High Sensitive C-Reactive Protein as a Predictor of Acute Heart Failure in Acute Myocardial Infarction

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Abstract

Background: The development of heart failure in the setting of acute myocardial infarction (AMI) results in significant risk far above that of AMI. Independently CRP level in the early phase of MI might be a simple marker for the magnitude of the inflammatory response to myocardial necrosis, potentially providing prognostic information regarding the risk of death and HF. However, it is not known whether inflammation plays a role in the time-course of heart failure (HF) in this clinical setting. Our aim was to study the relationship between high CRP levels and HF progression during the first week of hospitalization for AMI.

Methods: This study included 59 patients admitted with acute myocardial infarction to the coronary care unit of the Suez Canal University hospital. CRP was assessed on the first, third and seventh day after admission.

Results: 42% of the study population developed heart failure. Among the patients with AMI, CRP was significantly higher in patients with HF than in patients without HF at admission, after 48 hours and after 7 days of admission ($p=0.0001$ & $p=0.000$ and $p=0.001$ respectively). Prevalence of HF was significantly higher on admission in patients with initial CRP serum level $>17$mg/L. CRP levels after 48 hours of admission showed significant positive correlation with peak CKMB ($p=0.02$) and peak CK levels ($p=0.002$) but they showed significant negative correlation with left ventricular ejection fraction ($p=0.01$).

Conclusions: On admission, hs-CRP level is a strong predictor of the incidence of heart failure in AMI setting. Hs-CRP is a good predictor of the amount of myocardial damage in AMI and it may predict the left ventricular ejection fraction after AMI.

Key Words: Acute myocardial infarction – High sensitive C-reactive protein – Heart failure – Creatine kinase.

Introduction

The acute phase reactant, CRP, a simple downstream marker of inflammation has now emerged as a major cardiovascular risk factor [1]. More than simply a marker of inflammation, CRP may influence directly vascular vulnerability through several mechanisms [2]. Myocardial infarction results in necrosis of cardiac muscle, which is a stimulus for CRP production [3] and its level rises in parallel to the amount of muscle necrosis, peaking at around day 2 post-MI and then falling. Persistent elevations of CRP 14 days after MI, suggesting ongoing inflammation, predict recurrent events [4]. Increased levels of CRP provide prognostic information in the acute setting. Elevated serum levels on hospital admission have a poor prognosis among patients presenting with unstable coronary artery disease [5]. Although the prognostic value of CRP in patients with myocardial infarction has not been evaluated in large studies, several data indicate that CRP is an important marker of risk also in the clinical setting of MI [6]. The high incidence of heart failure during acute myocardial infarction and the strong influence of HF on mortality make it one of the most challenging problems to deal with in this clinical setting. This study was done to compare levels of high sensitive C-reactive protein (hs-CRP) in patients admitted to the Suez Canal University hospital with acute myocardial infarction and patients admitted with acute myocardial infarction complicated by acute heart failure. Also to study if there is relationship between hs-CRP in AMI and both the size of myocardial damage measured by serum enzymes (total creatine phosphokinase; CK and MB isoenzyme of creatine kinase; CK-MB) and the left ventricular systolic function (as determined by echocardiography).

Subjects and Methods

This is a cross sectional study that included 59 patients admitted to the CCU of Suez Canal University Hospital with AMI [either ST segment elevation (STEMI) or non-ST segment elevation (NSTEMI)]. On admission, patients were subjected to the following:
A - Study questionnaire: Including personal history and risk factors for coronary artery disease.

B - Clinical examination: Included blood pressure, heart rate, cardiac examination and chest examination.

C - Electrocardiogram (ECG): Upon admission and thereafter every 6 hours, 12-lead electrocardiogram was carried out for 48 hours. Starting from the third day of admission, it was performed daily.

D - Heart failure evaluation: The presence and degree of HF were assessed on the first, third and seventh day after admission following the Killip classification [7]. To describe the progression of HF during the first 7 days of hospitalization, patients were divided into 4 classes:
   Class 1: Killip class 1 in all examinations.
   Class 2: Killip class >1 at entry and then improving to Killip class 1 within the seventh day.
   Class 3: Killip class 1 on admission and then worsening to Killip class >1 in the following days.
   Class 4: Killip class >1 in all examinations.

E - Echocardiographic assessment:
   Transthoracic echocardiography of each patient was used to assess the left ventricular systolic function by measuring the left ventricular ejection fraction by the Teichholz method [8].

F - Laboratory measurements:
   1 - Cardiac enzymes: Upon admission and thereafter every 6 hours, serum enzymes (creatine phosphokinase and CK-MB) were carried out for the first 48 hours. Starting from the third day of admission, the serum enzymes were measured daily by using kinetic assay methods on Hitachi 912 automatic autoanalyzer [9].

   2 - High sensitive C-reactive protein (Hs-CRP): In all patients, blood samples were drawn on the first, third and seventh day for measurement of CRP. Sera were kept frozen at –20°C for further laboratory investigations. Hs-CRP was measured using a solid phase enzyme-linked immunosorbent assay (hsCRP ELISA) [10].

   All laboratory tests were done at the laboratory of the Suez Canal University hospital.

Results

This study included 59 patients admitted with acute myocardial infarction to the coronary care unit of the Suez Canal University hospital. 76% of them were males and the rest 24% were females. 71.2% presented with STEMI and 28.8% presented with NSTEMI. 42.4% of the patients developed HF. There was no difference in the incidence of HF between patients with STEMI and patients with NSTEMI. Patients who developed HF had significantly higher heart rates (p=0.001) in comparison to non-HF group.

CRP levels were significantly higher in patients with HF in comparison to patients without HF at admission, after 48 hours of admission and after 7 days of admission (p=0.0001, p=0.000 and p=0.001 respectively).

CRP levels were mildly higher after 48 hours and after 7 days of admission in STEMI who received thrombolytic therapy (p=0.75, p=0.45 respectively).

CRP levels after 48 hours had significant positive correlation with both CK (p=0.002) and CK-MB levels (p=0.02) but they had significant negative correlation with left ventricular systolic function (p=0.01).

According to ROC curve analysis, the CRP at admission cut-off value that best identified the patients prone to heart failure approximated 17mg/L (at this value: sensitivity=88%, specificity=51.2%).

Table (1): Baseline characteristics of the study population.

<table>
<thead>
<tr>
<th></th>
<th>Heart failure n=25</th>
<th>No heart failure n=34</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean ± SD</td>
<td>60.84±8.49</td>
<td>57.44±8.91</td>
</tr>
<tr>
<td>Sex:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18 (72%)</td>
<td>27 (79.4%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Female</td>
<td>7 (28%)</td>
<td>7 (20.6%)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>14 (56%)</td>
<td>24 (70.5%)</td>
<td>0.45</td>
</tr>
<tr>
<td>Previous MI</td>
<td>6 (24%)</td>
<td>6 (17.6%)</td>
<td>0.75</td>
</tr>
<tr>
<td>DM</td>
<td>10 (40%)</td>
<td>12 (35.3%)</td>
<td>0.79</td>
</tr>
<tr>
<td>HTN</td>
<td>10 (40%)</td>
<td>14 (41.2%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>22 (88%)</td>
<td>30 (88.2%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>127.2±34.79</td>
<td>121.32±21.19</td>
<td>0.4</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>79.8±19.82</td>
<td>76.02±12.89</td>
<td>0.3</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>100.12±21.92</td>
<td>73.26±18.14</td>
<td>0.00*</td>
</tr>
<tr>
<td>Time to CCU (hours)</td>
<td>7.48±4.93</td>
<td>7.5±4.9</td>
<td>0.9</td>
</tr>
</tbody>
</table>
These; 25.4% of the population had heart failure versus 22%.

Møller et al. was supported by Berton et al. [6]. Roe et al. [12] 

tim for patients to enter CCU. In our study, the average time of transporting patients to the CCU was 7.5 hours in comparison to Berton et al. [6], Hartford et al. [14] and Pietila et al. [15].

This study revealed that 42.4% of the study population developed HF in the AMI setting. Of these, 25.4% of the population had heart failure at admission. This finding is almost identical to Roe et al. [12]. Furthermore, 8.5% of our study population was in class 3 (which means that they developed in-hospital heart failure) which differs from Roe et al. [12] who reported that the incidence of in-hospital heart failure was 3.6% of their study population. This could be explained by the frequent usage of cardiac catheterization, percutaneous coronary intervention and CABG in contrast to our study where the usage of these procedures was very limited.

By analysis of levels of CRP; the admitting CRP, CRP after 48 hours of hospital admission and after 7 days of admission, were significantly higher in patients with heart failure in comparison to patients without heart failure (adjusted \( p=0.000 \), \( p=0.000 \) and \( p=0.001 \) respectively) which was confirmed by Berton et al. [6], Mariotti et al. [14] and Pietila et al. [15].

The evidence that patients with heart failure in the AMI setting had more myocardial damage is evident from our study by the significantly higher levels of cardiac biomarkers (CK and CK-MB) in HF group (2171.24±1634.59U/L and 278.8±179.04U/L respectively) in comparison to non-HF group (1394.59±1162.75U/L and 191.38±110.94U/L respectively) which was confirmed by Toshihisa et al. [16] (2681±1678U/L versus 1620±1505U/L, \( p<.0001 \)). Also our study showed that the peak levels of CRP are significantly correlated to CK (\( r=0.402 \), \( p=0.002 \)) and to CKMB (\( r=0.302 \), \( p=0.02 \)) which were confirmed by Toshihisa et al. [16] who mentioned that peak CRP levels showed a weak positive correlation with peak CK levels (\( r=0.27 \), \( p=0.0004 \)). These results were also confirmed by Brunetti et al. [17], Hartford et al. [18] and de Beer et al. [19].

Our study also revealed that there is significant negative correlation between peak CRP levels and left ventricular ejection fraction (\( r=-0.331 \), \( p=0.01 \)) which was supported by Hartford et al. [18] and Toshihisa et al. [16] but were opposed by Brunetti et al. [17] and Zebrack et al. [20] who reported no correlation between CRP and LVEF. This difference is because of the difference of study population between our study (which included STEMI and NSTEMI but not UA) in comparison to Brunetti et al. [17] which included patients with acute coronary syndromes (STEMI, NSTEMI and UA).

**Discussion**

In this study, the incidence of heart failure in AMI was found to be 42% among the study population. This figure was higher than that reported by Berton et al. [6] (39%) and Giuseppe et al. [11] (39%). This might be attributed to difference in timing for patients to enter CCU. In our study, the average time of transporting patients to the CCU was 7.5 hours in comparison to Berton et al. [6] study which was only average 3 hours.

Diabetes; according to our study results, is more common in heart failure group (40%) than non-heart failure group (35.3%) but without statistical significance. These results are confirmed by Roe et al. [12] (44.7% versus 28.5% respectively), Møller et al. [13] (18% versus 10%) and Berton et al. [6] (39% versus 17%) but without statistical significance.

Hypertension shows the same prevalence between the heart failure group (40%) and the non-heart failure group (41.2%) in our study which was supported by Berton et al. [6] but opposed by Møller et al. [13] who mentioned that hypertension is significantly more prevalent in HF group (28% versus 22%).

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**Conclusion:**

CRP level at admission is a strong predictor of the incidence of heart failure in AMI. Also CRP levels are positively correlated to the amount of...
myocardial damage in AMI (measured by cardiac enzymes) and negatively correlated to the left ventricular ejection fraction measured by echocardiography. A cut-off value of hs-CRP at admission of 17mg/L is the best identified to detect patients prone to heart failure.

References