

Heart type fatty acid binding protein H – FABP



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وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ

Heart-type Fatty Acid-Binding Protein (H-FABP) is a small cytoplasmic protein. The molecular weight is 15kDa – smaller than Myoglobin (18kDa), Troponin I (22kDa), Troponin T (37Da) and CK-MB (86kDa), released from cardiac myocytes following an ischemic episode.

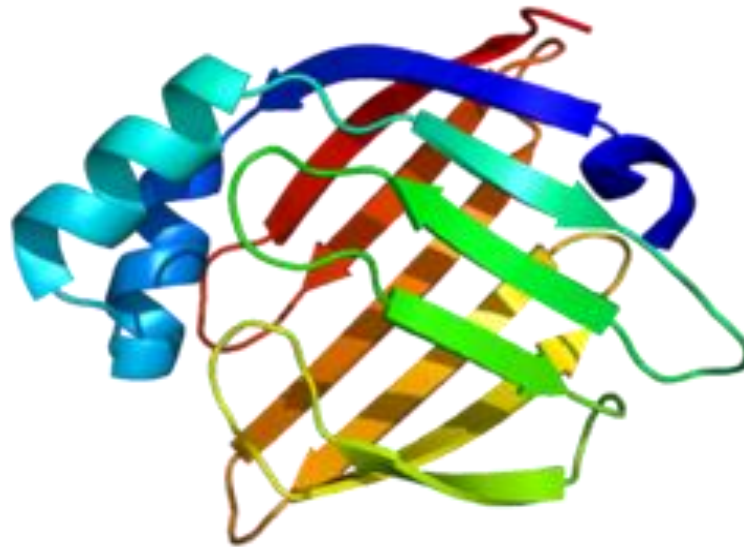
Like the nine other distinct FABPs that have been identified, H-FABP is involved in active fatty acid metabolism where it transports fatty acids from the cell membrane to mitochondria for oxidation.

The intracellular fatty acid-binding proteins (FABPs) also known as mammary-derived growth inhibitor, is a protein that in humans is encoded by the FABP3 which belongs to a multigene family.

FABPs are divided into at least three distinct types, namely the hepatic-, intestinal- and cardiac-type

They are thought to participate in the uptake, intracellular metabolism and/or transport of long-chain fatty acids. They may also be responsible in the modulation of cell growth and proliferation of mammary epithelial cells

QUATERNARY STRUCTURE



The diagnostic potential of the biomarker H-FABP for heart injury was discovered in 1988 by Professor **Jan Glatz** (Maastricht, Netherlands)

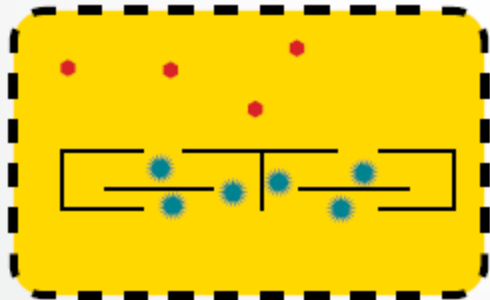
The normal serum/plasma value is much lower, compared to Myoglobin. H-FABP is highly specific to the heart – approximately 15-20 times more specific than Myoglobin.

Ischemia

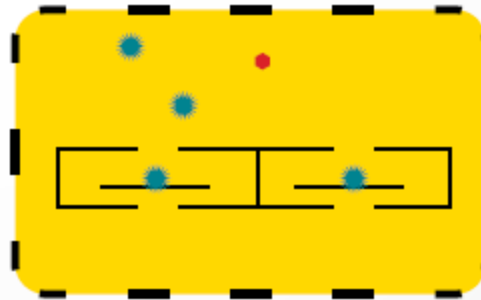
Necrosis

Endothelial Cell

Endothelial Cell



Cardiac Myocyte

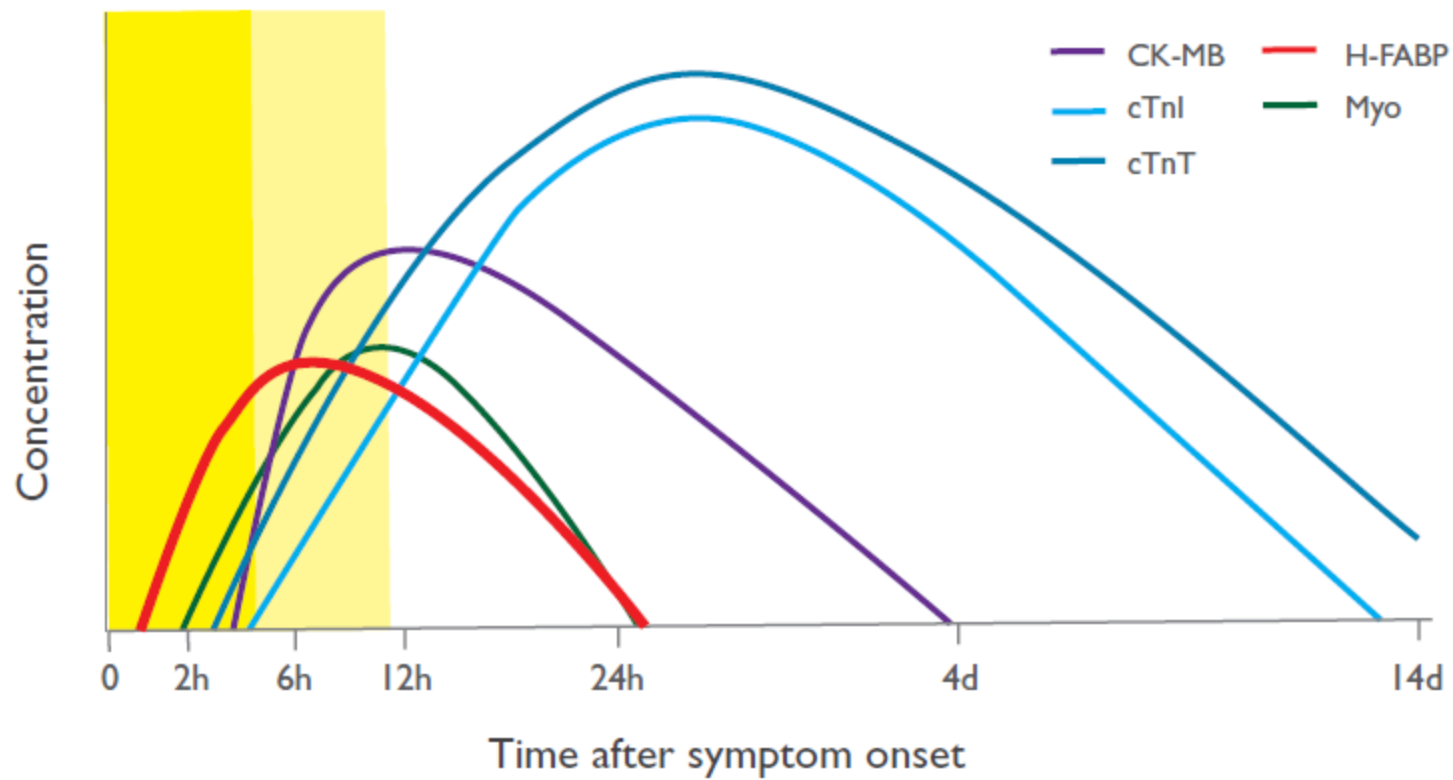


Cardiac Myocyte

- H-FABP
- Troponin

Due to the low molecular weight & cytoplasmic location of H-FABP, it is released extremely quickly after an ischemic episode – detectable as early as 30 minutes afterwards.

Furthermore, the rapid return to baseline within 24 hours, offers significant potential utility in patients with suspected re-infarction, instead of CK-MB






This sensitivity may be explained by the high concentration of H-FABP in myocardium compared to other tissues, the stability and solubility of H-FABP, its low molecular weight; its rapid release into plasma after myocardial injury - 60 minutes after an ischemic episode, and its relative tissue specificity.



In a recent study at two Emergency Departments in the UK, 1171 patients with suspected cardiac chest pain had single blood samples taken on presentation (0h) to assess the potential value of the combination of H-FABP, hsTnT & ECG to reliably rule-out AMI based on a single sample on presentation.


Protocol	Diagnostic cut-offs	Sensitivity	Specificity	PPV	NPV
H-FABP & hsTnT & ECG	95th centile = 2.5 ng/ml 99th centile = 14ng/l ECG negative	99.1%	59.3%	35%	99.7%

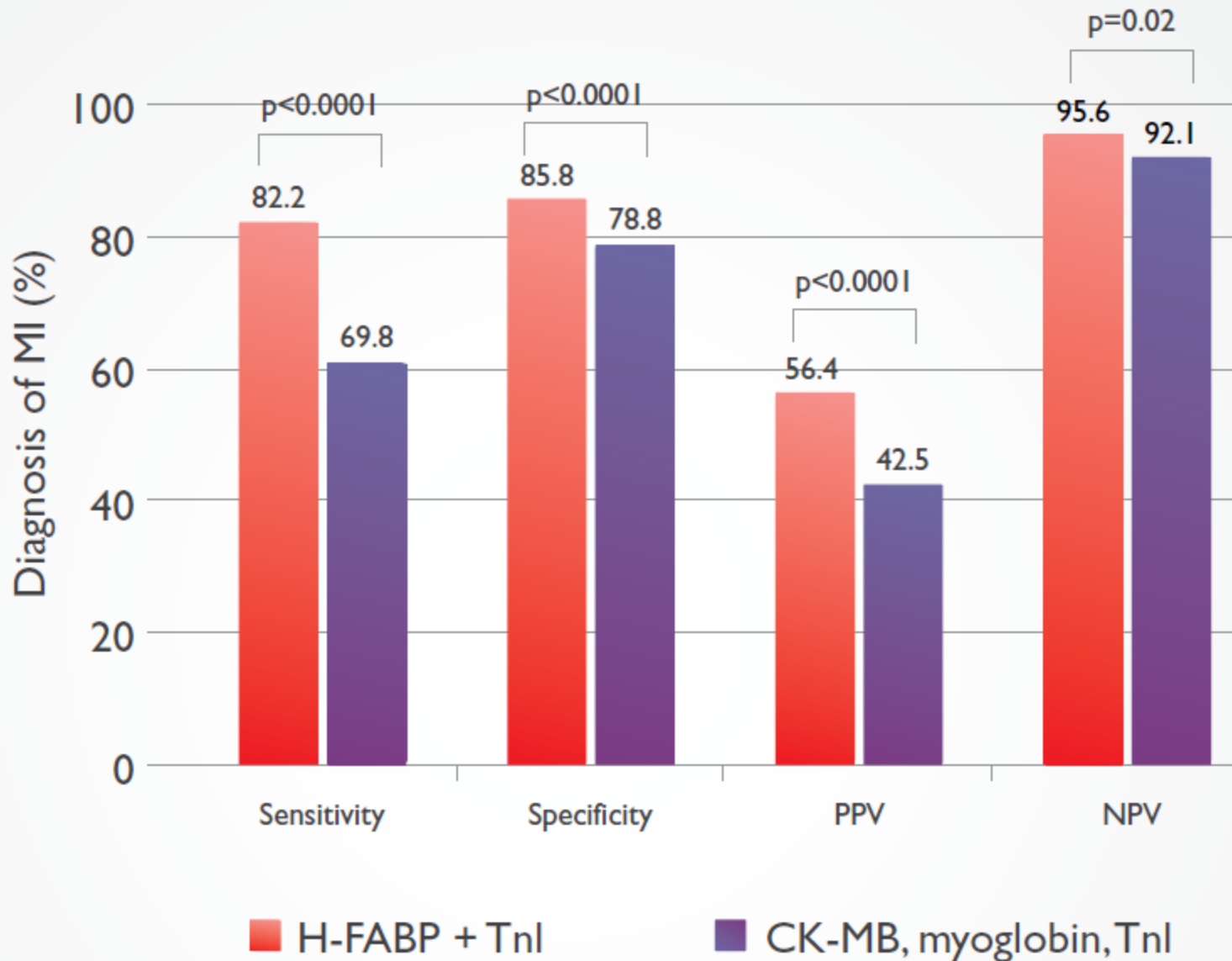




This protocol on presentation resulted in a **sensitivity** for AMI of **99.1%**, and a **NPV** of **99.7%** - and could have enabled AMI to be excluded in 48.8% of patients.

In addition, an economic analysis was undertaken on a subset of this cohort (n=473). The results showed that applying this protocol reduced the mean length of stay (4.1days vs. 5.3 days), and would have resulted in a projected saving of £327 per presenting patient.

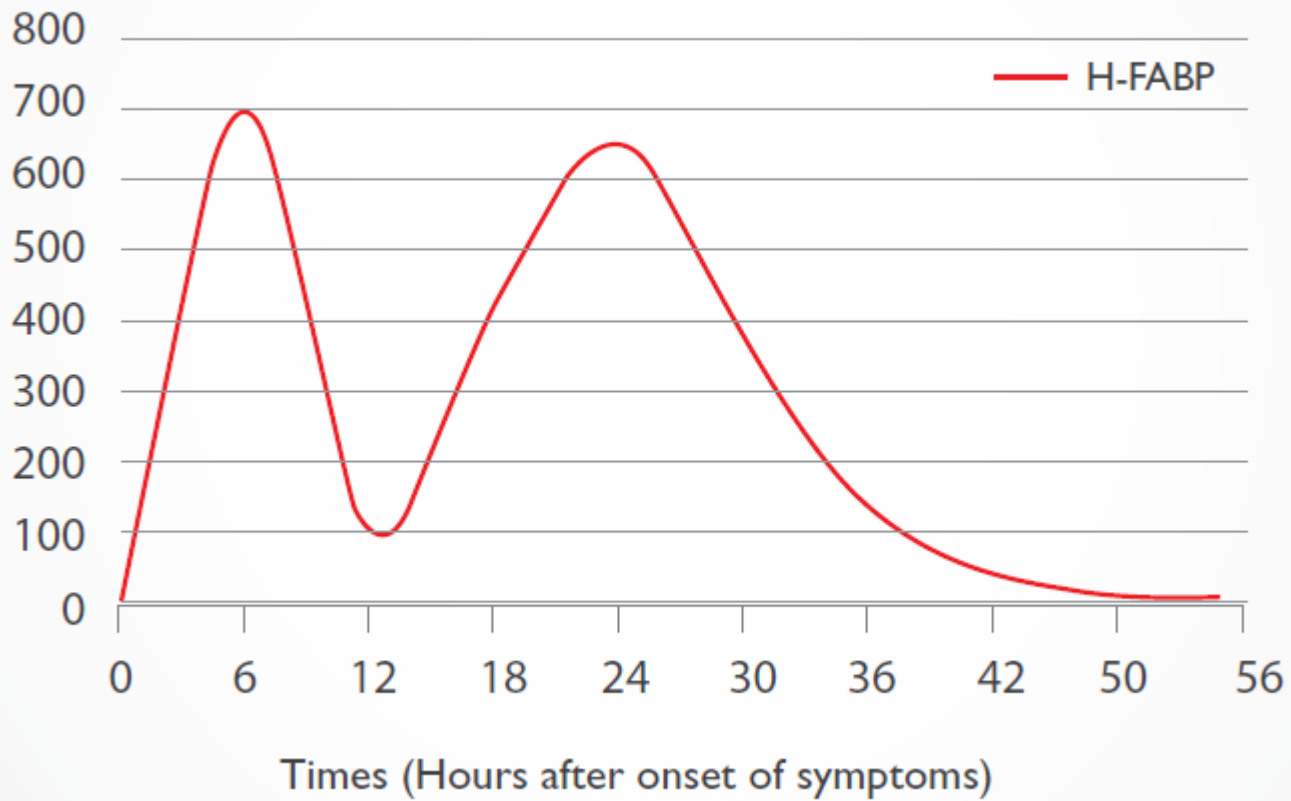


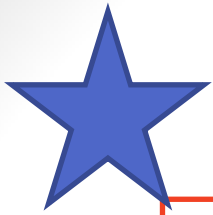


H-FABP's clinical diagnostic value is very limited in the presence of renal failure and skeletal muscle diseases as it is completely eliminated by kidney. In these conditions, the diagnosis of acute myocardial infarction (AMI) may be overestimated



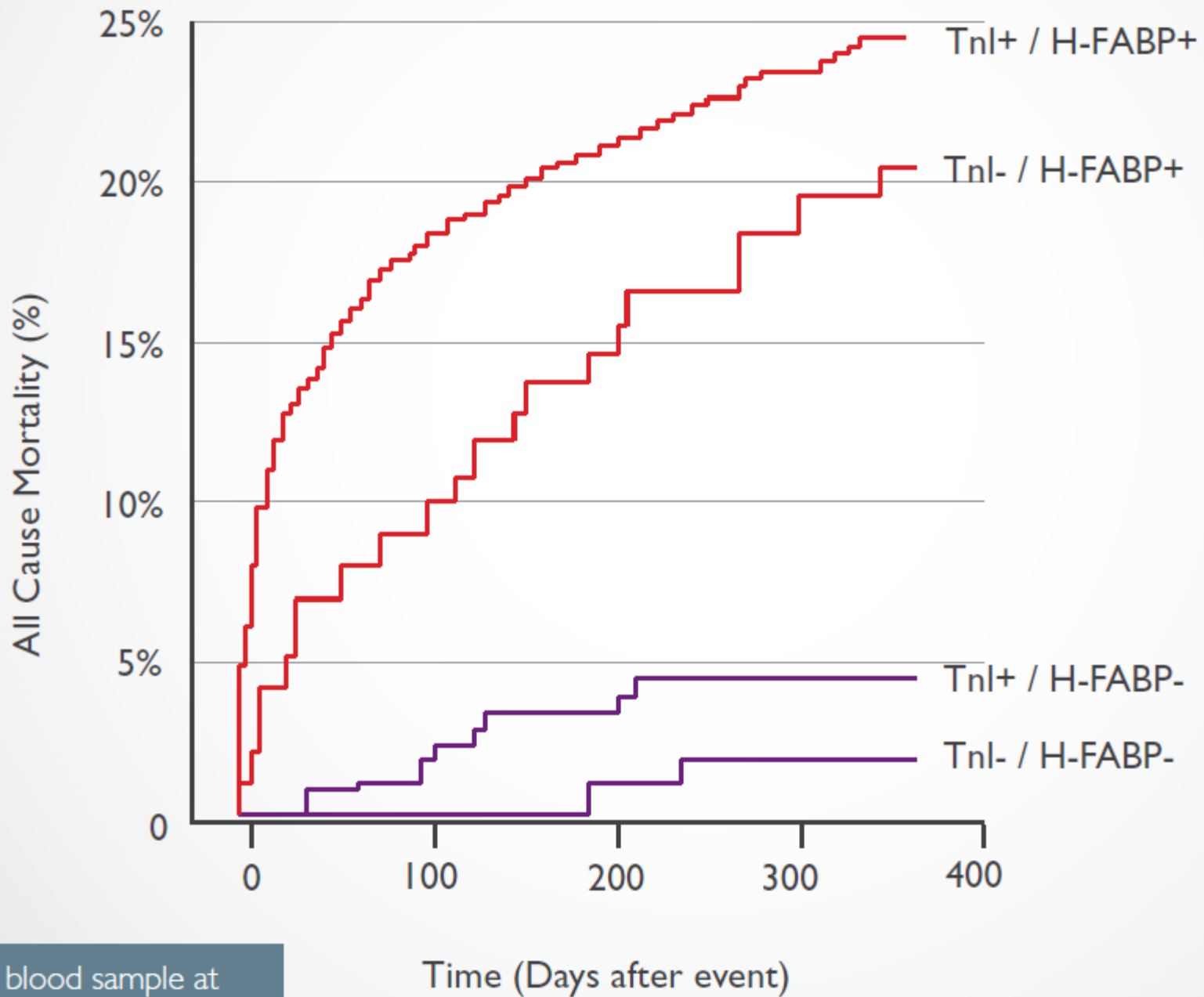
Furthermore, the rapid return to baseline within 24 hours, offers significant potential utility in patients with suspected **re-infarction**, instead of CK-MB





In addition to its diagnostic potential, H-FABP also has **prognostic** value. Alongside D-dimer, BNP and peak troponin T, it was the **only cardiac biomarker** that proved to be a statistically significant predictor of death or MI at one year.

This prognostic information was independent of troponin T, ECG and clinical examination.



Single blood sample at
after ACS system onset

The risk associated with raised H-FABP is dependent upon its concentration. Negative test result for both TnI and H-FABP was associated with 0% mortality at 6 months. Patients who were TnI negative but H-FABP positive had 17% increased risk of all-cause mortality within one year compared to those patients who were TnI positive but H-FABP negative.

Currently these TnI positive patients are prioritized for **angioplasty**, and the TnI negative patients are considered to be of a lower priority, yet the addition of the H-FABP test helps identify patients who are currently slipping through the net and allows physicians to more appropriately manage this hidden high risk group. If both biomarkers were negative, there is 0% mortality at 6 months

Serial measurements of H-FABP in the first 24 h after onset of AMI can:

(a) identify patients who are susceptible to reperfusion strategies,

(b) detect perioperative AMIs,

(c) distinguish patients who re-perfuse their infarct-related artery from those who do not, as early as 30 min after starting **thrombolytic** treatment.

(d) detect re-infarction if it occurs within **10 hours** after symptom onset, and

(e) permit an accurate estimation of myocardial infarct **size** providing important prognostic information

H-FABP in other diseases

H-FABP has been proven to significantly predict 30 day mortality in acute **pulmonary embolism**. H-FABP is more effective than Troponin T in risk stratifying **Chronic Heart Failure** patients. H-FABP is beginning to create interest with researchers who have found emerging evidence that indicates a role in differentiating between different **neurodegenerative diseases**

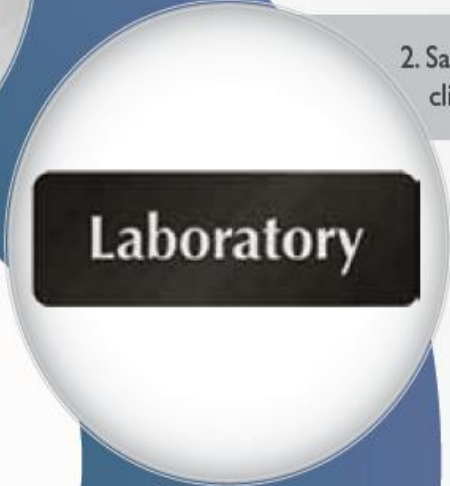
The serum concentrations of H-FABP were determined by latex enhanced **immunoturbidimetric** assay suitable for fully quantitative measurement of H-FABP in serum and plasma or using a recently developed **ELISA**

H-FABP testing process

1. Plasma or serum sample taken from patient



2. Sample sent to main clinical laboratory



Results delivered to the clinicians



3. The H-FABP assay consists of standard clinical chemistry reagents



Reagents run on a range of clinical chemistry analyzers and which typically provide results within 15-20 minutes



THANK YOU

