European Heart Journal (2005) **26**, 234–240
doi:10.1093/eurheartj/ehi033

Clinical research

B-type natriuretic peptide: a novel early blood marker of acute myocardial infarction in patients with chest pain and no ST-segment elevation

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Received 13 May 2004; revised 24 September 2004; accepted 30 September 2004; online publish-ahead-of-print 1 December 2004

See page 207 for the editorial comment on this article (doi:10.1093/eurheartj/ehi078)

KEYWORDS
Acute coronary syndrome;
Acute myocardial infarction;
Natriuretic peptide

Aims This study was undertaken to determine the diagnostic value of admission B-type natriuretic peptide (BNP) for acute myocardial infarction (AMI) in patients with acute chest pain and no ST-segment elevation.
Methods and results A prospective study with 631 consecutive patients was conducted in the emergency department. Non-ST elevation AMI was present in 72 patients and their median admission BNP level was significantly higher than in unstable angina and non-acute coronary syndrome patients. Sensitivity of admission BNP for AMI (cut-off value of 100 pg/mL) was significantly higher than creatine kinase-MB (CKMB) and troponin-I on admission (70.8 vs. 45.8 vs. 50.7%, respectively, $P < 0.0001$) and specificity was 68.9%. Simultaneous use of these markers significantly improved sensitivity to 87.3% and the negative predictive value to 97.3%. In multiple logistic regression analysis, admission BNP was a significant independent predictor of AMI, even when CKMB and troponin-I were present in the model.
Conclusion BNP is a useful adjunct to standard cardiac markers in patients presenting to the emergency department with chest pain and no ST-segment elevation, particularly if initial CKMB and/or troponin-I are non-diagnostic.

Introduction

During the last decade B-type natriuretic peptide (BNP) has been recognized as a useful marker for the detection of acute and chronic left ventricular dysfunction.[1–5] BNP is released by the ventricles as a neurohormonal response to increased wall stress and pressure and volume overload[2,6,7] and correlates very closely not only with heart failure functional class but also with clinical response to treatment and prognosis.[4,8–11]

Acute regional diastolic and/or systolic left ventricular dysfunction is a hallmark of sudden and prolonged myocardial ischaemia, and is one of the first steps in the ischaemic cascade that leads to cell necrosis.[12] Thus, BNP might be released by ventricular myocardium in settings of acute coronary occlusion and prolonged cardiac ischaemia. Morita *et al.*[13] were the first to demonstrate significantly elevated plasma BNP levels on admission in 50 patients with ST-elevation acute myocardial infarction (AMI) compared with

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controls. Peak levels were observed 16 h after admission with over one-half of the patients developing a second peak by the fifth day.

The purpose of the present study was to evaluate the diagnostic role of admission plasma BNP for AMI in patients presenting to the emergency department with chest pain suggestive of cardiac ischaemia without ST-segment elevation.

Methods

Study population

From 1 January 2002 to 30 September 2003 we examined 631 consecutive patients in our emergency department at Pró-Cardíaco Hospital with complaints of chest pain or discomfort in the preceding 12 h due to possible acute cardiac ischaemia and in whom the admission electrocardiogram did not present ST-segment elevation. These patients are routinely managed in our Chest Pain Unit with a systematic diagnostic protocol which recommends the following: (i) cardiac markers: admission and serial (every 3 h) serum creatine kinase-MB (CKMB) mass levels, admission serum troponin-I level (and a 9th-hour sample in most cases); (ii) admission 18-lead electrocardiogram followed by serial (every 3 h) 12-lead tracings; (iii) two-dimensional echocardiogram (in many patients); (iv) if no myocardial necrosis or rest ischaemia is detected, a stress test (either treadmill electrocardiogram or single-photon emission computed tomographic myocardial scintigraphy).

For the present prospective study, plasma BNP was incorporated into the diagnostic protocol and obtained on admission with the purpose of correlating BNP with the final discharge diagnosis. The study complies with the Declaration of Helsinki, its protocol was approved by the hospital ethics committee, and patients gave informed consent. The trial was financially supported by the hospital.

Biochemical analysis

Plasma BNP was immediately analysed on the same EDTA-anti-coagulated blood sample collected on admission for CKMB and troponin-I, using the quantitative immunofluorescence assay manufactured by Biosite (San Diego, CA, USA). The analytic sensitivity of the assay is <5 pg/mL and the upper normal limit is considered to be 100 pg/mL. Plasma CKMB mass was measured by immunofluorescence assay manufactured by Dade-Behring (Marburg, Germany). The analytic sensitivity of the assay is 0.6 ng/mL and the upper normal limit is considered to be 5.0 ng/mL. Plasma troponin-I was measured by immunofluorescence assay manufactured by Dade-Behring. The analytic sensitivity of the assay is 0.1 ng/mL and the upper normal limit for the diagnosis of AMI was considered to be 1.0 ng/mL.

Diagnostic endpoints

(i) Non-ST-segment elevation AMI was diagnosed when an elevation of troponin-I level (>1.0 ng/mL in any sample during the first 9 h post-admission) and/or a typical CKMB curve occurred, with or without ST/T changes in the electrocardiogram (ECG), in the absence of any other demonstrable cause for the chest pain.

(ii) Unstable angina was diagnosed when, in the absence of the above troponin-I or CKMB changes, suggestive chest pain longer than 20 min duration was associated with either ST-segment depression (≥ 0.1 mV) or T-wave inversion in the electrocardiogram, pre-discharge ischaemic stress test, or significant coronary artery disease in an angiogram.

(iii) Absence of acute coronary syndrome was diagnosed when complete diagnostic protocol was performed in the Chest Pain Unit and did not demonstrate myocardial necrosis or ischaemia. Patients who showed increased CKMB and/or troponin-I levels after the performance of percutaneous transluminal coronary angioplasty were not considered to have AMI.

Patients were followed throughout their hospital stay by a research nurse (M.V.N.) who collected all physicians' admission clinical data and laboratory test results, and monitored and adjudicated physicians' in-hospital final diagnosis and events according to pre-specified protocol definitions. In most cases the final diagnosis was reviewed by at least two physician investigators.

Statistical analysis

Sample size for this study was calculated after reviewing the data in the first 300 consecutive cases. By considering a relationship of two patients with BNP value <100 pg/mL for each patient with BNP >100 pg/mL, and a prevalence of AMI of 10 and 20% in each group, respectively, a sample size of 630 patients was found to be necessary to obtain 5% significance with a power of 90%.

All data analyses were performed using Statistica 6.0 and R-system 1.80 statistical packages. Differences in proportions were judged by the χ^2 method. Plasma concentrations of BNP are described as the median and interquartile range (IQR). All sample measurements had their 95% confidence interval (CI) calculated by the maximum likelihood estimations method.

The Mann–Whitney *U* test was used to compare BNP levels between two independent groups (patients with or without AMI and patients with or without heart failure on admission) whereas the Kruskal–Wallis one-way analysis of variance was used to test the equality of distributions in the four BNP groups (AMI, unstable angina, non-acute coronary syndrome, and non-AMI).

The bivariate analysis between BNP level quartiles and clinical variables and final diagnosis was calculated by the χ^2 method for trend. Analysis of linear correlation between continuous variables was based on a non-parametric method (Spearman's rho).

A receiver operating characteristics (ROC) curve was generated and the area under the curve (and its 95% CI) calculated to determine the best discriminating level of BNP and troponin-I obtained on admission for predicting the diagnosis of AMI. Respective values were 100 pg/mL and 0.28 ng/mL. Comparison of ROC curves and their sensitivities were performed as recommended by DeLong *et al.*[14]

Sensitivity, specificity, positive and negative predictive values, likelihood ratios, and risk ratios were calculated in the usual manner.

Logistic regression analyses were used to establish the predictive relationship between continuous or dichotomized BNP levels and diagnosis of AMI adjusted for the effects of clinical and laboratory variables. Initially, all significant variables identified by univariate analysis were included in the models. Selection of variables was done by the forward stepwise method guided by likelihood ratio, and respective c-statistics were calculated. Modelling was performed, refusing entry to variables with $P > 0.10$. By using the dichotomized BNP level, three models were obtained: one with all variables except CKMB and troponin-I obtained on admission; a second including admission

CKMB and troponin-I with a discrimination level of 5.0 and 0.28 ng/mL, respectively; a third with discriminative level for admission CKMB of 5.0 ng/mL and troponin-I of 1.0 ng/mL. A *P*-value (two-tailed) of >0.05 was considered statistically non-significant.

When appropriate, the Bonferroni adjustment was made for three consecutive tests and considered significant for *P*-values of <0.017 for overall comparisons.

Results

Demographic and clinical characteristics of the 631 studied patients are depicted in *Table 1*. The median (IQR) time from chest pain onset to hospital arrival was 120.0 min (60.0–300.0) (similar values for AMI patients). Seventy-two patients had a final diagnosis of non-ST elevation AMI: 11 by positive troponin-I alone, three by positive CKMB alone, and 57 by both (one patient who died of cardiac rupture shortly after hospital arrival had normal admission markers). Unstable angina was diagnosed in 183 patients while 174 had the final diagnosis of no acute coronary syndrome. The remaining 202 patients had the diagnosis of AMI ruled out but not the diagnosis of unstable angina (because a stress test or coronary angiogram could not be performed).

Table 1 Baseline characteristics of 631 study patients and 72 non-ST elevation AMI patients

Characteristics[a]	All	AMI
Age, mean ± SD	67.3 ± 13.6	75.2 ± 11.5
Male gender, *n* (%)	343 (54.4)	46 (63.9)
Present use of aspirin, *n* (%)	193 (30.8)	24 (34.3)
History of diabetes, *n* (%)	125 (20.1)	22 (31.0)
Smoking habit, *n* (%)	88 (14.2)	9 (12.7)
Previous infarction, *n* (%)	174 (28.0)	19 (26.4)
Previous history of heart failure, *n* (%)	51 (8.1)	13 (8.1)
Heart failure on admission, *n* (%)	55 (8.8)	16 (22.5)
Normal ECG (admission), *n* (%)	492 (81.3)	33 (50.8)
ST-depression (admission), *n* (%)	37 (6.1)	16 (24.6)

[a]Percentages reflect the total number of patients for whom data were available.
SD, standard deviation.

Association of BNP levels with clinical variables and final diagnosis

Patients with AMI had a median (IQR) BNP level of 203.5 pg/mL (52.1–494.5) whereas patients with unstable angina and patients without acute coronary syndrome had 77.9 (25.8–240.0) and 27.7 pg/mL (9.1–76.8), respectively ($P < 0.0001$). The 202 patients who could only be ruled out for AMI had BNP levels of 45.7 pg/mL (17.3–127.0). These differences remained significant only for patients who presented to the emergency department without clinical evidence of heart failure ($P < 0.0001$).

In bivariate analysis, higher baseline levels of BNP were directly associated with age, history of diabetes, previous infarction, previous history of heart failure, heart failure on admission, ST-segment depression on admission, and diagnosis of AMI and unstable angina on index hospitalization. An inverse association was seen with smoking history, normal ECG on admission and diagnosis of non-acute coronary syndrome (*Table 2*). Median admission BNP levels were significantly higher in patients with previous heart failure or myocardial infarction and with evidence of heart failure at the time of admission, than in their counterparts (data not shown). In relation to patients in the first BNP quartile, those in the second, third, and fourth quartiles had AMI risk ratios of 1.27 (95% CI 0.84–3.23), 1.81 (1.47–3.77) and 5.16 (4.97–7.12), respectively ($P < 0.0001$ for trend). Patients with elevated plasma troponin-I on admission (>1.0 ng/mL) had significantly higher median (IQR) BNP levels than patients with normal troponin-I: 164.0 (38.9–533.5) vs. 57.0 (19.1–149.0), respectively

Table 2 Relationship of clinical characteristics and final diagnosis with quartiles of BNP levels (in pg/mL)

Characteristics[a]	1st quartile (0–17.5)	2nd quartile (17.6–55.0)	3rd quartile (55.1–158.0)	4th quartile (>158.0)	*P*-value for trend
Age, mean ± SD	58.3 ± 12.9	63.9 ± 12.3	71.5 ± 11.6	75.8 ± 10.7	0.0001
Male gender, *n* (%)	101 (29.4)	80 (23.3)	81 (23.6)	81 (23.6)	0.0761
History of diabetes, *n* (%)	25 (20.0)	21 (16.8)	38 (30.4)	41 (32.8)	0.0022
Smoking habit, *n* (%)	18 (33.3)	17 (31.5)	13 (24.1)	6 (11.1)	0.0134
Previous infarction, *n* (%)	19 (10.9)	29 (16.7)	55 (31.6)	71 (40.8)	0.0001
History of heart failure, *n* (%)	3 (5.9)	5 (9.8)	12 (23.5)	31 (60.8)	0.0001
Heart failure on admission, *n* (%)	4 (7.3)	4 (7.3)	13 (23.6)	34 (61.8)	0.0001
Normal ECG (admission), *n* (%)	149 (30.3)	136 (27.6)	118 (24.0)	89 (18.1)	0.0001
ST-depression (admission), *n* (%)	2 (5.4)	4 (10.8)	14 (37.8)	17 (45.9)	0.0001
AMI, *n* (%)	8 (11.1)	10 (13.9)	14 (19.4)	40 (55.6)	
Unstable angina, *n* (%)	37 (20.2)	36 (19.7)	52 (28.4)	58 (31.7)	0.0020
No acute coronary syndrome, *n* (%)	64 (36.8)	52 (29.9)	37 (21.3)	21 (12.3)	

[a]Percentages reflect the total number of patients for whom data were available.

($P = 0.0002$) (similar results if using ROC curve recommended troponin-I cut-off level of 0.28 ng/mL measured on admission). However, no linear correlation was found between admission troponin-I and BNP levels in patients with AMI (rho = 0.08, $P = 0.503$). Of the 72 patients with final diagnosis of AMI, only 37 had fulfilled the diagnostic criteria by CKMB and/or cTnI on admission. The knowledge of an elevated BNP blood level at this point in time allowed for the identification of 22 more patients (i.e. 60% of undiagnosed AMI patients on admission). The rates of AMI diagnosis in patients with admission troponin-I levels below 0.28 and 1.0 ng/mL, according to admission BNP levels, are presented in *Figure 1*.

Patients arriving at the hospital within 2 h of chest pain onset had similar median BNP blood levels and similar BNP diagnostic performance to patients with more than a 2 h delay.

Diagnostic accuracy of BNP for AMI

ROC curve analysis confirmed 100 pg/mL as the best diagnostic cut-off value of BNP for AMI (area under the curve = 0.710, 95% CI 0.642–0.778). Sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios of BNP $\geq$ 100 pg/mL for the diagnosis of AMI are depicted in *Table 3*.

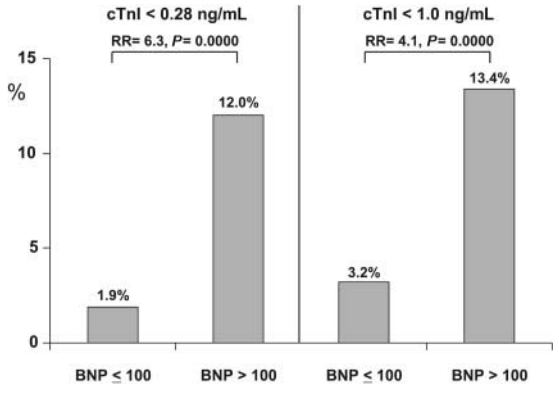

Figure 1 Rates of non-ST elevation acute myocardial infarction according to admission BNP and admission troponin-I levels. cTnI, troponin-I; RR, risk ratio.

Comparative diagnostic accuracy of BNP, CKMB, and troponin-I on admission

Although BNP had a significantly higher sensitivity than CKMB and troponin-I for the diagnosis of AMI, its specificity and positive predictive value fared significantly worse with similar values for negative predictive values (*Table 3*).

The combined use of BNP, CKMB, and troponin-I on admission (either one abnormal) significantly improved the sensitivities of isolated CKMB and troponin-I ($P < 0.0001$ for both) as well as their negative predictive values ($P = 0.0016$ for both) with a significantly lesser specificity and positive predictive value (*Table 3*).

The use of the ROC curve recommended a cut-off level of 0.28 ng/mL because admission troponin-I significantly improved sensitivity for the diagnosis of AMI (67.6%, $P < 0.0001$) in comparison with a value of 1.0 ng/mL, with a significant loss in specificity (93.7%, $P < 0.0001$) and no change in negative predictive value. With regard to combination of markers, only the sensitivity significantly improved (91.5%, $P = 0.0225$). Finally, the association of ST-segment depression with BNP, CKMB, and troponin-I did not further improve the diagnostic accuracy of these blood markers (data not shown).

In a logistic regression model in which we adjusted for other variables known to be predictors of AMI or related to an elevated BNP level (including age, previous history of heart failure, clinical evidence of heart failure on admission, serum creatinine level, and coronary risk factors) a BNP level >100 pg/mL on admission was an independent predictor of the diagnosis of AMI and free of interaction with plasma creatinine levels (*Table 4*). The addition of admission CKMB and troponin-I values to the regression model did not impact on the predictive power of BNP. The use of a 10-base logarithmic BNP value was also an independent predictor of AMI (odds ratio = 1.95, $P = 0.0157$).

Table 3 Diagnostic accuracy of admission BNP, CKMB, troponin-I or either one for non-ST elevation AMI

	BNP	CKMB	Troponin-I	Either
Sensitivity	70.8%* (67.2–74.4)	45.8% (41.9–49.7)	50.7% (46.4–54.8)	87.3%** (84.5–90.1)
Specificity	68.9%* (65.3–72.5)	98.4% (97.4–99.4)	98.8% (97.9–99.7)	65.7%* (61.8–69.6)
Positive predictive value	22.7%* (19.4–26.0)	78.6% (75.4–81.8)	85.7% (82.8–88.6)	27.0%* (23.3–30.7)
Negative predictive value	94.8% (93.1–96.5)	93.4% (91.5–95.3)	93.3% (91.2–95.4)	97.3%*** (96.0–98.6)
Positive likelihood ratio	2.28* (1.94–2.71)	28.63 (16.24–80.23)	42.25 (22.15–183.93)	2.55* (2.21–2.97)
Negative likelihood ratio	0.42 (0.35–0.50)	0.55 (0.51–0.60)	0.50 (0.45–0.55)	0.19* (0.14–0.25)
Risk ratio	4.38* (2.71–7.09)	11.85 (8.42–16.68)	12.71 (9.02–17.91)	9.91 (5.03–19.54)

Values in parentheses represent 95% CI.
*$P < 0.0001$ in relation to CKMB and troponin-I.
**$P < 0.0001$ in relation to BNP.
***$P = 0.0016$ in relation to CKMB and troponin-I.

Table 4 Logistic regression analysis showing odds ratios (95% CI) of baseline clinical variables for the diagnosis of non-ST elevation AMI

Variables	Model 1	Model 2	Model 3
ST-segment depression	8.87, $P < 0.0001$ (3.87; 20.32)	5.15, $P = 0.0015$ (1.87; 14.18)	6.00, $P = 0.0002$ (2.33; 15.48)
T-wave inversion	3.58, $P = 0.0145$ (1.29; 9.96)	$P = 0.4469$	$P = 0.3915$
Left bundle branch block	3.37, $P = 0.0088$ (1.36; 8.37)	$P = 0.8442$	$P = 0.8652$
BNP > 100 pg/mL	2.75, $P = 0.0027$ (1.42; 5.32)	2.89, $P = 0.0049$ (1.38; 6.05)	3.24, $P = 0.0026$ (1.51; 6.96)
Male gender	2.76, $P = 0.0021$ (1.45; 5.29)	$P = 0.2035$	$P = 0.0642$
Diabetes	2.06, $P = 0.0315$ (1.07; 3.97)	2.28, $P = 0.0389$ (1.04; 4.98)	2.47, $P = 0.0238$ (1.13; 5.43)
Age	1.04, $P = 0.0063$ (1.01; 1.07)	$P = 0.1756$	$P = 0.0802$
Previous infarction	0.45, $P = 0.0237$ (0.22; 0.90)	$P = 0.1683$	$P = 0.2367$
Troponin-I > 0.28 ng/mL	—	12.03, $P < 0.0001$ (5.63; 25.68)	—
Troponin-I > 1.0 ng/mL	—	—	36.66, $P < 0.0001$ (11.09; 121.16)
CKMB > 5.0 ng/mL	—	13.70, $P < 0.0001$ (4.78; 39.26)	11.96, $P < 0.0001$ (3.81; 37.58)

Model 1, all variables except CKMB and troponin-I; Model 2, all variables including CKMB >5.0 ng/mL and troponin-I >0.28 ng/mL; Model 3, all variables including CKMB >5.0 ng/mL and troponin-I >1.0 ng/mL.

Discussion

Patients with acute chest pain in the emergency department frequently constitute an analytical dilemma to physicians, particularly when the ECG is non-diagnostic. Although 60–70% of these patients are usually admitted to the hospital for investigation, less than one-third of them receive the final diagnosis of acute coronary syndrome.[15,16]

Non-ST elevation AMI is diagnosed by time-dependent rise of myocardial necrosis markers. As the sensitivities of these markers are low on admission[17–19] a delay in the patient's final disposition is unavoidable.

In the acute ischaemic cascade, myocardial cell death (and the release of its necrosis markers) is a final event.[11] One of the first steps in this process is systolic and diastolic dysfunction. BNP is produced by myocardial cells when submitted to wall stress or overload, especially if systolic dysfunction is present.[3,6,7] Previous studies have demonstrated plasma BNP elevation in patients with AMI, reflecting a biphasic behaviour in those with large infarct and/or significant systolic dysfunction.[13]

Recent studies in patients with ST-segment elevation AMI and non ST-elevation acute coronary syndrome have demonstrated BNP as a potent predictor of early and late cardiac events.[20–26] In these studies, BNP levels were measured hours to days after hospital admission. Jernberg *et al.*[27] collected blood samples of 775 acute chest pain patients without ST-segment elevation upon admission to their coronary care unit and demonstrated a significant trend in the rate of AMI diagnosis across BNP level quartiles. Patients with AMI had significantly higher median BNP levels than patients with unstable angina or non-cardiac chest pain. Admission BNP level also provided significant prognostic information in this study.

The present study demonstrates for the first time that plasma BNP measured in patients on arrival at the emergency department with chest pain, is significantly higher in those with non-ST elevation AMI compared with unstable angina and non-acute coronary syndrome patients. When compared with CKMB and troponin-I on admission, BNP was more sensitive for the diagnosis with a similar high negative predictive value. More importantly, when measured in association with these necrosis markers on admission, BNP levels added significantly to their diagnostic performance, increasing the sensitivity and negative predictive value to 87.3 and 97.3%, respectively. Only rest myocardial scintigraphic imaging has been found to have such a high diagnostic power for non-ST segment elevation AMI when done at hospital admission.[28] Even in patients with normal troponin-I (<1.0 ng/mL) on admission, a BNP greater than 100 pg/mL implied a four-fold greater risk of AMI than a normal BNP (the risk was six-fold greater if troponin-I was <0.28 ng/mL) (*Figure 1*). It should be stressed, however, that in patients with clinical left ventricular dysfunction on admission, absolute BNP values could not identify those who had or did not have AMI. It is important to stress that the relatively low positive and negative likelihood ratios of BNP do not allow its use instead of CKMB and/or troponin-I as the gold standard for the diagnosis of AMI.

The concept that ischaemia may be an important stimulus for BNP release is supported by several observations. In experimental models of infarction, BNP gene transcription is increased in both infarcted tissue and surrounding viable myocytes, which exhibit increased wall stress.[29] In patients referred for stress testing, it has been shown that BNP rises after exercise in proportion to the size of the ischaemic territory as assessed with nuclear single-photon emission computed tomographic imaging.[30] Finally, after percutaneous transluminal coronary angioplasty, BNP transiently increases, even when intracardiac filling pressures remain unchanged.[31]

The findings of this study confirm previous ones and bring important information regarding the pathophysiology of BNP elevation in patients with acute cardiac ischaemia. First, the biological continuum of myocardial hypoxia in acute coronary syndrome—where AMI represents a greater ischaemic burden than unstable angina—seems confirmed by the observation of the progressive increase in BNP levels in these subgroups of patients. Second, immediate BNP elevation seems not to be directly related to myocardial necrosis or to the amount of cell death as measured by initial troponin blood level as no linear correlation between them was found (although this could be due to a small number of patients with AMI, or a narrow range of BNP and troponin I values, etc.). Rather, BNP seems to be a marker of the ischaemic burden that results in ventricular dysfunction. Therefore BNP, while not a diagnostic tool for AMI, is a strong predictor of it, particularly in patients with chest pain and non-diagnostic ECG and CKMB/troponin blood levels.

Limitations

One possible limitation of this study is the use of a troponin-I level >1.0 ng/mL as one of the diagnostic criteria for AMI, as recommended by others,[28] despite the fact that no consensus exists on this issue at the present time (recommended decision limits varying from 0.1 to 2.5 ng/mL).[17–19,28,32–35] Although some patients with minor myocardial necrosis may have been misdiagnosed as non-infarction, the fact that only 3 out of 71 AMI patients were solely diagnosed by CKMB elevation makes this possibility very unlikely. Also, 11 of the 71 patients only had troponin-I elevation, a rate in accordance with previously published diagnostic studies of troponins.[17–19,28,35] Other limitations of the study are the fact that it does not shed any light on the possible role of sequential BNP measurements for the diagnosis of AMI, and whether acute left ventricular dysfunction is the real responsible mechanism for immediate BNP elevation in these patients. Finally, one possible drawback of our results would be related to the fact that AMI patients were compared with a mixed group of unstable angina and non-acute coronary syndrome patients. Given the fact that BNP is considered a marker of contractile dysfunction (here resulting from acute myocardial ischaemia), some unstable angina patients were misdiagnosed as false-positive cases. In the worst scenario this would only reduce the diagnostic specificity of BNP.

Although validation of the present findings with studies using larger samples and different clinical settings is necessary, it is concluded that plasma BNP is an early marker of AMI in patients with chest pain and non-diagnostic ECG and its use should be considered in patients with suspicion of cardiac ischaemia in the emergency department in association with serial CKMB and troponin measurements.

Acknowledgements

This study was funded by the Pró-Cardíaco Hospital, Rio de Janeiro, where all the data were collected.

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