

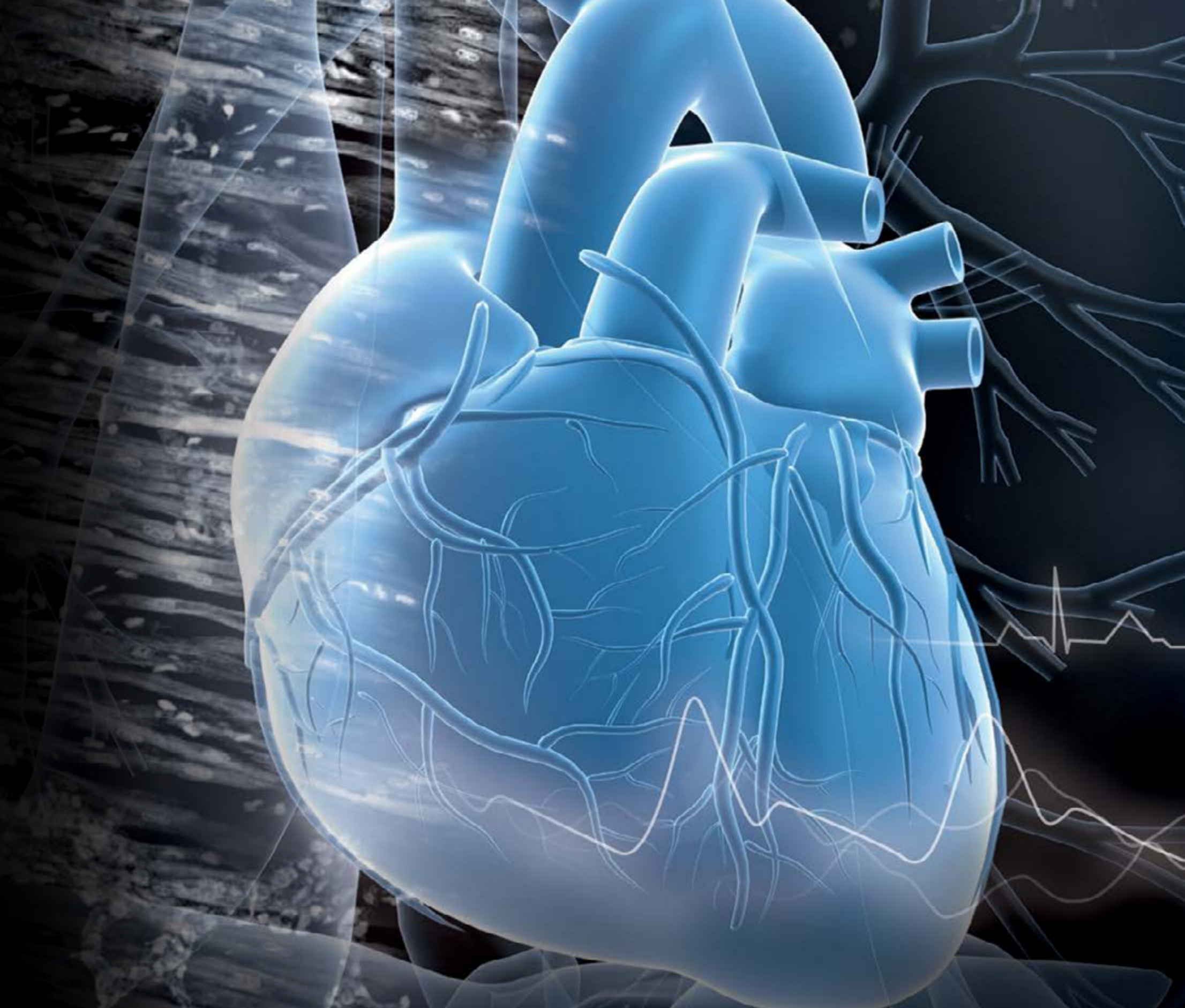
# H-FABP – A SENSITIVE BIOMARKER OF EARLY DIAGNOSIS AND PREDICTION OF MYOCARDIAL DAMAGE

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## Introduction

Differential diagnosis of acute chest pain and dyspnea patients is based on conventional cardiac biomarkers like cardiac troponins, creatine kinase-MB and myoglobin; however, these markers are not elevated in the initial hours. Natriuretic peptides are used for determination of myocardial overload and can distinguish cardiac and noncardiac dyspnea, based on age-dependent cut-off levels. Moreover, in patients with cardiac dyspnea, concentrations of natriuretic peptides are 10x-20x higher than the corresponding reference values [1].

Heart-type Fatty Acid-binding Protein (H-FABP) protects against free radical accumulation during myocardial ischemia. H-FABP concentration in blood reflects myocardial damage and increases within 2 hours, peak at about 4-6 hours and return to normal baseline value in 24 hours [2].

H-FABP exhibits an excellent efficiency in early diagnosis of acute myocardial infarction. H-FABP was shown to be associated also with chronic heart failure. Measurement H-FABP together with troponin exhibits increased sensitivity by 20.6% over troponin alone at 3-6 hours after chest pain onset and increases diagnostic accuracy [3].

In prognostic models containing 11 conventional risk factors plus NT-proBNP, hFABP mostly improved prognostic models for acute heart failure-related rehospitalization at 1 and 5 years, whereas troponin I mostly improved prognostic models for all-cause mortality [1, 4].

N-terminal pro-brain natriuretic peptide (NT-proBNP) is increased early after acute myocardial infarction. NT-proBNP on day 3 after admission correlates with acute and chronic infarct size and myocardial function after acute myocardial infarction [5,6].

## Conclusion

- ▶ Serum H-FABP levels were increased in patients with chest pain compared to healthy subjects.
- ▶ Serum NT-pro BNP levels were increased in patients with chest pain compared to healthy subjects.
- ▶ The results suggest that age-adjusted reference values should preferentially be used in H-FABP based diagnostics.

## References:

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## Materials and Methods

This study was focused on circulating H-FABP levels in healthy individuals and in patients suffering from dyspnea and chest pain. We used a new, high-sensitivity Human Heart FABP (FABP3) ELISA (BioVendor) to measure H-FABP in healthy subjects and in patients suffering from chest pain. In this assay, standards and samples are incubated in microplate wells pre-coated with polyclonal anti-human H-FABP antibody. After incubation and washing, biotin-labelled polyclonal anti-human H-FABP antibody is added and incubated with captured human H-FABP. After another washing, streptavidin-HRP conjugate is added. After incubation and the last washing step, the remaining conjugate is allowed to react with the substrate solution. The reaction is stopped by addition of acidic solution and absorbance of the resulting yellow product is measured. The absorbance is proportional to the concentration of H-FABP. A standard curve is constructed by plotting absorbance values against concentrations of standards, and concentrations of samples are determined using this standard curve.

The total assay time is less than 3.5 hours.

NT-proBNP serum levels were measured on Immulite 2000 Immunoassay system according to the instructions provided by the manufacturer.

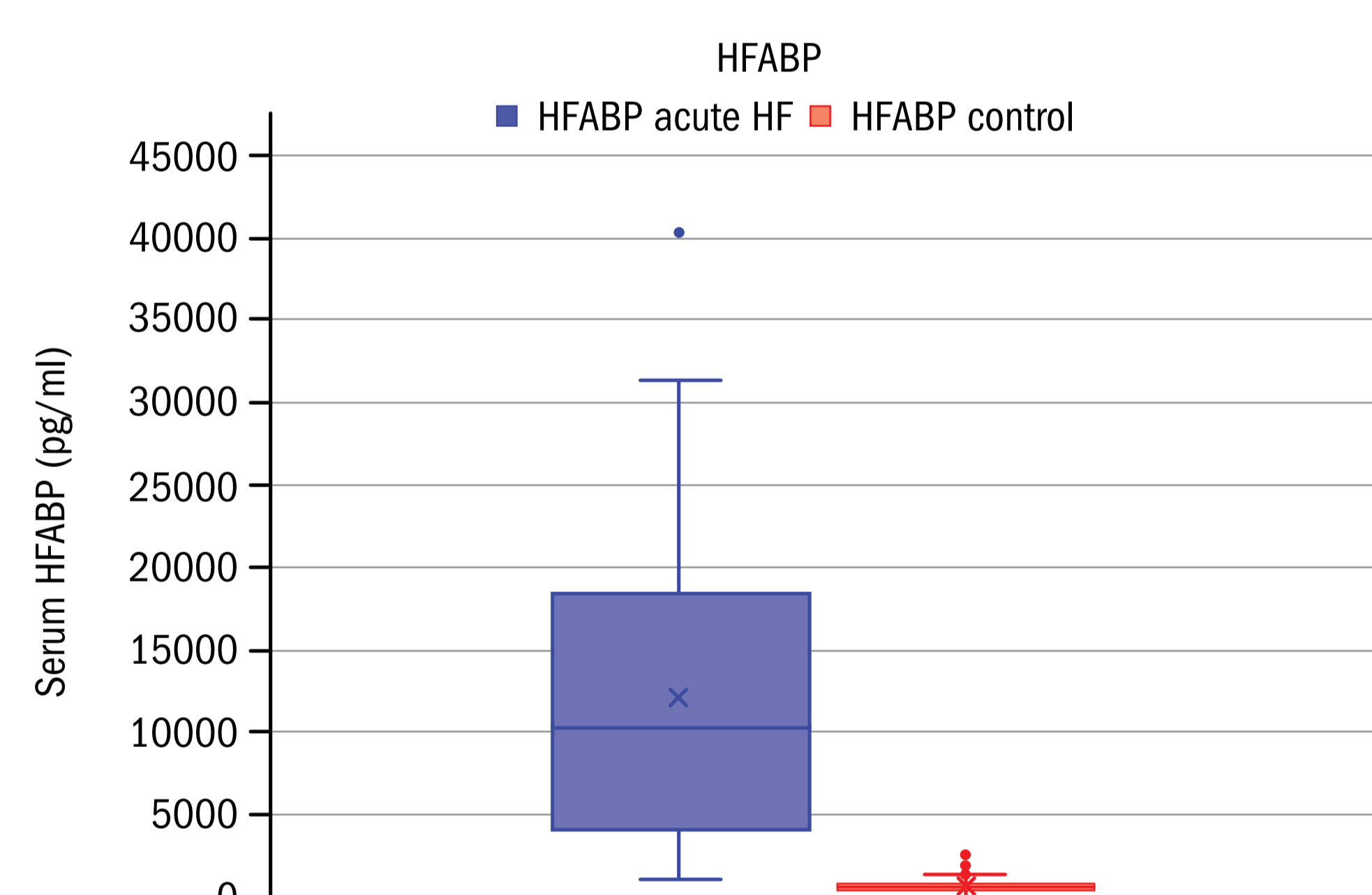
### Heart FABP (FABP3) Human ELISA Characteristics:

Intra-assay CV (n=8)	3.3 - 8.0 %
Inter-assay CV (n=6)	2.5 - 4.3 %
Dilution Linearity	86.7 - 109.8 %
Spiking Recovery	88.4 - 107.9 %
Sensitivity	5.6 pg/ml
Specificity	no crossreactivity with human FABP1, FABP2, FABP4, FABP5, FABP6, FABP7, FABP8, FABP9, FABP12

## Results

### A) Serum H-FABP levels in patients and healthy donors

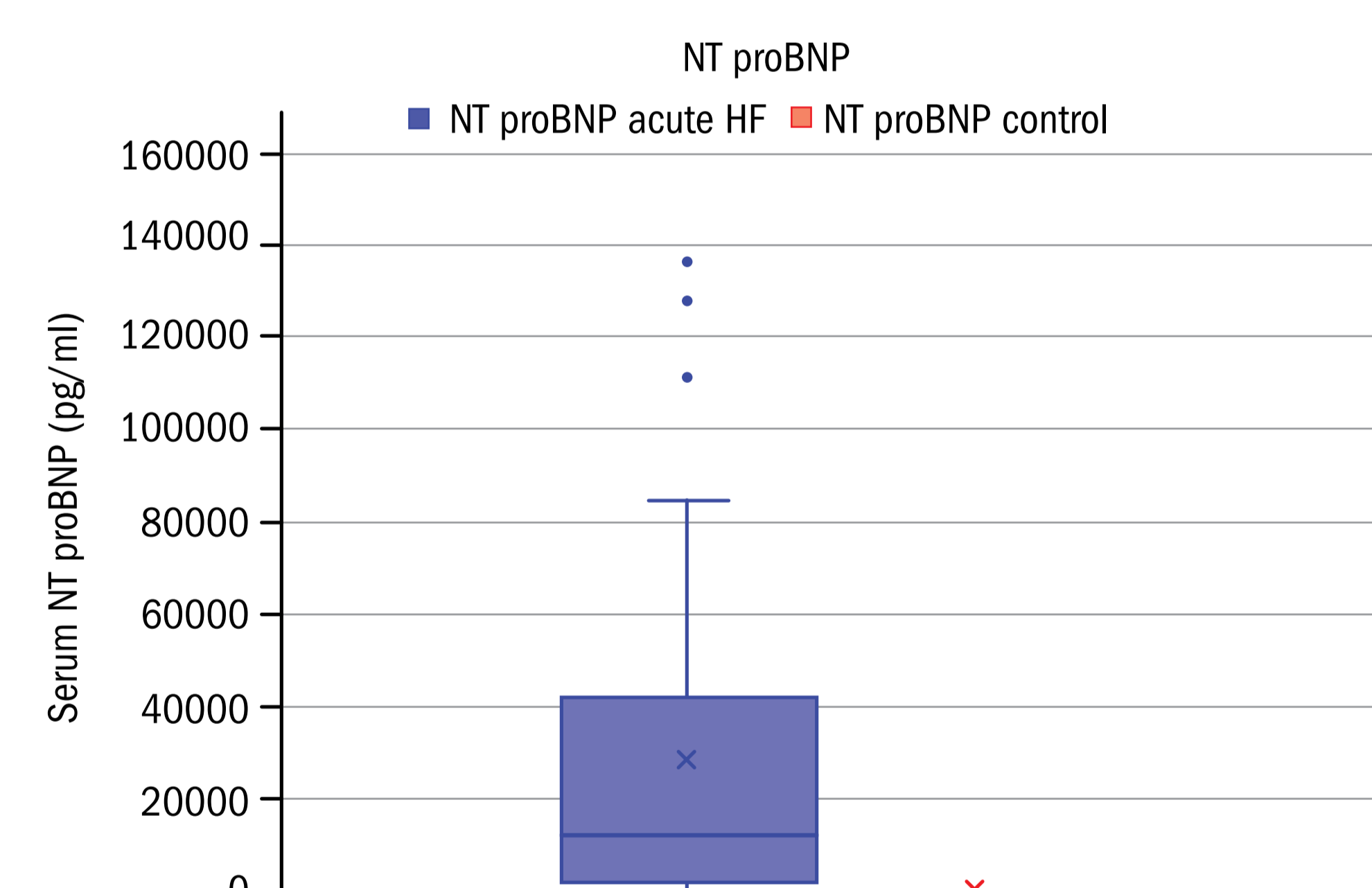
	n	Serum H-FABP (pg/ml)				
		Mean	Median	SD	Min	Max
Healthy subjects	148	727.2	649.0	399.0	20.0	2 829.0
Patients with chest pain	46	12 206.9	10 239.0	9 314.8	1 148.0	40 290.0



Serum H-FABP levels were increased in patients with chest pain compared to healthy subjects (mean: 727.2 pg/ml vs 12 206.9 pg/ml).

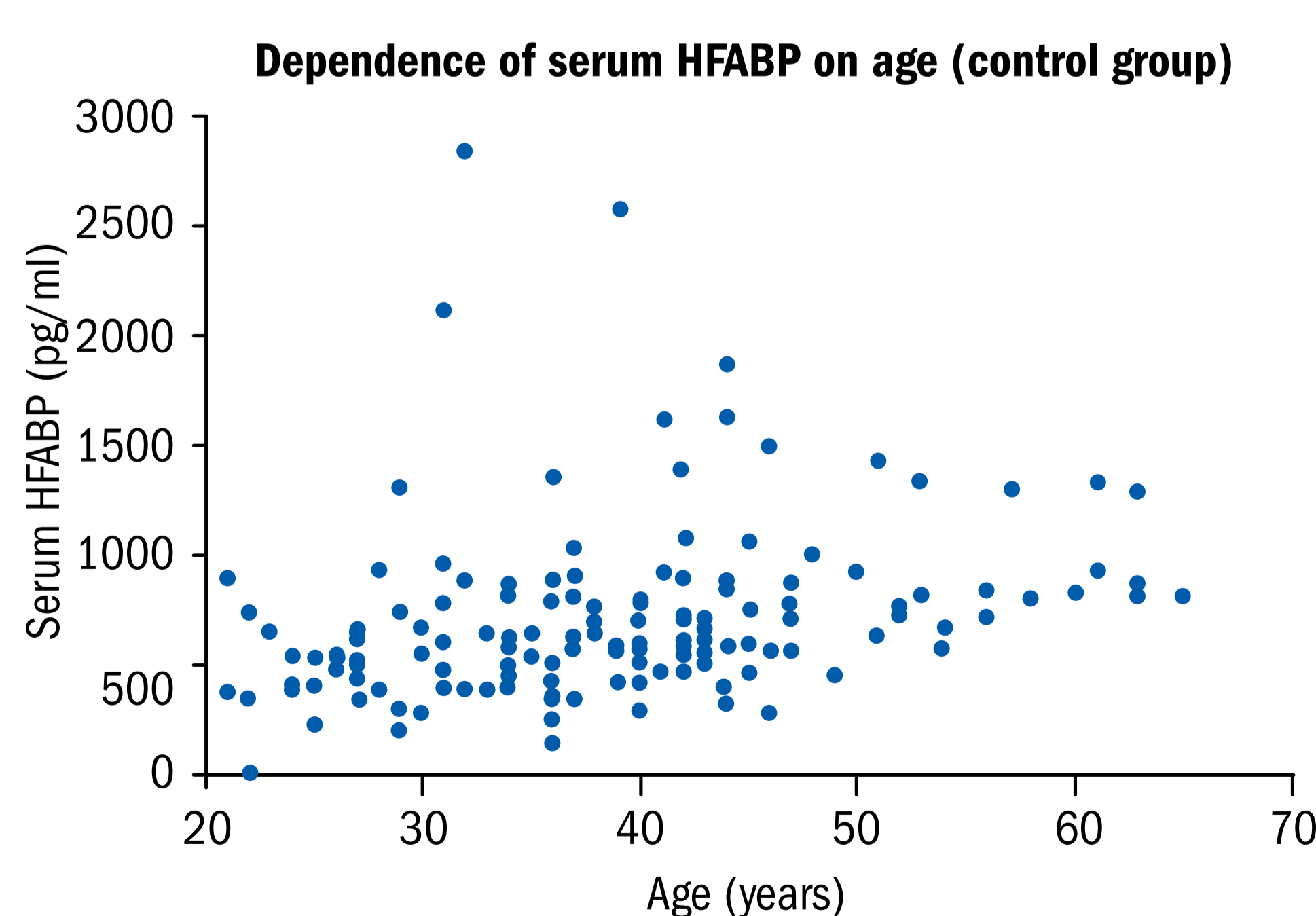
### B) Serum NT-proBNP levels in patients and healthy donors

	n	Serum NT-proBNP (pg/ml)				
		Mean	Median	SD	Min	Max
Healthy subjects	147	36.5	24.0	39.2	0.0	246.0
Patients with chest pain	46	27 601.9	12 313.1	35 220.0	91.0	136 178.0



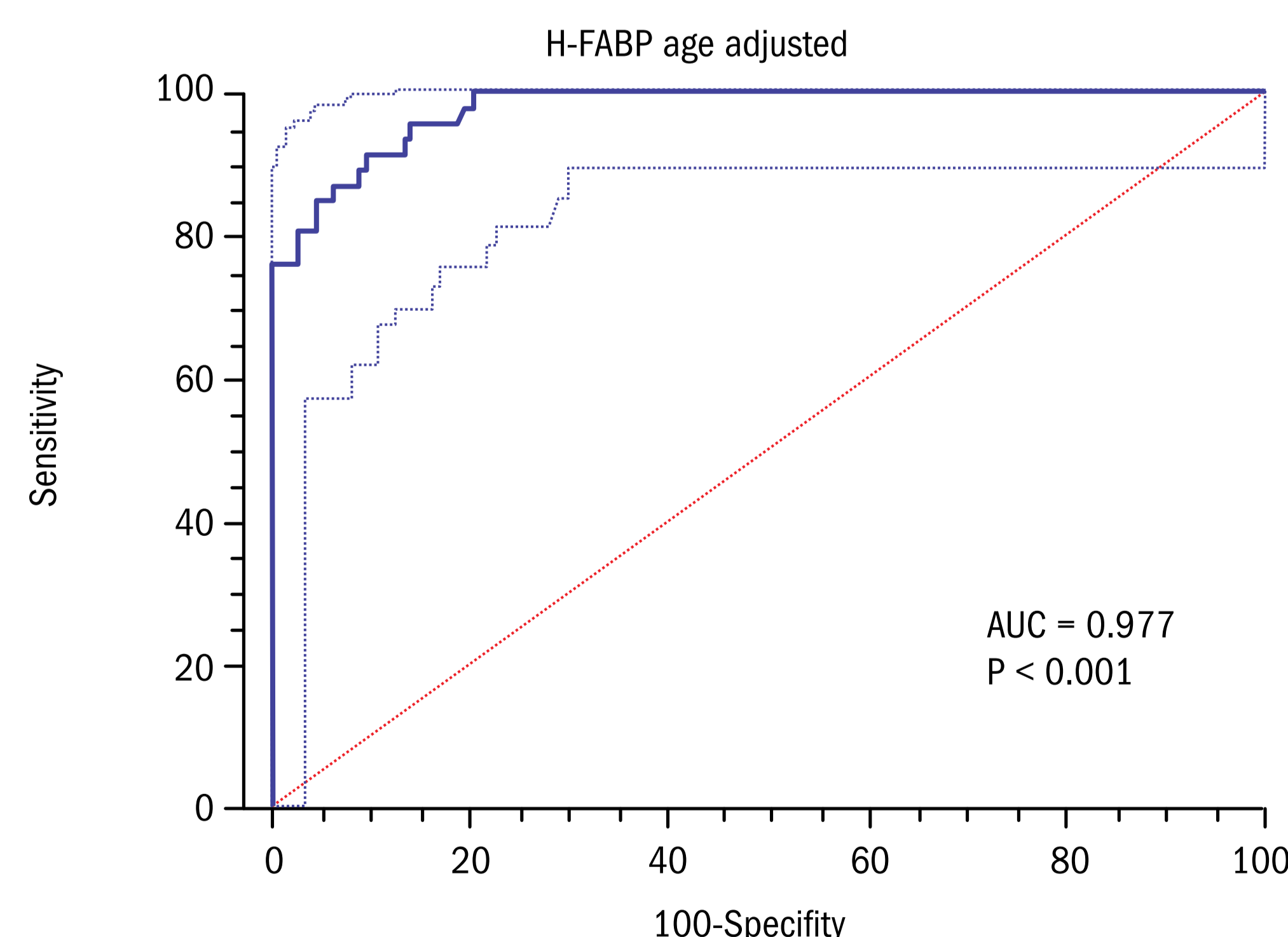
Serum NT-pro BNP levels were increased in patients with chest pain compared to healthy subjects (mean: 36.5 pg/ml vs 27 601.9 pg/ml).

### C) Dependence of H-FABP on age



HFABP serum levels were positively correlated with age in the group of healthy donors.

### D) Diagnostic potential of H-FABP



For evaluation of diagnostic potential of aged adjusted H-FABP, we constructed the receiver operating characteristic (ROC) curves according DeLong et al. method. The ROC curves reflected strong separation between groups with an AUC 0.977, sensitivity of 91.3% and specificity of 90.5%.