Measurement of Heart-Type Fatty Acid-Binding Protein Before Discharge

Takeshi Yamamoto, MD; Masahiro Yasutake, MD

Despite significant advances in interventional and pharmacological therapies, late mortality after acute myocardial infarction (MI) is still high. Survivors of MI face a substantial excess risk of further cardiac events. Therefore, it is very important to perform risk stratification for the long-term management of MI patients before discharge. The long-term prognosis for an individual varies markedly depending on the presence or absence of adverse cardiovascular factors, including left ventricular (LV) dysfunction, residual ischemia, or ventricular arrhythmias. Indeed, the 2008 guidelines of the Japanese Circulation Society for the management of patients with ST-elevation MI recommended that assessment of such adverse prognostic factors should be completed during the index hospitalization or early after discharge. However, a simpler and more convenient method for evaluation of long-term prognosis has been desired.

Biomarkers have come to play an increasingly important role in predicting unfavorable events such as LV remodeling, recurrence of angina, non-fatal MI and cardiac death after acute coronary syndrome or acute MI. In this issue of the Journal, Matsumoto et al. report on the long-term prognostic utility of heart-type fatty acid-binding protein (H-FABP) in patients surviving acute MI. H-FABP is a biomarker of myocardial injury and necrosis that offers several theoretical advantages over cardiac troponins. It is smaller in size (14–15 kDa) than troponin I or T (21–37 kDa) and is concentrated in the cytoplasm of cardiomyocytes. Therefore, H-FABP is released more quickly than the troponins into the circulation when membrane integrity is compromised in response to myocardial injury. Levels of H-FABP are detectable as early as 2–3 h and typically return to baseline levels within 12–24 h of the initial insult. Consistent with these findings, a growing number of studies have shown that H-FABP is a sensitive marker for the diagnosis of MI and might be more sensitive than troponin assays when measured in the early hours after symptom onset.

To date, H-FABP seems to provide incremental information for risk stratification that is independent of established risk factors and biomarkers such as cardiac troponin, B-type natriuretic peptide, and myoglobin. Recent studies have shown that elevated H-FABP in the acute phase of MI is associated with an increased risk of cardiac events. However, few reports have investigated the clinical significance of H-FABP level in the convalescent phase of MI. One of the features of the current study was to clarify this issue.

A total of 1,283 patients were subjected to blood sampling for determination of H-FABP concentrations at a median of 20 days after the onset of MI. The optimal cut-off value for discriminating all-cause mortality was estimated to be 6.08 ng/ml with a C-statistic of 0.68, which was a little less than the cut-off value for H-FABP to diagnose MI of 6.20 ng/ml. During a median follow-up period of 1,785 days, Kaplan-Meier curves showed that patients with elevated H-FABP levels had a significantly higher incidence of death (18.3% vs 3.8%, P<0.001) and readmission for heart failure (10.3% vs 2.6%, P<0.001) than those without. Multivariate Cox regression analyses also

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Division of Intensive and Cardiovascular Care Unit (T.Y.), Emergency and Integrated Medical Care Center (M.Y.), and Department of Cardiovascular Medicine (T.Y., M.Y.), Nippon Medical School Hospital, Tokyo, Japan
Mailing address: Takeshi Yamamoto, MD, Division of Intensive and Cardiovascular Care Unit, Nippon Medical School Hospital, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan. E-mail: yamamoto56@nms.ac.jp
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Table. Comparison of Long-Term Outcome Studies by Biomarkers in the Convalescent Stage

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Subjects</th>
<th>Biomarker</th>
<th>Cut-off level</th>
<th>Endpoint (follow-up period)</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matsumoto (2013)</td>
<td>20 days after AMI (n=1,283)</td>
<td>H-FABP</td>
<td>&gt;6.08 ng/ml</td>
<td>All-cause mortality (60 months)</td>
<td>1.91 (1.03–3.51)</td>
</tr>
<tr>
<td>Ang (2012)</td>
<td>7 weeks after ACS* (n=326)</td>
<td>High-sensitivity TnT</td>
<td>&gt;0.014 ng/ml</td>
<td>All-cause mortality (30 months)</td>
<td>3.99 (1.55–10.24)</td>
</tr>
</tbody>
</table>

ACS, acute coronary syndrome; AMI, acute myocardial infarction; CI, confidence interval; H-FABP, heart-type free acid-binding protein; HR, hazard ratio; TnT, troponin T. *ST elevation AMI (n=106), Non ST elevation AMI (n=156), unstable angina (n=64).
revealed that elevated serum H-FABP was associated with an increased risk of all-cause mortality (hazard ratio (HR) 1.91; 95% confidence interval (CI) 1.03–3.51; P=0.039) and readmission for heart failure (HR 2.49; 95% CI 1.15–5.39; P=0.020). Moreover, multivariate logistic regression analyses revealed that advanced age, diabetes, and decreased eGFR were significantly associated with elevated H-FABP levels. Although the precise mechanism for H-FABP elevation in the convalescent phase of acute MI remains uncertain, it may be reasonable to assume that ageing, metabolic disorders, or inflammatory reactions play a role in promoting ongoing myocardial damage and increasing risk for heart failure or death as a result. Interestingly, Narumi et al recently reported that insulin resistance and metabolic syndrome were similarly related to higher H-FABP levels in a screening study of healthy subjects.

In the present study, the predictive accuracy by H-FABP for all-cause mortality and readmission for heart failure was greater (0.730 and 0.724, respectively) than that by cardiac troponin T (0.634 and 0.600, respectively) or LV end-diastolic dimension (0.587 and 0.622, respectively) determined before discharge. In contrast, a similar study regarding the prognostic value of high-sensitivity troponin T in the convalescent stage after an acute coronary syndrome has been reported. High-sensitivity troponin T was measured at 7 weeks after the acute coronary event and adverse outcome was evaluated over a median duration of 30 months. An elevated level of high-sensitivity troponin T predicted adverse clinical outcomes independent of conventional risk factors and LV dysfunction. Table shows a comparison of the 2 long-term outcome studies of the biomarkers in the convalescent stage. It is extremely important to note that the clinical characteristics, including the significance of H-FABP and cardiac troponins, was considerably different between ST-elevation MI (acute MI) and acute coronary syndrome (non-ST elevation MI and/or unstable angina). Therefore, interpretation and comparison of the studies should be undertaken with caution.

The measurement of serum H-FABP in a single blood sample collected during the convalescent stage of acute MI appears to be a simple and useful method for long-term risk stratification. It would be interesting and clinically significant to carry out a similar study in patients with acute coronary syndrome. Furthermore, future studies should investigate the mechanism of sustained elevation of H-FABP during the convalescent stage and examine whether tailoring specific treatment to higher risk individuals as identified by an elevated H-FABP during the convalescence stage of MI would improve their clinical outcomes.

Disclosures

No conflict of interest.

References