratification of acute coronary syndromes (ACS). Detecting high risk patients and estimating the prognosis is considered as important as diagnosis of AMI.

Percutaneous coronary intervention (PCI) remains the gold standart test for assesment of coronary vascular diseases since it is currently the best tool in the evaluation of coronary luminal obstruction. The Gensini Scoring System is widely used to estimate the severity of CAD based on the lesion location, the degree of coronary vessel stenosis, and the number of stenotic artery segments.

The aim of this prospective study is to determine the correlation between the first cardiac biomarker levels of ST elevation myocardial infarction (STEMI) patients measured early after admission with Gensini score and mortality. These biomarkers include CKMB (Creatine kinase MB isoenzyme), hs-Troponin T (High-sensitivite troponin T) and BNP (Brain natriüretic peptide). In our study, we evaluated PCI findings of STEMI patients with their early cardiac biomarker levels to determine the correlation between cardiac biomarker levels and lesion stenosis degree on prognosis and mortality.

Materials and Method:

Study design and population

The study was performed prospectively through a six-month period between 1 January- 31 June 2015 on seventy STEMI patients admitted to emergency departments of Koc University and Sivas Cumhuriyet University Hospitals who had chest pain within the last six hours for the first time in their lives and underwent PCI. Patients' focused medical history, physical examination, twelve-lead electrocardiography (ECG) and chest radiography tests were performed and recorded upon arrival. Venous blood samples were taken from the patients for measuring cardiac biomarker levels.

The patients who had chest pain and/or discomfort lasting at least 30 minutes and ECG with STEMI according to 2013 ACCF/AHA guidelines were included in the study (3). All of the patients were checked with Transthoracic echocardiography (TTE) to look for whether focal wall motion abnormalities were present or not. Philips Epiq 7 Ultrasound Machine was used for TTE in this study. Patients who had renal failure (creatinine >2 mg/dL) or previous cardiac diseases were excluded from the study. All patients were given written informed consent and the study was approved by Koc University Medical School Ethical Committee.

Cardiac Biomarker Analysis

Venous blood samples from the antecubital veins of patients were obtained to measure serum levels of BNP, CKMB and hs-Troponin T. Serum BNP levels were measured by enzyme immunoassay (EIA) kit and with ELISA method (Biomedica Medizinprodukte GmbH, Wien, Divischgasse). Roche Creatine Kinase-MB Cobas Integra/cobas c systems was used to measure CKMB levels (normal range 0-25 IU/L) and Troponin T hs STAT Elecsys and Cobas e analyzers was used to measure hs-Troponin T levels (normal range <0.06 ng/ml). Patients who had BNP levels above the cut-off value of 80 pg/ml were considered as BNP positive, CKMB levels above the cut-off value of 25 IU/L as CKMB positive and hs- Troponin T levels above the cut-off value of 0.06 ng/ml as hs-Troponin T positive.

Angiographic Analysis

PCI studies of all patients were evaluated by cardiologists who were blind to patients' clinical and cardiac marker status. CAD severity was calculated using the Gensini score system (4). Patients who had stenosis ≥ 70% in their left anterior descending artery (LAD) were considered as high risk patients with LAD (+) lesion.

Gensini Scoring system

Gensini score was first described in 1980 and it is calculated by considering the geometrical severity of lesions found in angiography, multiple obstructions of coronary vessels and the amount of myocardium affected by ischemia. Each lesion was given a score considering the amount of stenosis as indicated by the reduction of lumen diameter. Then, the lesion score is multiplied with a number according to clinical significance of affected myocardial functional area due to ischemia caused by coronary artery vessel stenosis. The Gensini score is finalized by adding all of the lesion scores.

Gensini score is used to determine the severity of coronary lesions. Scoring is performed as follows: 5 points for left main coronary artery lesion, 2.5 points for proximal LAD and left circumflex artery (LCx) lesions respectively, 1.5 points for mid LAD lesion; 1 point each for the first diagonal branch (D1), obtuse marginal branch, and the right coronary artery lesions , 0.5 points for second diagonal (D2) or posterolateral branch of LCX lesions, 1 point for narrowing between 0-25%; 2 points for narrowing between 25-50%; 4 points for narrowing between 50-75%; 8 points for narrowing between 75-90%; 16 points for narrowing between 90-99%, 32 points for 100% totally occluded lesion. Then a defined coefficient for each segment of coronary stenosis is multiplied with a score corresponding to the degree of points (4).

Statistical Analysis

The data obtained from this study was analyzed by SPSS 20 software package. The Mann Whitney U test was performed to analyze the differences between

independent groups. P values less than 0.05 were considered as statistically significant. Spearman's correlation coefficient test was used to analyze associations between variables without normal distribution.

Results:

The clinical and demographic characteristics of the patients are listed in Table 1 and Table 2. The associations between Gensini score and BNP, CK-MB, hs-troponin T were evaluated. There was no significant difference between the value of BNP, CK-MB and hs-troponin T with Gensini score (p>0.05).

Table 1. Demographics and Clinical Characteristics of the Patients

		Number (n)	Percent %
Gender	Male	26	37.1
	Female	44	62.9
	Total	70	100.0
Diagnosis	Acute inferior MI	27	38.6
	Acute posterior MI	12	17.1
	Acute anterior MI	31	44.3
	Total	70	100.0
BNP (pg/ml)	<80	40	57.1
	>80	30	42.9
	Total	70	100.0
LAD (stenosis %)	<70	32	45.7
	>70	38	54.3
	Total	70	100.0
hs-Troponin T (ng/ml)	Negative	14	20.0
	Positive	56	80.0
	Total	70	100.0
CK-MB (IU/L)	Negative	9	12.9
	Positive	61	87.1
	Total	70	100.0

BNP: B-type natriüretic peptide, LAD: Left Anterior Descending artery, CK-MB: Creatine kinase MB isoenzyme, hs-Troponin T: High-sensitivite troponin T, MI: Myocardial Infarction

Table 2. Value Distributions of Variables

	Number	Mean	Median	Minimum	Maximum
Age (year)	70	60.53	60.00	33.00	87.00
BNP (pg/ml)	70	107.07	63.25	0.60	800.00
Hs Troponin T (ng/ml)	70	5.97	0.76	0.00	50.00
CK-MB (IU/L)	70	90.92	64.00	12.00	398.00

BNP: B-type natriüretic peptide, CK-MB: Creatine kinase MB isoenzyme, hs-Troponin T: High-sensitivite troponin T

CK-MB, BNP, hs-Troponin T were classified as positive and negative according to the cut-off values and re-evaluated for association with Gensini score. There was no significant difference between the value of BNP, CK-MB and hs-troponin T positivity with Gensini score (p>0.05) (Table 3).

The association between mortality with Gensini score was evaluated. No significant association was found between Gensini score and mortality (p>0.05) (Table 3).

Table 3. Associations between Gensini Score with Pozitivity of LAD, Cardiac Markers and Mortality

		BNP(+)	hs-Trop. T(+)	CKMB(+)	LAD(+)	Mortality
Gensini	r	-0.221	.025	-0.031	-0.003	-0.221
	p	0.066	0.839	0.801	0.981	0.066
	N	70	70	70	70	70

BNP: B-type natriüretic peptide, hs-Trop. T: high-sensitivite troponin T, CK-MB: Creatine kinase MB isoenzyme, LAD: Left Anterior Descending artery

The associations between mortality and BNP, CK-MB, hs-troponin T were evaluated. Higher BNP (p=0,005) and hs-Troponin T (p=0.002) values were related to increased mortality. CK-MB values were found to be higher in deceased patients although it was stastically insignificant (p> 0.05) (Table 4).

The effect of LAD lesion positivity (vessel stenosis>%70) on mortality was evaluated. There was no significant association between mortality and LAD lesion positivity (p>0.05) (Table 4).

Association between LAD (+) stenosis with cardiac marker levels and their positivity were evaluated. There was a significant association between LAD (+) stenosis with increased BNP levels and its positivity (p<0.05). There was no significant association between LAD (+) stenosis and other cardiac biomarker levels and their positivity (hs-Troponin T, CKMB) (p>0.05).

Table 4. Associations between Mortality with Cardiac Markers and LAD positivity

		BNP	hs-Trop. T	CK-MB	LAD(+)
Mortality	r	0.332	0.366	0.208	0.149
	p	0.005*	0.002*	0.084	0.217
	n	70	70	70	70

BNP: B-type natriüretic peptide, hs-Trop. T: High-sensitivite Troponin T, CK-MB: Creatine kinase MB isoenzyme, LAD: Left Anterior Descending artery

Discussion:

Early detection of high-risk patients and prediction of prognosis are as important as confirming the diagnosis of STEMI. The prognostic values of admission cardiac biomarker measurements in patients treated with PCI for STEMI is unclear. However, they are still used commonly in practice since they are relatively inexpensive and applicable tools (5).

Infarct size is considered as one of the most significant prognostic factors in AMI patients. Possible practical tools for assesing infarct size include methods for imaging, electrocardiographic interpretation and biochemical markers (6). In literature, there are only few studies performed for assesing the relationship between admission cardiac biomarker levels and its ability to guess prognostic outcome. For this reason, we examined admission cardiac biomarker levels and its association with coronary artery lesion severity on early period of STEMI and their prognostic significance. Large trials have shown the predictive value of elevated Troponin T and Troponin I (7, 8) and CK-MB (9) levels

regarding mortality in AMI patients who have underwent PCI (10). However there are only a few studies evaluating the clinical significance of BNP in patients with STEMI, NSTEMI and unstable angina (11-14). Elevated BNP levels are associated with a larger infarct size and increased mortality (12, 15-17). Jeong et al found that increased levels of admission BNP, cardiac troponin I (cTnI) and high sensitivity C - reactive protein (hs-CRP) are related with death, reinfarction and new or worsening congestive heart failure. However, Jeong et al concluded that the use of admission cardiac biomarker levels of patients with STEMI who had underwent PCI had only a minimal impact for predicting the long term cardiovascualar events (18).

In our study, admission hs- Troponin T and BNP levels were related with increased mortality similar to findings of the past studies (19-21).

Angiographic data may provide additional prognostic information for CAD patients. In our study we preferred to use the Gensini Scoring System to determine the severity of CAD because Gensini index classification is one of the most widely used scoring systems. It depends on vessel diameter stenosis and proximal/distal vessel lesion variety (22).

Limited data is available for correlation of cardiac biomarker levels with Gensini score in literature. Peppes et al. studied correlation between myocardial enzyme levels and inflamation markers with severity of CAD and Gensini score (23). They found a positive correlation between CAD severity and serum levels of myocardial enzymes (creatinine phosphokinase (CPK), aspartate aminotransferase (AST), lactate dehydrogenase (LDH)) and inflammatory indices (C-reactive protein (CRP), fibrinojen, white blood cells (WBC) and erythrocyte sedimentation rate (ESR)). In their study, laboratory evaluation of cardiac markers was performed in the first 48 hours of hospital stay (23).We investigated the association of cardiac biomarker levels taken within the first 6 hours with Gensini scores and mortality. We concluded that there were no association between cardiac biomarker levels, Gensini scores and mortality.

BNP levels greater than 80 pg/ml was found to be associated with tighter culprit vessel diameter stenosis. LAD lesions are thought to be more risky than the other vessel lesions. Proximal/mid LAD culprit lesions suggest larger extent of ischemia (15). Goyal et al observed significantly higher BNP levels in patients with LAD involvement than in patients with other coronary artery involvement (24). In our study, BNP levels were found to be higher in LAD stenosis positive patients however there was no association between LAD lesion positivity and other cardiac biomarker levels (CKMB, hs-Troponin T). Unlike past studies, there was no association between mortality and LAD (vessel stenosis >70%) positivity in our study.

Study Limitations

The number of patients in the study population was not in the desirable range; consequently the data obtained from the study should be carefully interpreted. Cardiac biomarker measurements were only performed in early period and were not evaluated with serial measurements. The extended follow-up period of patients would provide more comprehensive data on mortality. A prospective multi-center study of a larger population is desirable.

Conclusion:

Although coronary angiography remains the gold standard test to determine STEMI patients, cardiac biomarkers can also be used for identification and prognosis of STEMI patients. We evaluated the association of cardiac biomarkers with coronary artery lesion severity and the effects of these markers on mortality. In our study, we found that high levels of BNP and hs-Troponin T measured in early period of STEMI predicts high mortality risk for these patients. These findings suggest that STEMI patients with high BNP and hs-Troponin T levels require more serious treatment and close follow-up. Additionally, in our study, high BNP levels suggest the presence of LAD lesion positivity which is related with higher mortality and less favourable prognostic outcome. However, we found no association between LAD lesion positivity and other cardiac biomarkers. There was also no association between early period cardiac biomarker levels and mortality with Gensini scores of STEMI patients.

Therefore, this study highlights that the patients presented to the emergency department with STEMI should be evaluated with hs-Troponin T and BNP together. As a result, admission BNP and hs-Troponin T levels have a prognostic significance in STEMI patients, but they do not indicate the severity of lesion according to the current study.

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