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Research Article

CORRELATION OF BNP LEVELS WITH SELECTED CARDIAC ECHO PARAMETER PREDICT CARDIAC ISCHEMIA IN PATIENTS WITH ACUTE CORONARY SYNDROME

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ABSTRACT

Objectives: To estimate the valueof N-terminal pro brain natriuretic peptide(NT-proBNP) and echocardiography for predicting ventricular remodeling after Acute coronary syndrome and to investigate relationships between the NT-proBNP level and echocardiographic parameters. **Methods:** The study involved 70 patients with ACS admitted to cardiology care unite and 20 healthy matched subject. Clinical, laboratory characteristics, including B-type natriuretic peptide and echocardiographic parameter were measured within 24 hours of hospitalization, Twenty healthy subjects were considered as control group. The present study was conducted at the Department of Bio Chemistry, College of Medicine, University of Baghdad and Baghdad Teaching Hospital during the period from April 2013 to May 2014. **Results:** The patients with A.C.S. were found to have significantly higher mean (± SEM) value of serum NT-PRO BNP ($p<0.001$) compared with mean (± SEM)value of serum control group. Mean (± SEM) value of Dimension of left atrium, E/e, Deceleration time , EF%: Ejection fraction were Non significantly higher ($p\geq0.05$) compared with mean (± SEM) value of control groups except Mean (± SEM) value of Isovolumic relaxation time was significantly higher ($p\leq0.01$) compared with mean (± SEM) value of control groups, there was non significant positive correlation between the BNP levels and the estimated echo parameters: Dimension of left atrium , E/e, Isovolumic relaxation time, and deceleration time , except the mean of the Ejection fraction, there was significantly positive correlation between the BNP concentration with Ejection fraction. In Frequency distribution of NT-PRO BNP quintiles by Mitral Regurge (MR)-ECHO Finding . Largest number of the patients sample (11) have Mild Mitral Regurge in quintile 1 , followed by (9) in quintile 2, Chi-square test revealed significant differences($P\leq0.01$) . Largest number of the patients sample (5) have Moderate Mitral Regurge in quintile 1 , followed by (1) in quintile 2&3, Chi-square test revealed a significant differences($P\leq0.05$). **Conclusions:** Of many echocardiographic variables determined in patients that have suffered ACS, are treated with combined drugs and have no complications during hospitalization, the diastolic dysfunction is the best predictor of LVR with NT-proBNP at admission.

Keywords: B-type natriuretic peptide, ACS and echocardiography.

INTRODUCTION

B-type natriuretic peptide (BNP) is a neurohormone that is synthesized in ventricular myocardium and is released in response to increased wall stress. Its actions include natriuresis, vasodilation, inhibition of sympathetic nerve activity, and inhibition of the renin-angiotensin-aldosterone system. BNP is a useful diagnostic and prognostic marker among patients with heart failure. BNP has prognostic value across the full spectrum of patients with ACS, including those with UA/NSTEMI.InOPUS–TIMI16 patients with elevated levels of BNP (>80 pg/mL) or NT-proBNP had a twofold to threefold higher risk of death by 10 months,1 a finding that has

been confirmed.2,3 Together, these data suggest that measurement of natriuretic peptides in patients presenting with UA/NSTEMI adds importantly to current tools for risk stratification.several investigations focused on the clinical implications of neurohormonal activation after acute myocardial infarction (MI). BNP concentration rises rapidly over the first 24 hours after MI and then tends to stabilize; patients with a large infarct may have a second peak approximately 5 days later, perhaps reflecting the remodeling process.4 When measured 1 to 7 days after MI, BNP elevation identifies patients at risk for LV dysfunction, heart failure, and death. Here, as in chronic heart failure, the prognostic value of BNP seems to be greater than (but complimentary to) that of LVEF.5.

These initial studies of BNP in acute coronary syndromes (ACS) were small case-control studies, limited mostly to patients with ST-elevation MI, who are likely to have at least minor LV dysfunction. More recently, the prognostic application of BNP has been extended to include patients with unstable angina and non–ST-elevation MI (non–ST-elevation ACS). In a small case-control study of patients with non–ST-elevation ACS.6

METHODS

Study Design and Patient Population

The study was a single-center in which 70 patients with chest pain and potential ACS were consecutively admitted to the CCU Baghdad teating Hospital, Norway from april 2012 to may 2014. The main exclusion criteria were age <18 years or unwillingness or incapacity to provideinformed consent and prior inclusion in the present study. The primary outcome measure of the present study was , the general practitioner or nursery home were contacted to obtain relevant data. Clinical and laboratory parameters, including assessment of previous MI, angina pectoris, CHF, diabetes mellitus (defined as either whole blood fasting glucose concentrations above 6.1 mmol/L, two hour post glucose load concentrations above 10.0 mmol/L or medical treated diabetes mellitus), smoking status (stratified in categories of current smokers, previous smokers or patients who never smoked), hypercholesterolemia (defined as total cholesterol concentrations above 6.5 mmol/L or medical treated hypercholesterolemia) and arterial hypertension (defined as repeated blood pressure measurements above 140/90 mmHg or treated hypertension) were based on hospital records and personal interviews.Electrocardiographic (ECG) findings at admission were classified according to the presence of ST-segment changes (i.e. ST-segment depression or elevation, T-wave inversion or left bundle-branch block). The term ACS in the present study encompasses unstable angina (UAP), NSTEMI and STEMI. The following classification for the index diagnosis was used: STEMI; ST-segment elevation combined with TnT values > 0.05 ng/mL. NSTEMI; Transient ST-segment elevation, ST-segment depression, or T-wave inversion in at least 2 contiguous leads combined with TnT values >0.05 ng/mL. UAP; Transient ST-segment depression or Twave inversion and TnT values < 0.05 ng/mL. No-ACS; All other conditions (i.e. unspecific chest pain, arrhythmias, atrial fibrillation etc.) without ECG changes and with negativetroponins.Written informed consent was obtained from all patients and the study was approved by the Regional Board of Research Ethics and the Norwegian Health authorities and conducted in accordance with the Helsinki declaration of 1971, as revised in 1983.

Blood Sampling Procedures and Laboratory Measurements

Peripheral blood samples for determination of s-creatinine, s-glucose, s-lipids, and BNP were drawn immediately following admission by direct venipuncture with a minimum of stasis of an anticubial vein. A blood samples were centrifuged for 15 min with 2000 g and 20°C without delay. Serum for BNP were immediately frozen and stored at -80°C until the measurements were performed. For all other biochemical parameters, measurements were performed immediately following centrifugation.

BNP was analysed in serum using the Microparticle Enzyme Immunoassay (MEIA) Abbott AxSYM® (Abbott Laboratories, Abbott Park, Illinois, USA). The dynamic range was 0–4000 pg/mL and the within run coefficient of variation (CV) was 6.3% at 95 pg/mL and 4.7% at 1587 pg/mL.

Statistical Analysis

The patients were divided into quantiles on the basis of their NT-PROBNP. Approximately normally distributedvariables were given as mean and standard deviation (SD), The Chisquare test for association was applied between the NT-PRO BNP quantiles and categorical variables at baseline. The one way ANOVA test was used to test for equality of means of scale variables (e.g. age), and the two-sample t test and Mann Whitney test were

used for comparing the means of two samples, respectively.

RESULTS

Table 1: Demographic and base line clinical variables for Acs studied patients and control

Variables	Case	Control
Age (mean±SD)	58.7	33.4
Sex		
Male	52(74.3 %)	10(50 %)
Female	9(47.4 %)	10(50 %)
Risk factor		
Diabetes	35(50 %)	
Hypertension	44(62.9 %)	
Dyslipidemia	9(12.9%)	
Smoking	29(41.4 %)	
Obesity	22(31.4 %)	
(mean±SD)		
NT-PROBNP level(ng/L)	203.95±21.42,	107.79 ± 4.23

The patients with A.C.S. were found to have significantly higher mean (± SEM) value of serum NT-PRO BNP ($p<0.001$) compared with mean (± SEM)value of serum controlgroups as shown in Table1.

The table 2. shows Comparison between patients and control in ECHO Finding. Mean (± SEM) value of Dimension of left atrium, E/e, Deceleration time , EF%: Ejection fraction were Non significantly higher ($p\geq0.05$) compared with mean (± SEM) value of control groups except Mean (± SEM) value of Isovolumic relaxation time was significantly higher ($p\leq0.01$) compared with mean (± SEM) value of control groups.

Table 2: Compare between patients & control in ECHO Finding

Parameters	Mean ± SE		T-test value P-value
	Patients	Control	
DLA: Dimension left atrium(cm)	3.61 ± 0.07	3.35 ± 0.04	0.582 NS 0.219
E/e	9.29 ± 0.54	8.00 ± 0.42	2.178 NS 0.473
IVRT: isovolumic relaxation time(ms)	95.04 ± 4.48	75.00 ± 3.71	12.372 * 0.0348
DT: deceleration time(ms)	184.45 ± 9.11	175.00 ± 7.02	24.638 NS 0.862
EF%: Ejection fraction	46.66 ± 1.91	50.00 ± 2.57	8.924 NS 0.549

* ($P\leq0.05$), NS: Non-significant

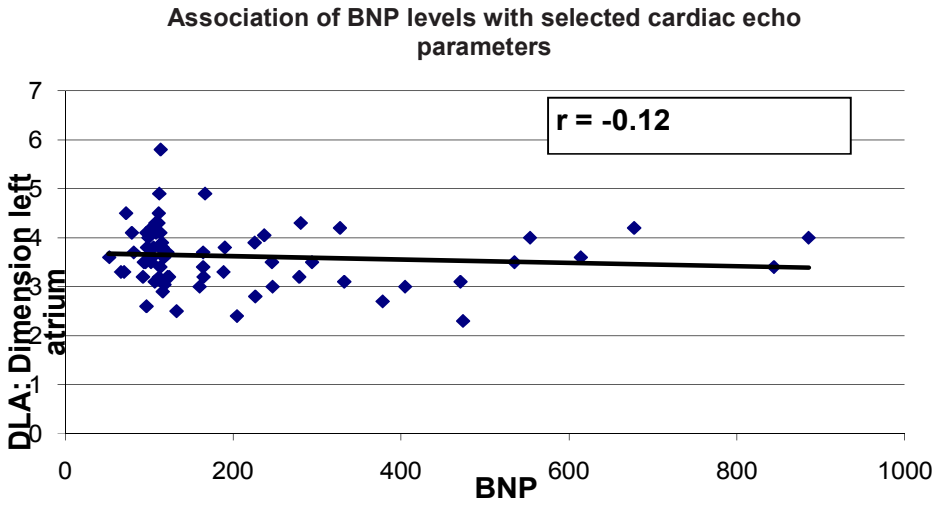

Fig. 1: correlation between the NT-PRO BNP(ng/l) levels and the Dimension of left atrium(cm), there was non significant positive correlation between the BNP levels and the Dimension of left atrium

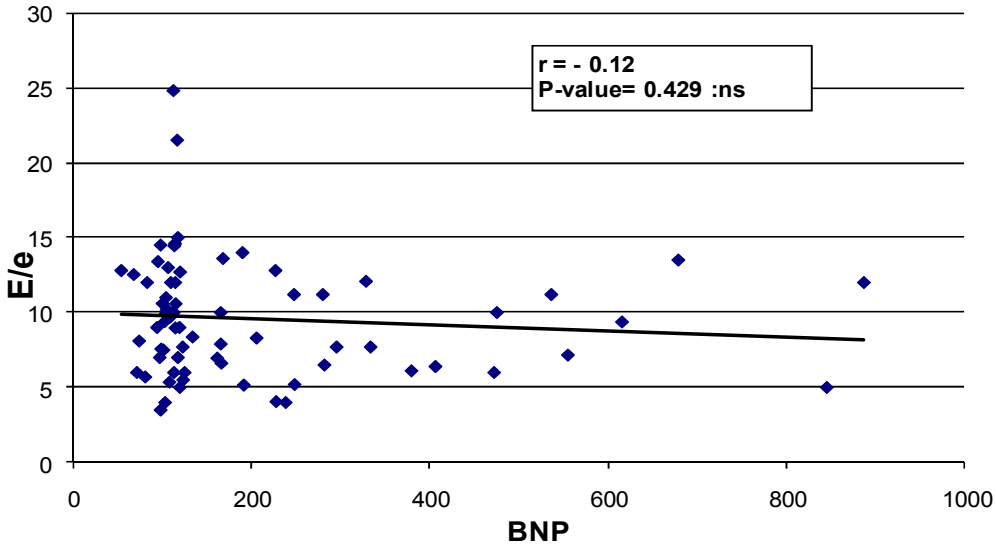

Fig. 2: Correlation between the NT-PRO BNP(ng/l) levels and the E/e ratio, there was non significant positive correlation between the BNP levels and the E/e.

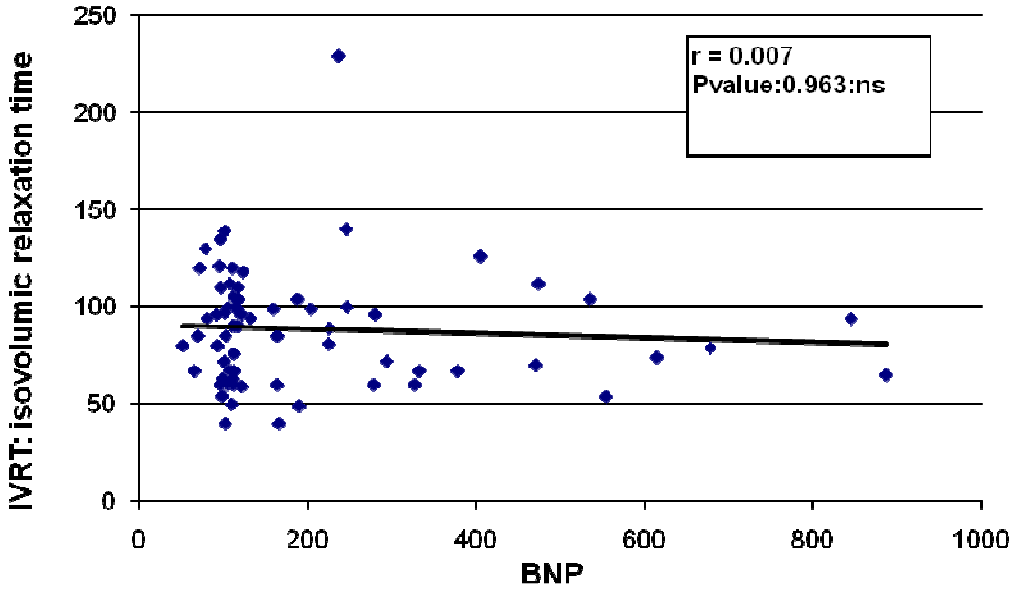

Fig. 3: Correlation between the NT-PRO BNP(ng/l) levels and theisovolumic relaxation time(ms),there was non significant positive correlation between the BNP levels and the Isovolumic relaxation time

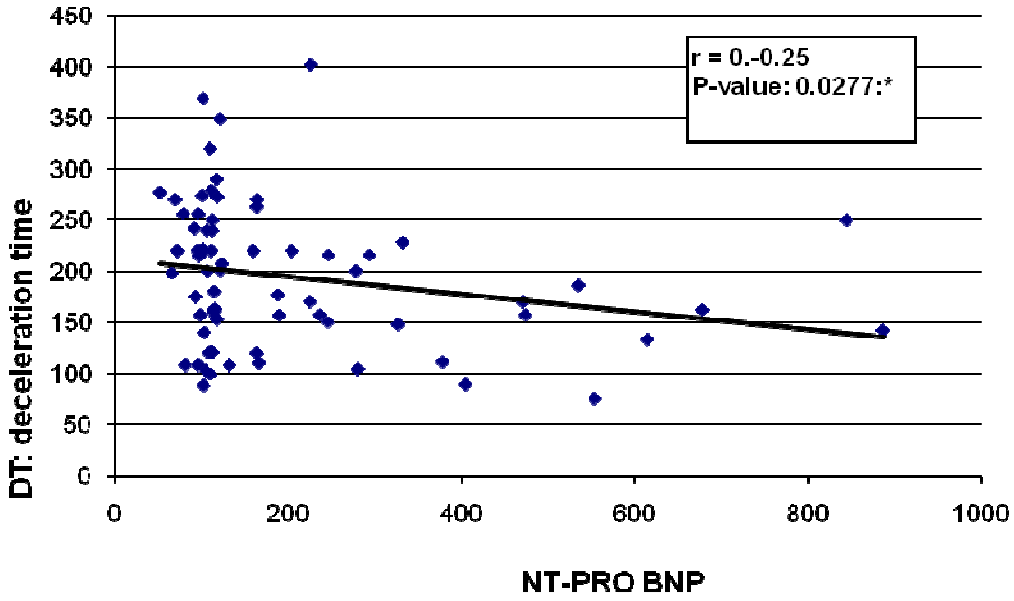

Fig. 4: correlation between the NT-PRO BNP(ng/l) levels and thedeceleration time(ms),there was non significant positive correlation between the BNP levels and deceleration time

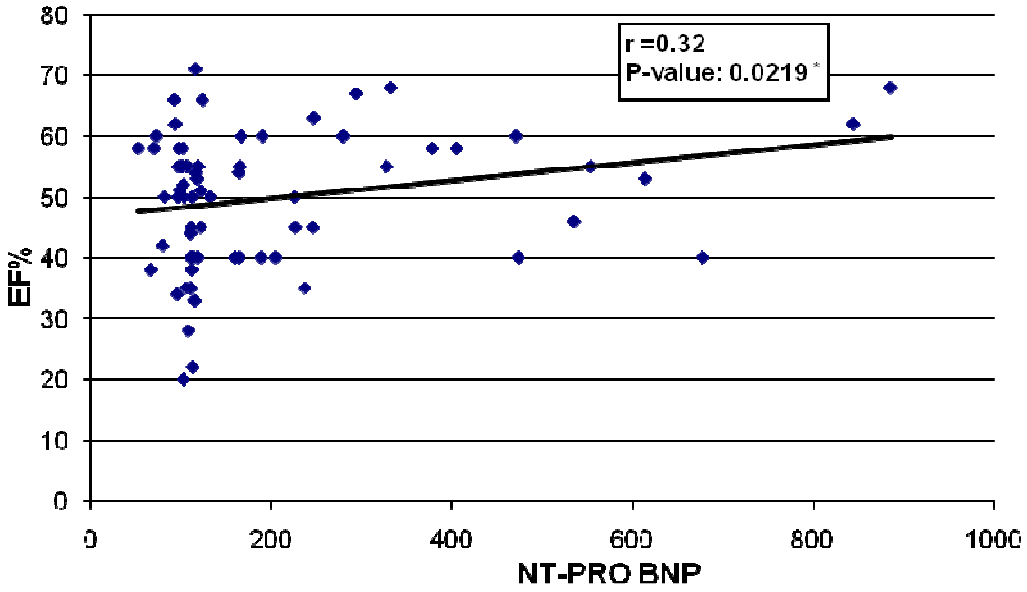

Fig. 5: Correlation between the NT-PRO BNP(ng/l) levels and the ejection fraction(%), there was significantly positive correlation between the BNP concentration with Ejection fraction

Table 3: Shows NT-PRO BNP level according to diastolic dysfunction Stages ,all 70 patients had diastolic dysfunction , there were significant difference in NT-PRO BNP level among stages of diastolic dysfunction, mean ± SE in stage 1 that include 43 patients higher than stage2 that include 18 patients and stage 3 that include 9 patients respectively.

Table 3: NT-PRO BNP level according to diastolic dysfunction Stages

SDD	No. of patients=70	Mean ± SE of BNP
1	43	217.51 ± 19.53
2	18	216.26 ± 13.95
3	9	114.59 ± 15.6
LSD value P-value	----	26.722 ** 0.0144

Table 4. shows Frequency distribution of (NT-PRO BNP) quintiles by Mitral Regurge (MR)-ECHO Finding , largest number of the patients sample (26) have no Mitral Regurge in quintile 2 , followed by (9) in quintile 1, Chi-square test revealed significant differences (P=0.001). Largest number of the patients sample (11) have Mild Mitral Regurge in quintile 1 , followed by (9) in quintile 2, Chi-square test revealed significant differences(P≤0.01). Largest number of the patients sample (5) have Moderate Mitral Regurge in quintile 1 , followed by (1) in quintile 2&3, Chi-square test revealed significant differences(P≤0.05).

Table 4: Frequency distribution of NT-PRO BNP quintiles by Mitral Regurge (MR)-ECHO Finding

MR	BNP			Chi-square value P-value
	quintile 1 ≥110ng/l (No. = 25)	quintile 2 110-400 ng/l (No. = 36)	quintile 3 ≥400 ng/l (No. = 9)	
0 (40)	9 (36.00%)	26 (72.22%)	5 (55.56%)	10.483 *** 0.0015
Mild (23)	11 (44.00%)	9 (25.00%)	3 (33.33%)	8.032 ** 0.0147
Moderate (7)	5 (20.00%)	1 (2.78%)	1 (11.11%)	5.469 * 0.0452
Chi-square value P-value	8.911 ** 0.0149	13.522 *** 0.0014	10.658 ** 0.0137	---
** (P≤0.01), *** (P≤0.001).				

DISCUSSION

The present study result showedmean (± SEM)ofNT-PROBNP was significantly higher(p<0.001) compared with mean (± SEM)value of serum control groups. NT-PRO BNP is a well known marker of left ventricular dysfunction and heart failure (HF), and it provides prognostic information beyond and above left ventricular ejection fraction (LVEF) in patients with acute coronary syndromes (ACS) [7]. This marker of neurohormonal activation plays a pivotal role across the spectrum of ACS, including patients with ST-elevation myocardial infarction (STEMI) and non ST-elevation myocardial infarction (NSTEMI). Moreover, elevated natriuretic peptides at presentation have been shown to identify patients with ACS who are at higher risk of death and HF and add information to that provided by the troponins [8-10].

The present study result showed there wasnon significant positive correlation between the BNP levels and the Dimension of left atrium ,this result disagreedwith José LópezHaldón et al[11]reported thatThe correlation of NTproBNP with echocardiographic variables that quantify left filling pressure, especially LAV, was better during the chronic phase than the subacute one subsequent to infarction. LAV did not show any correlation with NT-proBNP during the subacute phase, whereas it did during the chronic phase, although this was not intense. This difference probably is due to the fact that during the subacute phase insufficient time has elapsed for the elevation of filling pressure to dilate the atria.

The present study result showed there was non significant positive correlation between the BNP levels and the E/e.The E/e ratio, which reflects left filling pressure at the time of the study, showed a correlation with NT-proBNP both during the subacute and the chronic phase. However, this correlation was greater during the chronic phase (r=0.69) than at discharge (r=0.47). A possible explanation for this observation may be that NTproBNP values during the subacute phase are not only influenced by ventricular filling pressure, but also by ischemia. Therefore, in contrast to the E/ e ratio, NT pro-BNP is rather a marker of heart disease than of an increase in left filling pressure.[12]

The present study result showed there was non significant positive correlation between the BNP levels and the IVRT .Ioanna Zacharopoulou1 et al[13]in their study demonstrates that TIVRT-IVRTa provides a close prediction of NTpro-BNP in consecutive patients with an E/Ea ratio between 8 and 15, in sinus rhythm. In their series, the TIVRT-IVRTa index appears to be more accurate than the classical E/Ea index for the estimation of NTpro-BNP levels. The optimal cut-off value for prediction of NTpro-BNP levels >900 pg/ml was -25.5 ms. In their study, TIVRT-IVRTa correlated well with levels of NTpro-BNP, regardless of LVEF.

The present study result showed there wasnon significant positive correlation between the BNP levels and the deceleration time, this result disagreed withTretjak Met al. In thier studies found no correlation was demonstrated between natriuretic peptides and deceleration time.[14]

The present study result showed there wassignificantly positive correlation between the BNP concentration andEjection fraction.

Brij Mohan Goyalet al[15] reported thatthe main finding of thier study is that BNP levels are related also to the severity of coronary atherosclerosis: patients with multi-vessel disease showed higher BNP levels than subjects with only one or two vessel involvement. This trend was confirmed independently of the diagnosis of USAP or NSTEMI. Elevation of BNP levels appears strictly related to coronary artery disease, their results are in accordance with those of Sadanandan et al showing a correlation between TIMI flow, tightness of culprit stenosis and BNP levels.[16] However, with respect to the cited study, thier sample was characterized by

the absence of left ventricular dysfunction and enlargement, which are the main factors responsible for BNP increase.[17,18]

The present study result disagree withŠime Manola1,et al[19] in their study showed that that BNP in patients who underwent primary PCI due to STEMI with successful reperfusion could serve as a predictor of systolic dysfunction with LVEF<50%.

The table 3.Showed NT-PRO BNP level according to diastolic dysfunction Stages, there were significant difference in mean±SE of NT-PRO BNP level among stages of diastolic dysfunction, mean±SE in stage 1 that include 43 patients higher than stage2 that include 18 patients and stage 3 that include 9 patients respectively .All 70patients had diastolic dysfunction, thisresult agreed withA. Fazlinezhad1et al[20]in there study Plasma Brain Natriuretic Peptide (BNP) as an Indicator of Left Ventricular Function, Early Outcome and Mechanical Complications after Acute Myocardial Infarction Reported that no significant relationship between BNP level and grade of diastolic dysfunction was found.

Table 4.showed Frequency distribution of (NT-PRO BNP) quintiles by Mitral Regurge (MR)-ECHO Finding . Largest number of the patients sample (11) have Mild Mitral Regurge in quintile 1 , followed by (9) in quintile 2, Chi-square test revealed significant differences(P≤0.01) . Largest number of the patients sample (5) have Moderate Mitral Regurge in quintile 1 , followed by (1) in quintile 2&3, Chi-square test revealed significant differences(P≤0.05) . the present study result disagree withAnita Persson[21] study they used BNP, which has been found to be as accurate asNT-proBNP for identifying CHF.25 The volume overload andstretch of the atrial and ventricular myocardium associated with MR are potent stimuli for natriuretic peptide release, suggesting that in some patients the prognostic information obtained from BNP is partly derived from its reflection of MR grade. However, although MR is more common in patients with LV dysfunction, the association between MR grade and LVEF is not linear as unloading of the ventricle tends to increase LVEF.26

CONCLUSIONS

Of many echocardiographic variables determined in patients that have suffered ACS, are treated with combind drug and have no complications during hospitalisation, the diastolic dysfunction is the best predictor of LVR with NT-proBNP at admission, although it is associated with the development of remodeling, is an independent predictive factor when considered together with echocardiography.. However, correlation of NT-proBNP with echocardiographic variables that quantify left filling pressure, such as E/Em and LAV, was revealed early by diasystole more that systole.

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