Role of Heart-Type Fatty Acid-binding Protein in Early Detection of Acute Myocardial Infarction, Farooq Ghani,1,2 Alan H.B. Wu,3 Louis Graff,4 Christoph Petry,3 Glenn Armstrong,3 Florence Prigent,4 and Milton Brown1

Biochemical evidence of acute myocardial infarction (AMI) is delayed by the delay of appearance of serum cardiac markers in the blood after myocardial injury. Heart-type fatty acid-binding protein (H-FABP), a small (15 kDa) cytoplasmic protein (1) involved in lipid homeostasis, is abundant in heart muscle (2). H-FABP is ~10-fold lower in skeletal muscle than in heart muscle, and the amounts in the kidney, liver, and small intestine are even lower (3). After myocardial damage, H-FABP is released into the intercellular space and appears in the bloodstream (4). The magnitude of the increase in plasma H-FABP has also demonstrated a good correlation with the size of the infarction (5). Myoglobin, another small protein (18 kDa), appears in the plasma within 2–3 h after myocardial infarction and is considered a useful marker in the early detection of AMI (6). Myoglobin lacks specificity because myoglobin released from skeletal muscles cannot be distinguished from that released from the heart. Cardiac troponin I (cTnI) and creatine kinase MB isoenzyme (CK-MB) are more specific for myocardial injury but lack early sensitivity because their blood concentrations do not increase appreciably until 6–8 h after the onset of AMI (7).

The aim of this multicenter study was to compare H-FABP with myoglobin, cTnI, and CK-MB in the early detection of AMI in patients presenting with chest pain in the emergency departments of participating centers.

Serial plasma samples were collected from 460 consecutive patients (253 men, 207 women) presenting with chest pain in to the emergency departments of Hartford Hospital, Hartford, CT; New Britain General Hospital, New Britain, CT; and Winthrop University Hospital, Mineola, Long Island, NY 11501; * author for correspondence: fax 860-545-3733, e-mail fghani@harthosp.org)

We compared the diagnostic performance of H-FABP with myoglobin, CK-MB, and cTnI. At a specificity of 95%, the sensitivity of H-FABP was 39%, compared with 28% for myoglobin for the first sample at the time of admission. Performance of all the markers worsened after 12 h except for cTnI, whose specificity was still high at 48 h. Positive likelihood ratios (LR+) for H-FABP and myoglobin for the 0–4 h interval were 2.6 and 2, respectively.

There was no statistically significant difference in the myoglobin/H-FABP ratio for AMI (0.73; 95% confidence interval [CI], 0.41–0.53), non-AMI (0.46; 95% CI, 0.32–0.61), and healthy individuals (0.63; 95% CI, 0.50–0.79). The areas under the ROC curves (with 95% CI) at 0–4 h were as follows: H-FABP, 0.80 (0.73–0.85); myoglobin, 0.73 (0.65–0.79); CK-MB, 0.79 (0.72–0.85); and cTnI, 0.91 (0.87–0.94), as shown in Fig. 1A. Fig. 1B shows the improvement in the performance of CK-MB and cTnI at 5–8 h post admission. Van Nieuwenhoven et al. (9) have suggested that the ratio of plasma myoglobin to H-FABP could be used in the diagnosis of AMI. In our study, there was no statistically significant difference in the myoglobin/H-FABP ratio among the three groups because of considerable overlap in the values. For the diagnosis of AMI, the ratio did not add value to the measurement of H-FABP alone.
For H-FABP to be used as an early marker in detection of myocardial injury, the assay must have a fast turnaround time. Several biochemical assays of H-FABP have been described; however, these assays are of limited use for routine clinical practice because they are not automated. The sandwich immunoassay used in this study is a rapid and totally automated assay suitable for clinical use.

Because H-FABP appears early in the blood after myocardial damage, we were particularly interested in its diagnostic performance during the first 4 h. Our data show that although H-FABP has a somewhat better diagnostic performance than myoglobin, it did not demonstrate the sensitivity and specificity necessary to detect AMI significantly earlier than do the existing markers.

To make a meaningful difference in early detection of AMI, new cardiac biomarkers will need a higher sensitivity during the first 1–2 h after chest pain. Patients detected very early may have evidence of plaque rupture and reduced coronary artery blood flow, but may be detected substantially before the onset of irreversible damage that is characterized by release of enzymes and proteins. Tests that indicate the presence of inflammation, thrombus formation, platelet aggregation, and reversible ischemia are possible candidates for early markers for AMI (10).

References