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Research Article

Study of Global Longitudinal Strain And N-Terminal Pro Brain Natriuretic Peptide as Predictors of Outcome in Acute St-Segment Elevation Myocardial Infarction Patients Undergoing Primary Percutaneous Coronary Interventions

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Abstract

Objective: Acute ST-segment elevation myocardial infarction (STEMI) patients should be risk-stratified in order to enhance the outcome. Our study was designed to assess the prognostic value of N-terminal pro brain natriuretic peptide (NT-proBNP) and global longitudinal strain (GLS) of the left ventricle in patients presenting with acute STEMI and treated by primary percutaneous coronary interventions (PPCI).

Methods: the study included 100 STEMI patients treated by PPCI, their age was 55.69 ±8.70 years, all patients were subjected to analysis of NT-proBNP plasma level, and calculation of the GLS, and follow up was done for 6 months for major adverse cardiac events (MACE) occurrence.

Results: patients were divided into two groups according to MACE, group I (20 patients who had MACE), group II (80patients without MACE), the NT-proBNP was significantly higher and the GLS was significantly lower in group I, and by multivariate regression analysis GLS was shown to be the most significant predictor of MACE (p value=0.003).

Conclusions: Our study concluded that both GLS and NT-proBNP are significantly related to MACE, with GLS being the single most significant predictor for MACE in patients with acute STEMI treated by PPCI.

Keywords: acute ST elevation myocardial infarction; global longitudinal strain; NT-proBNP

Introduction

Acute ST-segment elevation myocardial infarction (STEMI) is one of the major contributors to adverse cardiovascular outcomes. Left ventricular ejection fraction (LVEF) is a predictive factor for outcomes in STEMI patients [1, 2]. However, the LVEF is both preload and afterload dependent, with substantial interobserver variability. Two-dimensional speckle tracking echocardiography (2D-STE) is a B-mode based approach that can assess regional myocardial deformation through measuring of global longitudinal strain (GLS), which has been shown to be less affected by loading conditions [3-7]. recent studies reported that myocardial deformation imaging by 2D-STE after acute myocardial infarction (AMI) predicts cardiovascular outcomes such as new onset heart failure (HF) and cardiovascular death [8, 9].

The plasma concentration of brain natriuretic peptide (BNP) increases after AMI, [10] and after acute coronary syndromes [11] and the levels of BNP and N-terminal pro brain natriuretic peptide (NT-proBNP) are recognized as new and useful biochemical markers for both the diagnosis and prognosis of HF [12-14]. However, data regarding the relationship between increased NT-proBNP level and adverse cardiac events after AMI is still limited. Our study is designed to assess the prognostic value of NT-proBNP and GLS of the left ventricle (LV) in patients presenting with acute STEMI and treated by primary percutaneous coronary interventions (PPCI).

Material and methods

Our study is a prospective cohort research and included 100 patients presented to our cardiology department (from march2019 to December 2019) by acute STEMI and underwent PPCI within 12 hour of the onset of chest pain, excluding those with LVEF≤40%, previous history of percutaneous coronary interventions(PCI)or coronary artery bypass graft (CABG), left bundle branch block, atrial fibrillation , significant valvular disease, also patients with non-cardiac causes that could interfere with NT-Pro BNP level were excluded .All patients included in the study were subjected to the followings:

Demographic and clinical data: Including age, gender, weight, height, body mass index (BMI), and history of clinical risk factors, and Killip class were also assessed.

12 lead electrocardiograms (ECG): Was done to all patients to diagnose STEMI [15].

Transthoracic echocardiography: It was performed within 48 h of admission to our institution and after patients were treated by PPCI. It was done using a Philips *iE33 xMATRIX* echo system, and the following parameters were measured:

- The LVEF, left atrial volume index (LAVI), early mitral inflow velocity (E), early mitral annulus diastolic velocity (e'), and (E/e').
- 2D-STE using a semiautomatic algorithm, a 2-dimensional clip acquisition of the LV in apical (4, 2, and 3 chamber) views by recording three consecutive heart cycles with offline analysis of the GLS as an average longitudinal strain of the 17 LV segments [16,17].

N T- pro BNP level: Peripheral samples of plasma were obtained on admission for measurements of NT-pro BNP, and analysis was performed using the Modular Analytics E170 NT-proBNP immunoassay (Roche Diagnostics, Mannheim, Germany) [18].

Follow up: for all patients for the occurrence of major adverse cardiovascular events (MACE) had been done for 6 months post discharge (by telephone at 1, 3, and 6 months). The primary end points for MACE occurrence in the study were (all-cause mortality, cardiovascular mortality, stroke, reinfarction, and hospitalization due to HF).

Statistical analysis

Data were analyzed using IBM SPSS software package version 20.0 **(**Armonk, NY: IBM Corp). Categorical variables were described using number and percent, compared using the chi-square test and continuous variables were described using mean and standard deviation, and compared using the Mann-Whitney test. The Spearman correlation coefficient, receiver operator characteristic (ROC) curve, and univariate and multivariate logistic regression tests were used, P<0.05 was considered statistically significant**.**

Results

Our study included 100 STEMI patients (their age 55.69 ±8.70 years, and 75% were males), all patients underwent PPCI with stent placement and all patients were kept on dual antiplatelet therapy, high intensity statins and by the end of 6-month patients were classified into 2 groups:

- Group I included 20 patients who reached the primary end points: [1 (1%) had all-cause mortality, 2 (2%) had cardiovascular mortality, 6 (6%) had reinfarction, and 11 (11%) had HF hospitalization.
- Group II included 80 patients who did not reach the primary end points.

Baseline clinical and laboratory characteristics: (Table1)

There was no statistically significant difference between the two groups regarding age, gender, presence of risk factors, site of infarction, and troponin level however the Killip class II-III (MCp= 0.002), and NT pro-BNP were significantly higher in group I of patients(P<0.001)

Angiographic characteristics: (Table1)

All patients underwent successful PPCI with stent placement, and TIMI grade 3 flow was achieved in all patients, there was no statistically significant difference between the two groups regarding the culprit coronary artery involved, the need for thrombus aspiration, or the total number of stenotic coronary vessels.

	All patients (NO=100)	Group I (NO=20)	Group II (NO=80)	P value
Age(mean±SD)	55.69 ±8.70	56.62 ± 7.0	54.06 ± 10.72	0.205
Gender (Male)	75	15	60	0.932
Body surface area(/m2)	1.8±0.3	1.9±0.4	2.0±0.3	0.223
Smoking	55	15	40	0.742
Diabetes Mellitus	38	10	28	0.846
Hypertension	60	16	44	0.697
Family history for CAD	19	5	14	0.865
History of stable CAD	19	4	15	0.725
Anterior AMI by ECG	55	12	43	0.826
Killip class (No) I II III	 72 24 4	 5 11 4	 67 13 0	 MCp= 0.002*
Troponin T(ng/ml) (Mean ± SD)	0.607 ± 0.719	0.41 ± 0.37	0.37 ± 0.32	0.253
N proBNP (pg/ml.) (Mean ± SD)	(2090.1 ± 1375.8)	3008.8 ± 1387.0	1647.8 ± 1140.4	<0.001*
Coronary angiography findings				
Single vessel disease	68	16	52	
Two vessel disease	17	4	13	MCp= 0.265
Multi vessel disease	15	6	9	
Distribution of PPCI according to revascularized coronary artery				
LAD	55	12	43	MCp= 0.432
RCA	30	7	23	
LCX/OM	15	3	12	

Table 1: Clinical , laboratory, and angiographic characteristics of the two groups of patients

Echocardiographic characteristics: (Table2)

	All patients (NO=100)	Group I (NO=20)	Group II (NO=80)	P value
Echocardiographic findings				
LVEF (%) (Mean ± SD)	47.73 ± 5.72	44.85 ± 4.27	46.11 ± 5.85	0.123
LAVI (ml/m2) (Mean ± SD)	30.24 ± 6.65	34.04 ± 5.59	26.50 ± 6.69	0.002*
E(cm/sec) (Mean ± SD)	61.67 ± 20.87	61.80 ± 19.70	65.0 ± 17.86	0.403
E'(cm/sec) (Mean ± SD)	6.63 ±2.0	5.44 ± 1.28	7.44 ± 2.05	0.007*
E/E'(Mean ± SD)	10.70 ± 4.72	14.19 ± 5.54	9.02 ± 3.15	<0.001*
GLS (%) (Mean ± SD)	10.41 ± 3.59	6.65 ± 1.92	12.22 ± 2.68	<0.001*

Table 2: Echocardiographic characteristics of the two groups of patients

- There was no statistically significant difference between the two groups regarding LVEF, however, the E' velocity and the GLS were significantly lower in group I of patients. The LAVI and E/E' were significantly higher in group I of patients.
- According to ROC curve analysis we found that GLS cut off value **of (≤-8)** and NT-pro BNP cut off value of **(>2318pg/ml)** were able to discriminate patients with MACE with the superiority of the GLS (AUC=0.971, p value<0.001, CI="0.940-1.001", sensitivity=90%, specificity =91.67%, PPV=78.3%, NPV=96.5%) ,(AUC=0.802, p value<0.001, CI= "0.685-0.920", sensitivity=89%, specificity=75%, PPV=51.6%, NPV=91.8%) respectively. (Figure 1).

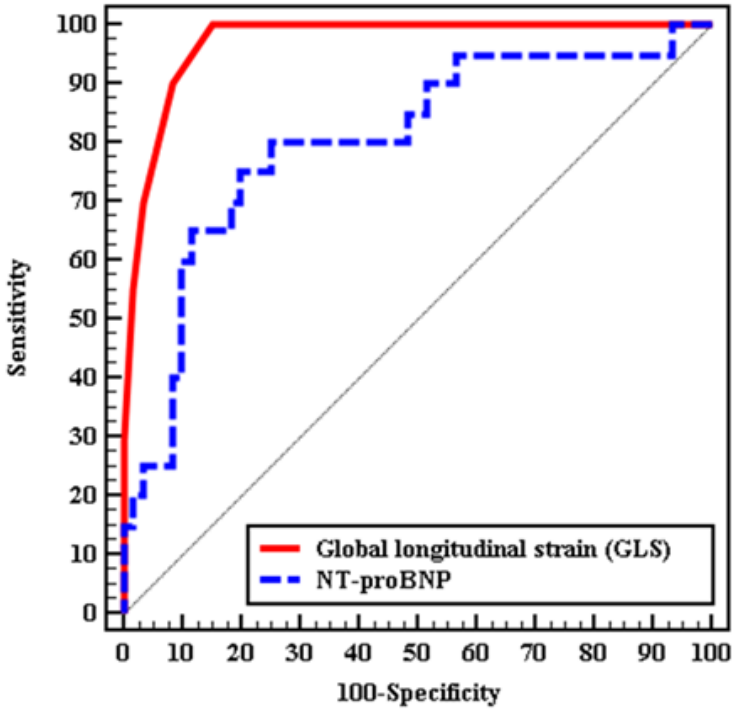

Figure 1: overlapping ROC curve for both GLS and N-proBNP to predict patients with MACE

- Correlation between the GLS and NT-ProBNP revealed a statistically significant inverse correlation between both of them (r=-0.492*, p value<0.001). (Figure 2).

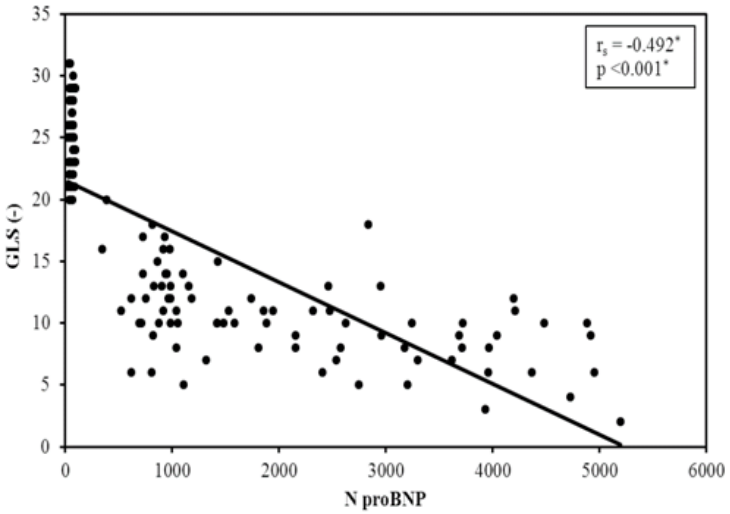

Figure 2: Correlation between NT-proBNP and GLS in cases group.

- Also, there was a statistically significant inverse correlation between LVEF and NT-ProBNP (r=-0.251, p value=0.025) and a statistically significant direct correlation between LVEF and GLS (R=0.346, p value=0.002).

We performed univariate and multivariate COX regression analysis for the parameters affecting MACE. In univariate analysis, the highly significant predictors were the NT-pro BNP level, E/E', and GLS with a p value <0.001 for all. In multivariate regression analysis, the GLS was shown to be the most significant predictor for MACE in patients with STEMI (p value=0.003, OR "95%C. I" = 0.721 (0.580 –0.896)).

Discussion

One of the primary causes of mortality worldwide is AMI though the use of early PPCI is growing and has greatly reduced mortality [19]. The evaluation of GLS, which depicts the function of longitudinally oriented cardiac fibers within the subendocardium and is particularly susceptible to ischemia, has received the majority of attention [4, 5)]. According to recent studies, GLS has been linked to regional cardiac function recovery and in-hospital outcomes in patients with AMI [20.21]. Also, it has been reported that the plasma level of BNP, a neurohormone that increases immediately after AMI in response to increased wall tension [22,23]. The combination of NT-proBNP with GLS improved risk stratification for MACE reduction, and in our study we found that both GLS and NT-proBNP were among the main predictors of MACE w(p value <0.001), and the multivariate analysis showed that GLS was the single most significant predictor of adverse outcome, and our findings are in agreement with many published studies, Sun Hwa Lee et al. [24] who studied a total of 171 patients with anterior STEMI who underwent successful PPCI , concluded that GLS is a powerful parameter related to development of HF, which is totally in agreement with our results. Mingzhu Xu et al. [25] who studied clinical outcomes in 405 patients with STEMI treated by PPCI, they found that the level of NT-BNP was an independent predictor for in-hospital HF incidence in AMI patients with preserved LVEF. In our study NT-ProBNP was a significant predictor of MACE in univariate regression but not in multivariate model. Also, Richards, et al. [26] who studied the prognostic value of levels of BNP, (NT-proBNP), and radionuclide LVEF in 666 patients with AMI. The B-type peptides and LVEF were significant predictors of mortality, HF, and new myocardial infarction. The combination of NT-proBNP (or BNP) with LVEF substantially improved risk stratification beyond that provided by either alone. And this was completely in agreement with our results as we found that NT-proBNP is among the univariate significant predictors of MACE in AMI patients, however, our study included only patients with EF > 40% unlike Richards et al who included patients regardless of their EF. Actually, the relationship between GLS and NT-proBNP reflects a pathophysiological association between longitudinal myocardial fiber dysfunction and the secretion of natriuretic peptides. This couldn't be explained by LVEF, which quantifies volume displacement, without an accurate assessment of myocardial function [27, 28]. our study is one of the few studies evaluating the incremental prognostic value of both NT pro BNP and GLS in patients presented with acute STEMI with preserved LVEF, but several studies are evaluating each one of them separately and this was in agreement of the study done by Ersbøll et al. [21] who studied 548 patients with AMI Within 48 hours of admission, assessment of GLS was performed, and NT- pro-BNP was measured, they found that GLS is significantly impaired in patients with in-hospital HF with LVEF > 40%, and multivariate analysis suggests that reduced GLS is the single most powerful predictor of HF occurrence.

Conclusions

Our study concluded that both GLS and NT-proBNP are significantly related to MACE, with GLS being the single most significant predictor for MACE in patients with acute STEMI treated by PPCI.

Study limitations

The present study has some limitations including; the study cohort was relatively small with short follow up time, and GLS, and NT-proBNP hasn't been assessed at time of follow up for endpoints.

List of abbreviations

2D-STE	Two-dimensional speckle tracking echocardiography
A	Late mitral inflow velocity
AMI	Acute myocardial infarction
BNP	Brain natriuretic peptide
CAD	Coronary artery disease
e'	Mitral annulus early diastolic velocity
ECG	Electrocardiogram
HF	Heart failure
LAD	Left anterior descending coronary artery
LAVI	Left atrial volume index
LCX/OM	Left circumflex coronary artery/obtuse marginal
LV	Left-ventricle
LVEF	Left ventricular ejection fraction
MACE	Major adverse cardiovascular events
NT-proBNP	N-terminal pro brain natriuretic peptide

PCI	Percutaneous coronary interventions
PPCI	Primary percutaneous coronary interventions.
RCA	Right coronary artery
STEMI	ST-segment elevation myocardial infarction

Ethics approval and consent to participate

The Ethics Committee of faculty of Medicine, Alexandria University had approved the Study, and informed consent was obtained from all individual participants included in the study.

Competing interests

The authors declare that they have no competing interests.

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Author contributions

GM did the acquisition and interpretation of echocardiography data, write and revised the article, FM performed data collection, and analyzed the data ST, and MH had performed the final data analysis. All authors had read and revised the article critically for important intellectual content and final approval of the version to be published.

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