Little information is available about the potential role of brain (type B) natriuretic peptide in patients with acute myocardial infarction. We therefore analyzed peptide levels, measured at discharge from our coronary care unit, in 56 patients admitted with a diagnosis of acute myocardial infarction. We examined peptide concentrations in the light of different features in our patients, and found a significant association between natriuretic peptide levels and the two most important prognostic factors: left ventricular ejection fraction, and the severity and extent of coronary disease. Type B natriuretic peptide was a good predictor of these features, and we conclude that concentration of type B natriuretic peptide, measured at discharge from the coronary care unit, provides important clinical and prognostic information in patients with acute myocardial infarction.

Key words: Natriuretic peptides. Myocardial infarction. Ventricular dysfunction.

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INTRODUCTION

Brain (or type B) natriuretic peptide (BNP) is a potent neurohormonal regulator with natriuretic and vasodilatory action. It also inhibits the activity of the sympathetic nervous system and the renin-angiotensin axis. The peptide is secreted by cardiac muscle (largely the ventricular muscle), mainly in response to pressure or volume overloads (or both). In chronic heart failure (CHF), BNP can be used as a marker of neurohormonal activity, and its determination is of diagnostic and prognostic value. It is also of use in the monitoring of treatment. Studies on the behavior and clinical importance of BNP in acute myocardial infarction (AMI), however, are rare, although high levels have been related to a greater incidence of CHF, systolic dysfunction, ventricular remodeling and, in general, poorer prognosis. The aim of the present work was to determine the relationship between BNP levels at discharge from the coronary department and variables of interest in risk stratification before discharge in patients who had suffered AMI.

PATIENTS AND METHODS

The study subjects were 56 consecutive patients aged ≤65 years (53.6±9.4 years) who were discharged from the coronary department with a diagnosis of AMI according to new criteria. At discharge, the plasma BNP level of all patients was recorded using a fluorescence immunoanalyzer (Triage BNP Test®; Biosite). This system brings a reactive strip into
TABLE 1. Patient Baseline and Clinical Characteristics

| Clinical characteristics (n=56)                      | Age, years 53.6±9.46 | Male 49 (87.5%) | Previous AMI 18 (32%) | Previous and/or inferior AMI 32 (57%) | Other site 6 (11%) | ACS with elevated ST segment 44 (78.6%) | ACS without elevated ST segment 12 (21.4%) | CK peak 1.258.4 | Thrombolysis 21 (38%) | Primary PTCA 2 (3.6%) | Coronary angiography 44 (78.6%) | LVEF on release 52.5±13.9 | Length of stay, days 11.7±6.7 | Death 1 (1.8%) | Background Smokers 28 (50%) | High blood pressure 25 (44.6%) | Diabetes 13 (23.2%) | Hypercholesterolemia 21 (37.5%) | Ischemic heart disease 11 (19.6%) | Myocardial infarction 9 (16.1%) | Brain natriuretic peptide (BNP) Time taken to run tests, h 60.64±17.9 | Values, pg/mL 318.2±369.4 |

*PTCA indicates percutaneous transluminal coronary angioplasty; LVEF, left ventricular ejection fraction; AMI, acute myocardial infarction; ACS, acute coronary syndrome; CK, creatine kinase.

Statistical Analysis

Quantitative results are expressed as means±standard deviations, categorical results as absolute frequencies and percentages. The Student t test was used to determine the significance of differences between pairs of means; analysis of variance was used to examine differences between several means. Relationships between quantitative variables were analyzed by linear regression. Multiple regression was used for multivariate analysis. Significance was set at P=.05. All calculations were made using SPSS v.11 software.

TABLE 2. Mean Brain Natriuretic Peptide Levels According to Baseline and Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mean BNP in Groups, pg/mL</th>
<th>Cases, %</th>
<th>BNP, pg/mL</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Prior ischemic heart disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated ST in acute phase</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum Killip class &gt;1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF on release ≤40%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extent of disease &gt;1 vessel</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

*BNP indicates left ventricular ejection fraction; BNP, brain natriuretic peptide.

RESULTS

Table 1 shows the patients’ baseline characteristics and clinical characteristics at release. Brain natriuretic peptide levels were analyzed with respect to these clinical characteristics (Table 2), and were significantly higher in patients with prior ischemic heart disease, diabetes mellitus (DM), CHF, left ventricular dysfunction, or existing coronary disease.

Brain Natriuretic Peptide, Heart Failure and Left Ventricular Ejection Fraction

Univariate analysis showed significant differences between mean BNP levels at discharge according to the presence and severity of CHF during hospitalization (maximum Killip class reached; P<.0001), and between the mean BNP values of patients with and without left ventricular dysfunction (Table 3).

In multivariate analysis, the BNP level was the only variable related to post-AMI LVEF (P=.01; Table 4).
Nogales JM, et al. Neurohormonal Prediction of Post-Infarction Ventricular Dysfunction and Coronary Disease

A model for predicting the LVEF was produced based on the mean BNP level at discharge from the coronary department. After the stepwise regression analysis of all the variables (age, masculine sex, DM, prior ischemic heart disease, anterior AMI, acute coronary syndrome with elevation of the ST segment, BNP, and maximum Killip class attained) that might affect LVEF, BNP at discharge was found to have the greatest predictive power (LVEF=59.26-0.02 BNP [pg/mL]). Introducing the remaining clinical variables into the model led to no significant improvement. Figure 1 shows the linear association between BNP levels and LVEF.

The diagnostic exactness of BNP levels in the detection of patients with post-AMI left ventricular dysfunction was examined using ROC analysis. The area under the curve was 0.82. The optimum cut-off point was 533 pg/mL. Figure 2 shows the diagnostic validity indices for different cut-off points.

**Table 4. Association of Clinical Variables With LVEF on Release From Coronary Department***

<table>
<thead>
<tr>
<th>Clinical Variables</th>
<th>Univariate, <em>P</em></th>
<th>Multivariate, <em>P</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>.93</td>
<td>.25</td>
</tr>
<tr>
<td>Male</td>
<td>.45</td>
<td>.45</td>
</tr>
<tr>
<td>Diabetes</td>
<td>.24</td>
<td>.61</td>
</tr>
<tr>
<td>Prior ischemic heart disease</td>
<td>.36</td>
<td>.30</td>
</tr>
<tr>
<td>Prior AMI</td>
<td>.26</td>
<td>.66</td>
</tr>
<tr>
<td>ACS with elevated ST segment</td>
<td>.17</td>
<td>.15</td>
</tr>
<tr>
<td>BNP</td>
<td>&lt;.0001</td>
<td>.01</td>
</tr>
<tr>
<td>Killip</td>
<td>.009</td>
<td>.87</td>
</tr>
</tbody>
</table>

*AMI indicates acute myocardial infarction; ACS, acute coronary syndrome; BNP, brain natriuretic peptide.

The diagnostic exactness of BNP levels in the detection of patients with post-AMI left ventricular dysfunction was examined using ROC analysis. The area under the curve was 0.82. The optimum cut-off point was 533 pg/mL. Figure 2 shows the diagnostic validity indices for different cut-off points.

**Brain Natriuretic Peptide and Extent of Coronary Disease**

Coronary angiography was performed in 44 patients (78.6% of the sample). A clear relationship was seen between BNP levels and the extent of coronary disease, the number of diseased blood vessels, and significant anterior descending coronary artery (ADCA) disease (Table 3). In univariate analysis, the number of vessels with significant lesions was related.
only to DM, BNP levels and prior ischemic heart disease. After adjusting for these variables, the BNP level was the only characteristic at discharge that remained independently associated with the number of diseased vessels and significant ADCA disease ($P=.001$ and $P=.01$ respectively).

DISCUSSION

The discovery of the natriuretic peptides confirmed the heart as an endocrine organ capable of regulating hemodynamic status in conjunction with other systems (the central nervous system, baroreceptors, the kidney, etc). Brain natriuretic peptide is a perfect marker of neurohormonal status in patients with CHF. Independent of other variables such as age, LVEF or gender, high BNP levels are indicative of a poor prognosis.

After an AMI, BNP levels increase over the course of the next 24 hours, becoming stable in the subacute phase. Advanced age is also a cause of high BNP levels. Several studies conclude that patients with increased BNP levels in the subacute phase of AMI have a worse prognosis, and suffer a greater incidence of left ventricular dysfunction, CHF, ventricular remodeling and death in the mid-long term.

In the present study, we determined BNP levels in the subacute phase of AMI in young patients, and thus avoided the early peak in the plasma concentration and the influence of age.

The levels of BNP at release from the coronary department correlated with LVEF. This, plus the demonstrated mid-long term prognostic value of BNP levels, could help select or prioritize patients for an echocardiogram in the coronary department when this cannot be made available to all who present with AMI (of course, the determination of BNP levels can never replace an echocardiogram). Further, since BNP levels seem to be related to the extent and severity of coronary disease (number of diseased vessels or ADCA disease or both) knowing them could help when making decisions on whether to follow invasive or conservative management strategies.

The behavior of BNP in AMI could be influenced by certain treatments (as seen in CHF), by residual ischemia or the size of the AMI etc. This work does not examine these possibilities although it is unlikely that the conclusion would change. Patients with high BNP levels show greater left ventricular dysfunction and extensive coronary disease (or both) and might benefit from invasive management. The determination of BNP levels on discharge from the coronary department (at some moment during the second to the fourth day post-AMI), is a simple technique that provides important information on clinical status (with respect to CHF) as well as prognostic information (LVEF and extent of coronary disease). In addition, it is a marker of great predictive power in the detection of post-AMI ventricular dysfunction, which must be taken into account when taking decisions on patient management.

REFERENCES