Biomarkers on Admission for the Prediction of Cardiovascular Events After Primary Stenting in Patients with ST-Elevation Myocardial Infarction

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ABSTRACT

Background: Several cardiac biomarkers have been shown to have predictive values for the development of cardiovascular disease and clinical outcome after events, and are now broadly used by clinicians. Little is known about the utility of these biomarker values on admission in ST-elevation myocardial infarction (STEMI) cases of primary drug-eluting stent (DES) implantation and intense medical therapy.

Hypothesis: Because little is known about the utility of these biomarkers on admission in ST-elevation myocardial infarction (STEMI) in cases primary drug-eluting stent (DES) implantation and intense medical therapy, we evaluated clinical outcomes.

Methods: We enrolled 207 consecutive STEMI patients treated with primary stenting (mean age, 57.3 ± 12.0 y). We evaluated the association between B-type natriuretic peptide (BNP), cardiac troponin I (cTnI), high-sensitivity C-reactive protein (hs-CRP) on admission, and death, reinfarction, and new or worsening congestive heart failure (CHF) through 1 y.

Results: In backward-elimination models including all biomarkers, only the cTnI level was retained as a predictor of 1-y CHF (odds ratio [OR]: 1.017, 95% confidence interval [CI]: 1.001–1.034, $p = 0.039$). There were no predictors in terms of 1-y death, reinfarction, and composite endpoint. When we applied a simple score system, in which patients were categorized on the basis of the number of elevated biomarkers, the 1-y risks of death ($p = 0.600$), reinfarction ($p = 0.185$), and composite endpoint ($p = 0.620$) did not increase in proportion to the number of elevated biomarkers on admission. One-y CHF only tended to increase according to the number of elevated biomarkers ($p = 0.067$).

Conclusions: The use of cardiac biomarkers on admission, in each or in combination, had only a minimal impact for the prediction of long-term cardiovascular events after primary stenting in STEMI patients.

Key words: biomarker, thrombolysis in myocardial infarction risk score, ST-elevation myocardial infarction, drug-eluting stent

Introduction

Several cardiac biomarkers have been shown to have predictive values for the development of cardiovascular disease and clinical outcome after events, and are now broadly used by clinicians.^{1–4} However, for assessing risk according to enrolled patients and clinical situations, the use of multiple biomarkers does not have a consistent additive impact on standard risk factors.¹ Since elevated levels of B-type natriuretic peptide (BNP), cardiac troponin I (cTnI), and high sensitivity C-reactive protein (hs-CRP) levels are associated with higher rates of cardiac events after acute coronary syndrome (ACS), these biomarkers with different pathophysiological mechanisms have been used to assess the risk and prognosis of ACS.^{5–8} Little is known, however, about the utility of the biomarkers on admission, in each or in combination, in cases of ST-elevation myocardial infarction (STEMI) or of primary

drug-eluting stent (DES) implantation and intense medical therapy.

We hypothesized that simultaneous assessment of these biomarkers would provide more complementary information for clinical outcomes after primary stenting in patients with STEMI. Therefore, we evaluated the relationships between 3 biomarker values on initial admission and clinical outcomes after immediate DES implantation against STEMI.

Methods

Study Population

We enrolled 207 consecutive STEMI patients who underwent primary DES implantation between June 2004 and June 2006: 181 patients (87.4%) were treated with a Cypher sirolimus-eluting stent (SES) (Cordis/Johnson and Johnson, Warren, NJ, USA) and 26 patients (12.6%) were

treated with a Taxus paclitaxel-eluting stent (PES) (Boston Scientific Corp., Natick, Mass., USA) at the doctor's discretion during the procedure. All patients had available BNP, cTnI, and hs-CRP results. The inclusion criteria were lasting chest pain ≥ 30 min refractory to nitrates, ST-segment elevation ≥ 1 mm in at least 2 contiguous leads in electrocardiogram on admission, and primary percutaneous coronary intervention (PCI) < 12 h from the onset of pain. They were transported immediately to a catheterization room. Informed consent was obtained from all enrolled patients. The study protocol was approved by the regional ethics committee.

Biomarker Test

Peripheral blood samples were obtained by direct venipuncture of an antecubital vein upon admission to the emergency department. The BNP was measured within 15 min using a Triage BNP Test (Biosite Incorporated, San Diego, Calif., USA). It is a direct chemoluminescence assay for the quantitative determination of BNP in whole blood specimens. The range of the BNP assay is 2.0 to 5000.0 pg/ml. We used the decision limit (80 pg/ml) as assessed in previous studies.^{7,9} Positive cTnI on admission was defined as any value above the upper range (1.5 ng/ml; ADVIA Centaur, Bayer, Tarrytown, NY, USA). The hs-CRP value was assessed using an immunoturbidimetric assay (Integra 800, Roche, Lewes, Sussex, UK). The decision limit (5 mg/l) was previously assessed in other studies.^{10,11}

Procedure and Medical Treatment

All PCI procedures were performed through a femoral approach. All patients received 300 mg loading of aspirin and 600 mg loading of clopidogrel immediately before procedure. After administration of 5,000 IU of heparin and conventional wire crossing, balloon predilation was carried out, and direct DES implantation was performed whenever possible. Use of either glycoprotein IIb/IIIa inhibitors or a device for thrombus aspiration was left to the doctor's discretion. Routine administration of aspirin (100 or 200 mg daily) indefinitely and clopidogrel (75 mg daily) for at least 1 y were recommended. Additional medical therapy, including β -blockers, nitrates, calcium antagonists, angiotensin-converting enzyme inhibitors/angiotensin receptor blockades, and statins was left to the discretion of the attending physicians.

Clinical Endpoints

In-hospital mortality and reinfarction were evaluated. In-hospital reinfarction was defined as a new increase in the plasma cTnI levels to $\geq 50\%$ above the previous value after an initial peak. Signs of acute heart failure on admission (Killip class II–IV) were assessed from in-patient records reviews. One-y major adverse cardiovascular events (MACE), including death from any cause, nonfatal myocardial infarction

(MI), and new or progressive congestive heart failure (CHF), were obtained from out-patient record reviews or telephone interviews. New MI after discharge was defined as a new episode of chest pain ≥ 30 min, with new electrocardiographic changes (ST-T changes or new Q-waves, or both, in ≥ 2 contiguous leads), and an increase in plasma cTnI concentrations (> 99 percentile of normal). Information on the endpoint of new or worsening heart failure was collected from the case-record forms. Stent thrombosis was defined according to the Academic Research Consortium (ARC) criteria.¹²

Statistical Analysis

Statistical analysis was performed with SPSS 13 software (SPSS Inc, Chicago, Ill., USA). Patients were divided into quartiles and dichotomized using a decision limit (80 pg/ml) based on initial BNP values. Patients were also divided into quartiles and dichotomized using a decision limit of cTnI (1.5 ng/ml) and hs-CRP (5 mg/l) levels on admission. The baseline characteristics with and without elevated biomarkers were compared using the Student *t* test or Wilcoxon rank-sum test for continuous variables, and the chi-square test or Fisher's exact test (if an expected frequency is < 5) for categorical variables. The relationships between biomarkers and clinical outcomes were assessed using the chi-square or Fisher exact test for dichotomized comparisons and the chi-square test for trend across quartiles. Multivariate analysis for comparison between biomarkers and thrombolysis in myocardial infarction (TIMI) risk scores, and clinical outcomes were performed using a stepwise logistic regression model. A *p*-value < 0.05 was considered statistically significant.

Results

Baseline Characteristics

The study population was comprised of 169 men (81.6%) and 38 women (18.4%) with a mean age 57.3 ± 12.0 y (range, 23–88 y). The mean time from the onset of symptoms to sampling was 4.7 ± 3.0 h (range, 1–12 h). The BNP level on admission was 121.7 ± 260.7 pg/ml (range, 2–1,764 pg/ml: median, 32 pg/ml), hs-CRP level was 9.3 ± 26.8 mg/l (range, 0.3–202.3 mg/l: median, 2.5 mg/l), and cTnI level was 7.8 ± 23.2 ng/ml (range, 0.1–258.2 ng/ml: median, 0.3 ng/ml). There were weak relationships between sampling time and BNP level ($r = 0.231$, $p = 0.001$), cTnI level ($r = 0.291$, $p < 0.001$), and hs-CRP level ($r = 0.172$, $p = 0.013$).

Patients with elevated BNP levels (> 80 pg/ml; 27.5%) were older, female, and more likely to have a longer time from symptom onset, high TIMI risk scores, and higher cTnI and hsCRP levels (Table 1). Elevated BNP levels were positively correlated with cTnI ($r = 0.225$, $p = 0.001$) and hs-CRP levels ($r = 0.543$, $p < 0.001$). They were also more likely to have a history of diabetes, a lower level of total cholesterol, and TIMI flow < 3 after PCI.

TABLE 1: Baseline characteristics in sub groups by BNP level

	BNP ≤ 80 pg/ml (n = 150)	BNP > 80 pg/ml (n = 57)	p-value
Demographics			
Age (y)	54 $\pm$ 11	65 $\pm$ 10	<0.001
Male	132 (88.0%)	37 (64.9%)	<0.001
Time from chest pain onset (h)	3.4 $\pm$ 2.6	8.0 $\pm$ 5.1	<0.001
LV ejection fraction (%)	49.0 $\pm$ 11.2	49.1 $\pm$ 9.4	NS
Medical history			
Hypertension	47 (31.3%)	26 (45.6%)	NS
DM	21 (14.0%)	15 (26.3%)	0.042
Current smoker	47 (31.3%)	16 (28.1%)	NS
Hypercholesterolemia (> 200 mg/dl)	61 (40.7%)	21 (36.8%)	NS
Prior PCI	3 (2.0%)	1 (1.8%)	NS
Prior CABG	0 (0%)	1 (1.8%)	NS
TIMI risk score	3.2 $\pm$ 1.9	5.2 $\pm$ 2.2	<0.001
Age 65–74 y	27 (18.0%)	20 (35.1%)	<0.001
>75 y	2 (1.3%)	10 (17.5%)	<0.001
History of angina, hypertension, and DM	51 (34.0%)	31 (54.4%)	0.011
Systolic blood pressure < 100 mm Hg	19 (12.7%)	4 (7.0%)	NS
Heart rate > 100 bpm	10 (6.7%)	14 (24.6%)	0.001
Killip class II–IV	84 (56.0%)	34 (59.6%)	NS
Weight < 67 kg	53 (35.3%)	30 (52.6%)	0.025
Anterior ST-elevation or LBBB	89 (59.3%)	38 (66.7%)	NS
Time to treatment > 4 h	36 (24.0%)	43 (75.4%)	<0.001
Biochemical tests			
Peak CK-MB (ng/ml)	241.5 $\pm$ 167.7	194.7 $\pm$ 151.0	NS
Troponin I (+) on admission	38 (25.3%)	44 (77.2%)	<0.001
High-sensitivity CRP (ng/ml)	0.3 $\pm$ 0.5	2.5 $\pm$ 4.7	<0.001
Serum creatinine (mg/dl)	1.0 $\pm$ 0.2	1.0 $\pm$ 0.5	NS
Total cholesterol (mg/dl)	194.2 $\pm$ 41.8	181.1 $\pm$ 40.4	0.045
LDL cholesterol (mg/dl)	118.0 $\pm$ 32.7	107.6 $\pm$ 30.9	NS
HDL cholesterol (mg/dl)	39.6 $\pm$ 11.2	42.9 $\pm$ 10.0	NS
Triglyceride (mg/dl)	182.8 $\pm$ 145.2	153.2 $\pm$ 140.0	NS

TABLE 1: (Continued)

	BNP ≤ 80 pg/ml (n = 150)	BNP > 80 pg/ml (n = 57)	p-value
Angiography			
Multivessel disease	25 (6.7%)	13 (22.8%)	NS
IRA			NS
LAD	78 (52.0%)	33 (57.9%)	
LCX	12 (8.0%)	4 (7.0%)	
RCA	56 (37.3%)	16 (28.1%)	
LM	4 (2.7%)	4 (7.0%)	
SES implantation	132 (88.0%)	49 (86.0%)	NS
Direct stenting	14 (9.3%)	3 (5.3%)	NS
Number of stents	1.4 $\pm$ 0.6	1.5 $\pm$ 0.7	NS
TIMI grade 3 flow after stenting	146 (97.3%)	51 (89.5%)	0.028
Treatment during hospitalization			
IABP	8 (5.3%)	6 (10.5%)	NS
Glycoprotein IIb/IIIa inhibitors	12 (8.0%)	2 (3.6%)	NS
Heparin	146 (97.3%)	55 (96.5%)	NS
Aspirin	150 (100%)	57 (100%)	NS
Clopidogrel	150 (100%)	57 (100%)	NS
β -blocker	150 (95.5%)	53 (93.0%)	NS
ACE inhibitor/ARB	64 (42.7%)	30 (52.6%)	NS
Statin	147 (98.0%)	56 (98.2%)	NS
<p>Abbreviations: ARB = angiotensin receptor blockade; BNP = B-type natriuretic peptide; CABG = coronary artery bypass graft; CK = creatin kinase; CRP = c-reactive protein; DM = diabetes mellitus; HDL = high-density lipoprotein; IABP = intra-aortic balloon pump; IRA = infarct-related artery; LAD = left anterior descending artery; LBBB = left bundle branch block; LCX = left circumflex artery; LDL = low-density lipoprotein; LM = left main artery; LV = left ventricular; NS = not significant; PCI = percutaneous coronary intervention; RCA = right coronary artery; SES = sirolimus-eluting stent; TIMI = thrombolysis in myocardial infarction.</p>			

Biomarkers and In-hospital Outcomes

The BNP level on admission did not differ significantly between the 6 patients who died during hospitalization (91.0 $\pm$ 90.8 pg/ml) and the 201 survivors (122.7 $\pm$ 264.7 mpg/ml, $p = 0.770$), and between the 2 patients who did and the 205 patients who did not experience reinfarction during hospitalization (25.0 $\pm$ 19.8 versus 122.7 $\pm$ 262.5 pg/ml, $p = 0.600$). However, the BNP level on admission for the 118 patients with signs of acute heart failure (Killip II–IV) was significantly higher than in the 89 patients without signs of acute heart failure (165.2 $\pm$ 330.0 versus 64.1 $\pm$ 91.9 pg/ml, $p = 0.005$). Baseline cTnI level did not increase in cases of death (8.7 $\pm$ 18.7 versus 7.8 $\pm$ 23.4 ng/ml, $p = 0.926$),

reinfarction (2.1 $\pm$ 2.6 versus 7.9 $\pm$ 23.3 ng/ml, $p = 0.725$), and acute heart failure (9.7 $\pm$ 29.0 versus 5.4 $\pm$ 11.7 ng/ml, $p = 0.190$). Baseline hs-CRP level also did not differ according to events of death (2.4 $\pm$ 2.1 versus 9.5 $\pm$ 27.2 mg/l, $p = 0.524$), reinfarction (3.1 $\pm$ 2.8 versus 9.3 $\pm$ 26.9 mg/l, $p = 0.743$), and acute heart failure (9.8 $\pm$ 25.0 versus 8.5 $\pm$ 29.2 mg/l, $p = 0.718$). There were 2 cases of in-hospital stent thrombosis, but no relationship with biomarker levels on admission.

Biomarkers and One-y Outcomes

All patients were followed up for 1 y. Any event of stent thrombosis after discharge did not occur during follow-up.

When we applied a simple score system, in which patients were categorized on the basis of the number of elevated biomarkers¹¹ (Table 2), we found that the 1-y risks of death ($p = 0.600$), reinfarction ($p = 0.185$), and MACE ($p = 0.620$) did not increase in proportion to the number of elevated cardiac biomarkers on admission. However, 1-y CHF tended to increase according to the number of elevated biomarkers ($p = 0.067$).

Baseline BNP levels did not differ between the 8 patients who died (3.9%) compared with those who were alive at 1 y (85.9 ± 81.7 versus 123.2 ± 265.4 pg/ml, $p = 0.692$), between the 4 patients who had recurrent MI (1.9%) compared with those free of infarction within 1 y (13.8 ± 10.5 versus 123.9 ± 262.9 pg/ml, $p = 0.404$), or between the 13 patients with new or worsening CHF (6.3%) compared with those who did not develop CHF within 1 y (244.7 ± 342.7 versus 113.5 ± 253.3 pg/ml, $p = 0.079$). In addition, BNP level on admission did not differ between the 25 patients who had MACE (12.1%) compared with those free of MACE at 1 y (156.9 ± 264.5 versus 116.9 ± 260.6 pg/ml, $p = 0.473$). In terms of baseline cTnI and hs-CRP levels, there were only significant differences of value among patients who had new or worsening CHF and those in whom CHF did not develop (27.8 ± 70.5 versus 6.5 ± 15.4 ng/ml, $p = 0.001$), and among patients who had any MACE and in those without any MACE (16.7 ± 52.0 versus 6.6 ± 15.6 ng/ml, $p = 0.042$).

When treated dichotomously, positive cTnI (> 1.5 ng/ml) was associated with a higher risk of CHF at 1 y (3.2 versus 11.0%, $p = 0.024$) (Table 3). Treated as quartile scale, biomarkers did not show any significant trend across quartiles (Table 4). Patients with BNP quartiles 3 and 4 had a 3.3-fold higher risk of death at 1 y compared with quartiles 1 and 2, and patients with cTnI quartiles 3 and 4 showed a 3.7-fold higher risk of CHF at 1 y compared with quartiles 1 and 2. In a multiple logistic regression analysis including these 3 biomarkers, only cTnI level was retained as predictors of 1-y CHF (odds ratio [OR]: 1.017, 95% confidence interval [CI]: 1.001–1.034, $p = 0.039$). In terms of 1-y death, MI, and MACE, there were no predictors in cardiac biomarkers. When we included both classic TIMI risk score and cardiac biomarkers, only TIMI risk score was a predictor of 1-y death (OR: 1.533, 95% CI: 1.091–2.155, $p = 0.014$) and MACE (OR: 1.232, 95% CI: 1.019–1.490, $p = 0.032$). Baseline cTnI level did not measure up as a predictor of 1-y CHF (OR: 1.015, 95% CI: 1.000–1.031, $p = 0.052$).

Discussion

The major finding of this study was that the use of cardiac biomarkers on admission, in each or in combination, STEMI had only minimal impact in predicting long-term cardiovascular events in cases of primary DES implantation and intensive medical therapy. Cardiac biomarkers provided only additional prognostic information in cases of 1-y CHF. Furthermore, these biomarkers on admission did not show

any predictive value added on the validated TIMI risk score in assessing adverse cardiovascular events.

Major adverse cardiac events, death from any cause, nonfatal MI, and new or progressive CHF at 1 y occurred in 12.1% of patients. It included 8 cases of death (3.9%), 6 cases of nonfatal MI (1.9%), and 13 cases of new or progressive CHF (6.3%). In addition, in-stent thrombosis only occurred in 2 patients during hospitalization (0.97%). The results of our study may be within the acceptable ranges compared with previous studies. Furthermore, because all patients were treated with 2 kinds of DES, their constitution was homogenous to some extent.

Wang et al. demonstrated that the use of multiple biomarkers added only moderately to the overall prediction of risk based on conventional cardiovascular risk factors.¹ These findings highlight the strengths and limitations of the use of current biomarkers for the prediction of cardiovascular risk in ambulatory persons. Likewise, because there have been many debates whether simultaneous assessment of cardiac biomarkers on admission would provide more complementary information for clinical outcomes after primary PCI in STEMI patients, we evaluated the relationships between cardiac biomarkers on initial admission and clinical outcomes after immediate DES implantation against STEMI.

The BNP is activated in response to left ventricular overload following acute ischemic injury and needs time to reach the level of decision limit.^{3,8} There have been strong relationships between plasma BNP concentration during the subacute phase of ACS and mortality as well as CHF.^{2,13} In addition, the prognostic value of BNP in non-ST-segment elevation ACS has been well researched.^{3,8,11,14} In studies done to evaluate the value of biomarkers for STEMI, most measurements were made after 12 h, providing enough time for elevation after the event.^{15,16} Few data are available for the predictive value of BNP levels obtained on admission in patients with STEMI, before introducing primary PCI.¹⁷ Grabowski et al. recanalized the 126 STEMI patients with primary PCI using uncoated stent implantation (81.7%) and balloon angioplasty (18.3%).¹⁷ During 42 d follow-up after procedure, 10 (7.9%) patients died. Their mortality rate was somewhat higher than expected from current data^{18,19} and was 2.0-fold higher compared with 1-y death from our data (3.9%). Therefore, we thought that their results might not reflect real-world practices, especially in the DES era. The cause of discrepancy in their study may be due to inclusion of myocardial revascularization using balloon angioplasty, less intensive medical therapy, and higher incidence of no-reflow phenomenon after PCI. Our patients were more intensively treated after PCI with dual antiplatelet regimen (aspirin 100% versus 96.8%; clopidogrel 100% versus 92.9%) and statins (98.1% versus 86.5%). These drugs have been convincingly shown to reduce the risk of cardiovascular events and should be used if no contraindications are present in STEMI. Of Grabowski's patients, 14.3% showed no-reflow phenomenon

TABLE 2: Relative 1-y risks of clinical outcomes stratified by the number of elevated cardiac biomarkers (BNP, cTnI, and hs-CRP)

No. of elevated biomarkers	0	1	2	3	p-value
Death	1	0.9	1.5	0	0.600
Reinfarction	1	0.6	0	0	0.185
CHF	1	2.3	3.1	3.7	0.067
MACE	1	1.2	1.5	1.1	0.620

Congestive heart failure indicated a new or worsening CHF after discharge. Major adverse cardiac events included death, reinfarction, and new or progressive CHF. *Abbreviations:* BNP = B-type natriuretic peptide; CHF = congestive heart failure; cTnI = cardiac troponin I; hs-CRP = high-sensitivity C-reactive protein; MACE = major adverse cardiac event.

TABLE 3: Association between biomarkers on admission and 1-y clinical outcomes (dichotomous grouping)

	Level on admission		p-value
BNP concentration (pg/ml)	≤80	>80	
Number	150	57	
Death (%)	5 (3.3)	3 (5.3)	0.521
Reinfarction (%)	4 (2.7)	0 (0)	0.214
CHF (%)	7 (4.7)	6 (10.5)	0.195
MACE (%)	16 (10.7)	9 (15.8)	0.342
cTnI concentration (ng/ml)	≤1.5	>1.5	
Number	125	82	
Death (%)	5 (3.3)	3 (5.3)	0.901
Reinfarction (%)	4 (3.2)	0 (0)	0.103
CHF (%)	4 (3.2)	9 (11.0)	0.024
MACE (%)	13 (10.4)	12 (14.6)	0.389
hs-CRP concentration (mg/l)	≤5	>5	
Number	151	56	
Death (%)	8 (5.3)	0 (0)	0.080
Reinfarction (%)	3 (2.0)	1 (1.8)	0.926
CHF (%)	9 (6.0)	4 (7.1)	0.756
MACE (%)	20 (13.2)	5 (8.9)	0.478

Congestive heart failure indicated a new or worsening CHF after discharge. Major adverse cardiac events included death, reinfarction, and new or progressive CHF. *Abbreviations:* BNP = B-type natriuretic peptide; CHF = congestive heart failure; cTnI = cardiac troponin I; hs-CRP = high-sensitivity C-reactive protein; MACE = major adverse cardiac event.

TABLE 4: Association between biomarkers on admission and 1-y clinical outcomes (grouping by quartile scale)

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p-value
BNP					
Concentration (pg/ml)	<15	15–31	32–97	>97	
Death (%)	1.8	1.9	6.1	6.0	0.162
Reinfarction (%)	3.6	3.8	0	0	0.087
CHF (%)	5.5	3.8	6.1	10.0	0.297
MACE (%)	10.9	9.4	12.2	16.0	0.379
cTnI					
Concentration (ng/ml)	<0.2	0.2–0.3	0.4–4.7	>4.7	
Death (%)	3.8	3.8	6.3	1.9	0.736
Reinfarction (%)	3.6	3.8	0	0	0.086
CHF (%)	2.5	2.9	10.4	9.6	0.060
MACE (%)	9.7	10.5	16.7	11.5	0.637
hs-CRP					
Concentration (mg/l)	<1.1	1.1–2.5	2.6–5.4	>5.4	
Death (%)	6.1	5.7	3.8	0	0.093
Reinfarction (%)	0	3.8	1.9	1.9	0.678
CHF (%)	8.2	3.8	5.7	7.7	0.955
MACE (%)	14.3	13.2	11.3	9.6	0.437

Congestive heart failure indicated a new or worsening CHF after discharge. Major adverse cardiac events included death, reinfarction, and new or progressive CHF. *Abbreviations:* BNP = B-type natriuretic peptide; CHF = congestive heart failure; cTnI = cardiac troponin I; hs-CRP = high-sensitivity C-reactive protein; MACE = major adverse cardiac event.

after PCI (our data 4.8%). This may be associated with enrollment of higher risk patients and, in part, procedure expertness performed by attending physicians. Drug-eluting stent introduction supported by intensive medical therapy may attenuate the impact of BNP level on admission for long-term cardiovascular outcomes.

Differences of baseline characteristics in the dichotomous sub-group by BNP level (Table 1) were similar with those of Grabowski's results. Although we could not suggest the proper explanations on all variables, the differences might be related to time to treatment and disease severity. Older patients and patients with diabetes mellitus generally have more diffuse and multivessel coronary artery diseases. In addition, their sensation and response to chest pain lag behind. These allowed more time from chest pain to hospital and worse clinical status (higher TIMI risk score), followed by increase of cardiac biomarkers and worse angiographic outcome after PCI.

In studies assessing the prognostic value of initial cTnI and hs-CRP in STEMI, elevated levels were associated with adverse prognosis and lower rate of recanalization after fibrinolysis or PCI (balloon angioplasty or uncoated stent),^{4,6,20,21} but negative correlations also coexisted.^{7,10} There are no published data on the value of initial cTnI and hs-CRP level for predicting clinical outcomes after primary DES implantation in STEMI. In the present study, we demonstrated that cTnI and hs-CRP levels on admission give no additive information on classic TIMI risk score for predicting long-term cardiovascular outcomes in STEMI patients treated with primary DES implantation and intensive medical therapy.

The findings of this study, performed in a real-world population setting, including routine use of stent and advanced intensive medical therapy, raise important questions regarding whether cardiac biomarkers on admission in STEMI have predictive values on validated TIMI risk scores.

Limitations

Our study had several limitations. It was retrospective and nonrandomized in design and included a relatively small population, thus possibly introducing significant biases. We selected some biomarkers on the basis of previous studies. Therefore, we might have missed other biomarkers that could provide additional information.

Conclusions

The use of cardiac biomarkers on admission, in each or in combination, in STEMI has only a minimal impact in predicting long-term cardiovascular events in cases of primary DES implantation and intensive medical therapy. Furthermore, these biomarkers on admission do not show any predictive value added on the validated TIMI risk score in assessing adverse cardiovascular events.

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