Original Article

Assessment of BNP before PCI and its association with major adverse cardiac events in acute coronary syndrome with heart failure

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ABSTRACT
Objective - To study the association of pre PCI BNP values and MACE(Death,MI,Stroke,HF) in patients presenting with ACS and clinically evident heart failure.

Methods : BNP was checked in 150 patients presenting with ACS and clinically evident heart failure who underwent PCI within 5days of index event. MACE was evaluated during hospitalisation and at 30days post discharge.

Result : 60% of the patients in this study were males. Mean age of the patients was 48.5±3 years. Smoking (45.33%) and hypertension (40%) were the main risk factors. This study had more number of STEMI (50%) while NSTEMI was present in 30% and unstable angina in 20%

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1.Introduction
Acute coronary syndromes (ACS) encompass a continuum of cardiac ischemic events, ranging from unstable angina pectoris with no biochemical evidence of myocardial necrosis to ST-elevation acute myocardial infarction (AMI). The common denominator of ACS is a pathophysiologic process characterized by rupture of an atherosclerotic plaque, altered coronary vasomotor tone, platelet aggregation, and thrombosis. The prognosis of patients with ACS varies widely, and clinical, electrocardiographic, and biochemical markers of adverse prognosis have been used to identify high-risk individuals in need of aggressive and early intervention. Recently, B-type natriuretic peptide (BNP) has been shown to provide valuable prognostic information in patients with ACS.

Brain natriuretic peptide (BNP) is a 32-amino acid polypeptide secreted in response to excessive stretching of heart muscle cells (cardiomyocytes). The release of BNP is modulated by calcium ions. After the description of BNP elevation in patients with chronic heart failure, 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. When measured post MI, BNP elevation identifies patients at risk for LV dysfunction, heart failure, and excess death.

BNP differs from other biomarkers used for risk-stratification in ACS, such as troponins and creatine kinase-MB, in that it is a counter-regulatory hormone that may play an active role in the response to ischemic injury. The level of BNP may reflect the size or severity of the ischemic insult, even when myocardial necrosis has not occurred. The 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 myocardial infarction (NSTEMI).  

Several studies have come up showing that basal BNP levels in acute MI patients predict short term and long term prognosis. This study was planned to assess whether BNP levels are independent predictors of percutaneous intervention (PCI) outcomes in patients presenting with acute coronary syndrome and heart failure in terms of major adverse cardiac events (MACE).

2. MATERIAL AND METHODS

2.1 Study population

The study was conducted in the Department of Cardiology, PGIMER & Dr. Ram Manohar Lohia Hospital, New Delhi between November 2013 to February 2015. 150 patients presenting with acute coronary syndrome and clinical heart failure who underwent PCI within 5 days of index event were included in this study.

2.2. Inclusion criteria.

Patients of Acute coronary syndrome (ST elevation Myocardial Infarction, Non ST elevation Myocardial Infarction, Unstable angina) with clinical evidence of heart failure who would undergo PCI within 5 days of index event.

2.3. Exclusion criteria:

1. Patients of acute coronary syndrome with ongoing ischaemic chest pain suitable for primary PCI
2. ACS patients with renal failure
3. ACS patients with renal failure
4. ACS patients with renal failure
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6. ACS patients with renal failure
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9. ACS patients with renal failure
10. ACS patients with renal failure
11. ACS patients with renal failure

2.4. Study design

This study is a prospective study. A detailed history & physical examination was carried out along with routine investigations. BNP values were done prior to PCI. BNP was done by fluorescent immunoassay (Alere Triage Cardio Profiler panel). However BNP levels was not a determining factor for the timing of PCI. Post PCI evaluation was done at time of discharge and after 30 days post discharge.

The follow up was in terms of Major adverse cardiac events (MACE), i.e
1. Death due to cardiovascular cause or unexplained death
2. Recurrent nonfatal MI
3. Rehospitalisation due to heart failure
4. Stroke

This study conforms to widely accepted ethical principles guiding human research and also this study was approved by institutional ethics committee.

2.5. Statistical analysis:

1. Data is presented by mean±standard deviation (SD). All data analyzed by SPSS.
2. The baseline characteristics of patients with BNP <400 and BNP ≥400 pg/ml were compared using the independent student test for continuous variables.
3. Categorical variables or percentage of patients with BNP <400 pg/ml or ≥400 pg/ml was analyzed by Pearson’s χ² test.

4. RESULTS AND OBSERVATIONS

This study recruited a total of 150 patients of acute coronary syndrome (STEMI, NSTEMI, UA) with clinically evident heart failure who underwent PCI within 5 days of index event and were evaluated for MACE at hospital discharge and at 30 days followup.

4.1. Baseline characteristics

Ninety patients (60%) were males and 60 (40%) were females. Mean age of the patients was 48.5 ± 5 years. 90 (60%) patients were in 31-50 years and 45 (30%) were in 50-70 years age group. 5 (3.3%) patients were <30 years and 10 (6.66%) were >70 years. Sixty patients (40%) had STEMI, 60 (40%) had NSTEMI and 30 (20%) had unstable angina. Out of 150 patients, 31 (11.8%) were diabetics, 82 (31.2%) were hypertensive, 35.33% were dyslipidemic and 169 (64.3%) were smokers.

4.2. BNP values

Out of 150 patients 90 (60%) had BNP values less than 400 pg/ml and 60 (40%) had more than 400 pg/ml

4.3. Major adverse cardiac events (MACE) & Mortality

There were total 6 (4%) deaths. MACE were found in 29 (19.3%) patients. (fig 1) Individual components of MACE are described in table 1.2. MACE was 22.26% in STEMI cases, 15.55% in NSTEMI cases and 16.66% in unstable angina cases. (P value 0.962)

![Figure 1 - Major adverse cardiac events (MACE) & Mortality according to BNP](image)

<table>
<thead>
<tr>
<th>Table 1 : Major adverse cardiac events (MACE)</th>
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<tbody>
<tr>
<td>MACE</td>
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<tr>
<td>---------------------------------------------</td>
</tr>
<tr>
<td>Death due to cardiovascular cause or unexplained death</td>
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<td>Recurrent nonfatal MI</td>
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<td>Rehospitalisation due to heart failure</td>
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<tr>
<td>Stroke</td>
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<td><strong>TOTAL</strong></td>
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Table 1: Major adverse cardiac events (MACE)

<table>
<thead>
<tr>
<th>BNP</th>
<th>At discharge % (n)</th>
<th>At 30 days % (n)</th>
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<tbody>
<tr>
<td></td>
<td>Death</td>
<td>Recurrent nonfatal MI</td>
</tr>
<tr>
<td>&lt;400 pg/ml</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&gt;400 pg/ml</td>
<td>3.3% (2)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>1.33% (2)</td>
<td>0</td>
</tr>
<tr>
<td>P value</td>
<td>0.158</td>
<td>0.158</td>
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</tbody>
</table>

4.4. Age and MACE

MACE was highest in >70 yr age group followed by 50-70 yr age group. (P value 0.001) (Fig. 2)

Figure 2 - Age and MACE

5. Discussion

Most of the patients in this study were males (60%). Mean age of the patients was 48.5 ± 3 years. Most of patients (60%) were in age group of 31-50 yrs. Smoking (45.33%) and hypertension (40%) were the main risk factors. This study had more number of ST elevation myocardial infarction (50%) while non ST elevation myocardial infarction was present in 30% and unstable angina in 20% cases. Majority of patients (60%), had BNP values of less than 400 pg/ml. Mean BNP level was 360 ± 5 pg/ml. Therefore total MACE was 19.33% and total death were 4%. Total deaths were more in high BNP group (>400 pg/ml) versus low BNP group (<400 pg/ml) [4 (6.66%) versus 2 (2.22%) p <0.001]. Major adverse cardiac events were more in high BNP group versus low BNP group [35% versus 8.9% p<0.0001] So high serum BNP values was associated with higher MACE rates. Aylin Yildir etal13 also showed similar results in 95 patients with one-year follow-up. Plasma BNP levels were significantly higher in patients with MACE compared to those free of MACE (P<0.001)

STEMI had highest major adverse cardiac events 22.26% with p value of 0.962 which is statistically insignificant. Patients in age group >70 years had maximum incidence of MACE (70%) followed by 50-70 yr age group (MACE-51.1%) (p<0.001). So higher MACE was observed in elderly population with statistically significant p value. So increased age predicts poor prognosis. Similar result was found in a study conducted by Ertan Okmen.12 In this study ACS patients were treated with PCI. Increased age and high BNP were found to be independently associated with higher morbidity and mortality at 1 year

Both at the time of discharge and at 30 days death due to cardiovascular causes were more in higher BNP group. Death at 30 days is significantly associated with higher BNP values (P 0.038) while there is trend towards more deaths at time of discharge in patients with higher BNP values. At discharge recurrent nonfatal MI was more in high BNP group (>400 pg/ml) versus low BNP group(<400 pg/ml) with p value of 0.158. Even at 30 days recurrent nonfatal MI was more in high BNP group (>400 pg/ml) versus low BNP group(<400 pg/ml) with p value of 0.315. So there is trend towards more recurrent nonfatal MI at discharge and at 30 days in patients with higher BNP values. Even in NawsadSalehetal11 same findings were seen. NT-pro-BNP levels in the highest quartile (>490 mg/L) were identified as independent factors for nonfatal myocardial infarction after PCI.

At 30 days recurrent hospitalization due to heart failure was more in high BNP group (>400 pg/ml) versus low BNP group (<400 pg/ml) with p value of 0.227. So recurrent hospitalization due to heart failure is significantly associated with higher BNP values. At 30 days stroke was more in high BNP group (>400 pg/ml) versus low BNP group (<400 pg/ml) with p value of 0.4. So there is trend towards more stroke in patients with higher BNP values. Similar results were found in Kyung Kee-Baeketal14. NT-proBNP level were obtained on admission from 78 patients with ST-elevation myocardial infarction (STEMI), 32 with non-ST elevation MI (NSTEMI) and 66 with unstable angina (UA). The mean NTproBNP level was significantly lower in the event-free survivors than in those with events (1342±1598 versus 6129±6522 pg/mL, p<0.0001).

This study concluded that MACE and mortality rate at 30 days post discharge were significantly associated with higher pre PCI BNP values in acute coronary syndrome with heart failure. Among MACE recurrent recurrent hospitalization due to heart failure is significantly associated with higher BNP values while there was trend towards increased recurrent nonfatal MI and stroke in higher pre PCI BNP group. Even elderly age was significantly associated with higher MACE. Our study differed from other studies in the sense that patients from all 3 types of acute coronary syndrome were included in the study along with clinically evident heart failure.

6. CONCLUSION

This study concluded that pre PCI BNP and elderly age are strong predictors of major adverse cardiac events at 30 days post discharge in patients presenting with acute coronary syndrome with clinically evident heart failure.

7. LIMITATIONS

1. The number of patients in this study was less, so larger study population is required to give a conclusive result
2. Follow up period was only 30 days, so long term follow-up can give a better picture of the outcomes in these patients.

8. References

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