NATRIURETIC PEPTIDES

CARDIAC MARKERS IN HEART FAILURE

Definition of heart failure

- A complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood (CAD, hypertension, valve disease, myocarditis)

Manifestations

- Dyspnea
- Fatigue
- Fluid retention can lead to pulmonary congestion and peripheral edema

New York Heart Association Functional (NYHA) Classification Used to Classify the Extent of Heart Failure

NYHA	Symptoms
I	Cardiac disease, but no symptoms and no limitation in ordinary physical activity
II	Mild symptoms and slight limitation during ordinary activity
III	Marked limitation in activity due to symptoms
IV	Severe limitation, symptoms even at rest

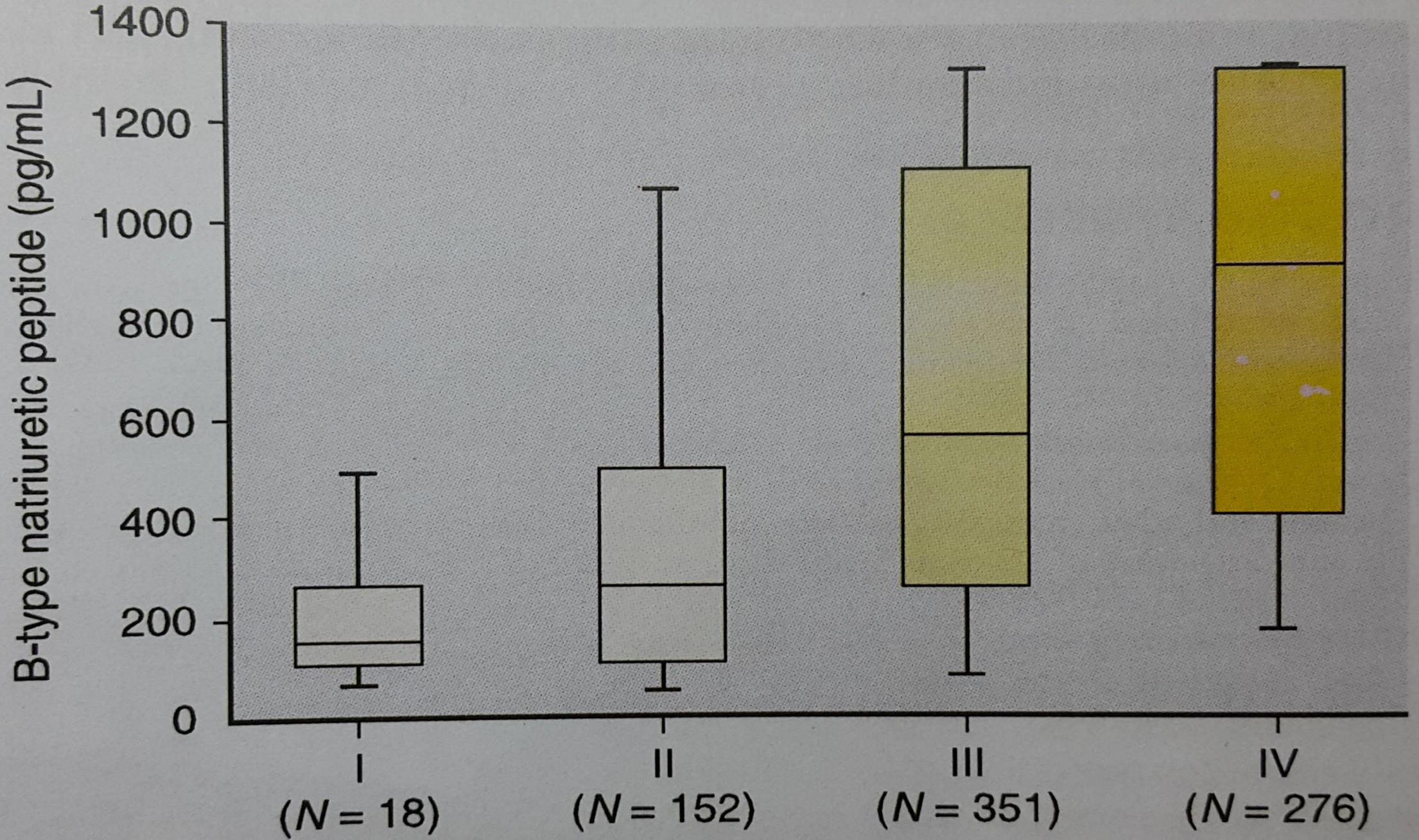
- **The symptoms and signs of HF are non specific, an objective test for HF would be extremely useful**
- **The biomarker would increase progressively with increasing severity of disease and not be increased or decreased in condition that mimic HF**
- **Rapid assays**

Natriuretic Peptides

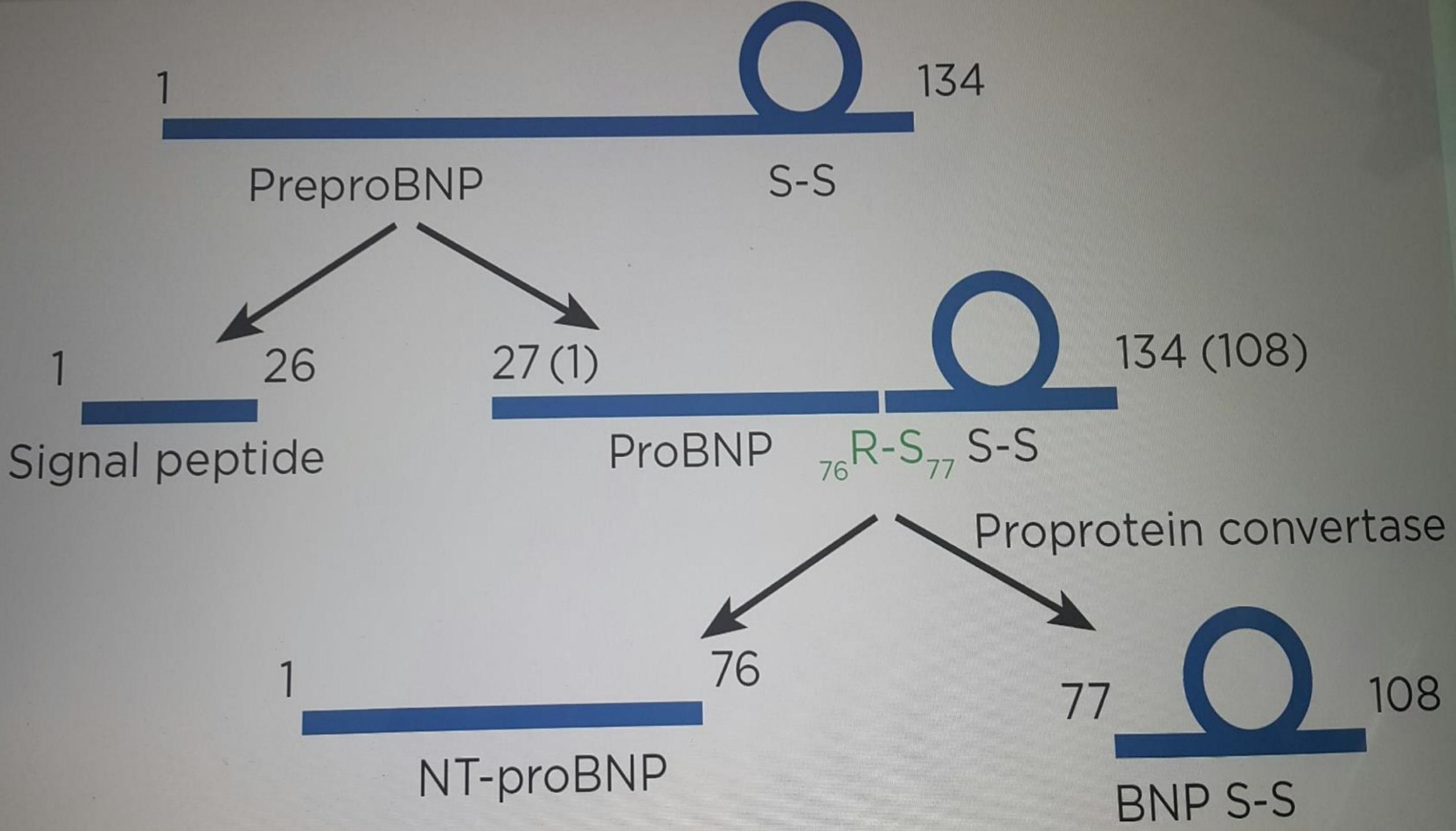
- **History**
  - 1981: Rat heart atria
  - 1984: Human heart atria (ANP)
  - 1988: Porcine brain (BNP)
  - 1990: Endothelial cells (CNP)
  - 1991: Human cardiac ventricle (B type NP)
  - 1992: Green mamba snake (DNP)

- B-type natriuretic peptide is a hormone that is mainly released from myocardial ventricle
- BNP ↑
- Volume overload
- Ventricular stretch

- Fluid and electrolyte hemostasis
- Down regulate the renin-angiotensin-aldosterone(RAAS)
- Decrease sympathetic nerve activity in the heart and kidney
- Increase renal blood flow
- Increase sodium excretion


B-type natriuretic peptide (pg/mL)
1400
1200
1000
800
600
400
200
0
I
(N = 18)
II
(N = 152)
III
(N = 351)
IV
(N = 276)
New York Heart Association class

B


1
134
PreproBNP
S-S
1
26
Signal peptide
27 (1)
134 (108)
ProBNP
76R-S77 S-S
Proprotein convertase
1
76
NT-proBNP
77
108
BNP S-S

- **The major circulating forms are NT-proBNP (unknown function) and BNP (physiological active)**
- **Circulation half-life BNP : 22 min**

NT-proBNP : 60-120 min

Applications

- Distinguishing HF from lung disease
- Monitoring HF
- Risk stratification of patients with ACS
- Screening for ventricular dysfunction in selected population
- Testing for drug cardiotoxicity

IFCC Guidelines

- Reference intervals (based on age and by sex)

Inverse relationship between concentration and body index

- Receiver operating characteristic curve (ROC)

Should be stablished to evaluate clinical effectiveness

- Total imprecision <15%

- **Preanalytical**
  - **Effects of storage time and temperature**
  - **Influence of different anticoagulants**
  - **Influence of gel separator tubes**
  - **Need for plastic blood collection tubes for BNP, for NT-proBNP, either glass or plastic is acceptable**

- **Analytical**
  - **Identification of the epitopes**
  - **Cross reactivity with related NPs**
  - **Interference from heterophile antibody, RF, HAMA**
  - **Description of calibration material**

- **BNP**

At a decision threshold of 100 pg/ml

PPV : 79%

NPV : 92%

>75 years old: have concentrations above 100

- **NT-proBNP**

  For patients younger than 75 years: 125 pg/ml

  NPV : 96.7%

  PPV : 80.6%

  For patients older than 75 years : 450 pg/ml

- **Conclusion**

- **The European society of cardiology has included the use of NP in their guidelines for the diagnosis or rule out of HF**