Azerbaijan Society of Cardiology

natriuretic peptides in the management of patients with heart failure

Azerbaijan, AZ

Dr. Aysel ISLAMLI, MD, FESC, FHFA ESC

Baku Health Center

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ayselislamli29@gmail.com

@islamliaysel

Dr. Aysel İSLAMLI

before we start ..

- Biomarkers are a support to clinical judgment
- But they do not replace clinical judgment
- In unclear clinical situations, in the patient's bedside can guide the treatment way

it is also important to say that

1. Natriuretic peptides is useful to defined worsening heart failure
2. Epidemiology of WHF
3. Prognostic role of BNP in WHF
4. Differential effect of drugs based on baseline BNP levels

the heart as an endocrine organ ?

The American Journal of Medicine

Vol. 36 JANUARY 1964 No. 1

Editorial

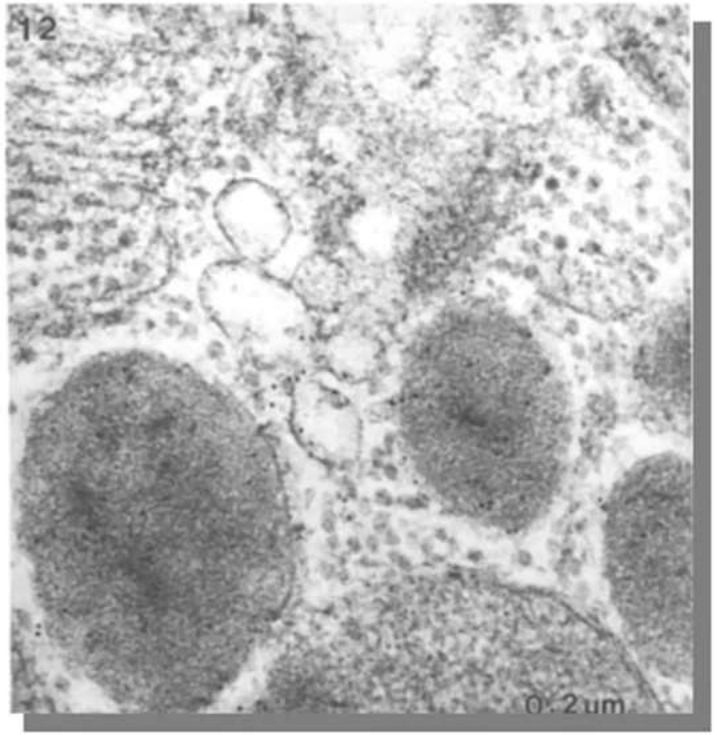
The Heart as an Endocrine Organ

The work of William Harvey in the seventeenth century established the prime function of the heart as a pump, but a number of experiments carried out during this century can be interpreted to show that, under certain circumstances, the heart may also subserve an endocrine function. In 1921 Otto Loewi stimulated the cardiac sympathetic nerves of the isolated perfused turtle heart and noted that the rate and force of contraction of the heart were augmented. In addition, nerve stimulation also resulted in the release of a sympathomimetic substance into the perfusion fluid. Thus, Loewi observed that the fluid perfusing a turtle heart that had undergone sympathetic stimulation was capable of enhancing the contraction of another isolated turtle heart [1]. These experiments not only served as the basis for modern concepts of the mechanism of adrenergic neurotransmission, but they also demonstrated that the quantity of active adrenergic neurotransmitter substance released by an organ after sympathetic nerve stimulation could be sufficient to have a perceptible effect on the function of a tissue which is not stimulated directly.

Twelve years later Cannon and Rosenblueth extended Loewi's observation by showing that in the cat, which had been sensitized to the action of nerve stimulation by cocaine, stimulation of the cardioaccelerator nerve resulted in contraction of the denervated sinus rhythm [2]. It was believed that a chemical substance was released within the heart and was carried by the blood to the sensitized sinus rhythm. Additional support for this concept was provided by Simeone and Saraoff who found that the contraction of the sinus rhythm following cardioaccelerator nerve stimulation could be prevented by treatment with the adrenergic blocking drug, dibenamine [3]. Hoffmann and collaborators demonstrated that the administration of acetylcholine to an isolated mammalian heart resulted in the liberation of an epinephrine-like substance capable of stimulating the contraction of a hypodynamic frog heart [4].

Cannon also showed that extracts of the heart have many of the biological properties of adrenaline [5]. von Euler demonstrated that the sympathomimetic compound in cattle heart was in fact norepinephrine [6]; Goodall measured its concentration [7], and Raab and Gilge showed that norepinephrine is also present in the human heart [8]. The close relationship between the sympathetic nerves and the norepinephrine content of the heart was suggested by the depletion of myocardial norepinephrine stores following postganglionic sympathectomy and degeneration of the sympathetic nerves to the heart [9,10]. It now appears likely that the norepinephrine stores of the mammalian heart are contained in the sympathetic nerves, particularly in the nerve endings, rather than in the muscle cells. Large quantities of epinephrine and norepinephrine are present in the abundant chromaffin cells which line the cavity of the hearts of some primitive vertebrate forms [11,12]. This finding provides strong morphologic evidence that the heart contains cells capable of secreting catecholamines in organisms which are at a relatively low level on the phylogenetic scale.

1



Braunwald, American Journal of Medicine, 1964

ESC
European Society of Cardiology
European Heart Journal (2021) **42**, 3599–3726
doi:10.1093/eurheartj/ehab368

2021 ESC Guidelines
treatment of acute a

Developed by the Task Force
and chronic heart failure of th

With the special contributio
(HFA) of the ESC

Authors/Task Force Members: Ther
Kingdom), Marco Metra * (Chairp
Coordinator) (Italy), Roy S. Gardne
Andreas Baumbach (United Kingdo
(Switzerland), Javed Butler (United
(Lithuania), Ovidiu Chioncel (Romania), John G.F. Cleland (United Kingdom),
Andrew J.S. Coats (United Kingdom), Maria G. Crespo-Leiro (Spain),
Dimitrios Farmakis (Greece), Martine Gilard (France), Stephane Heymans

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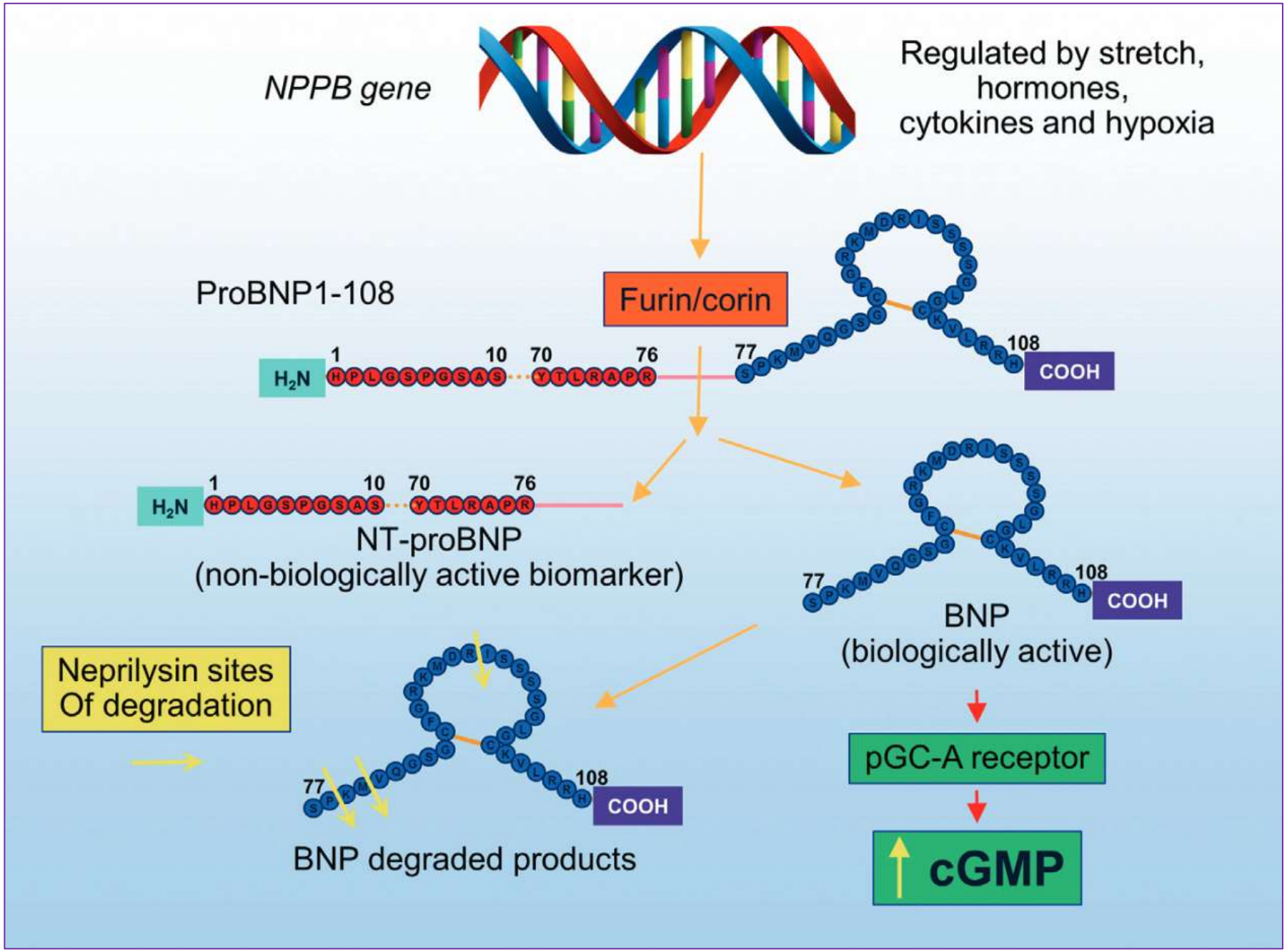
ESC GUIDELINES

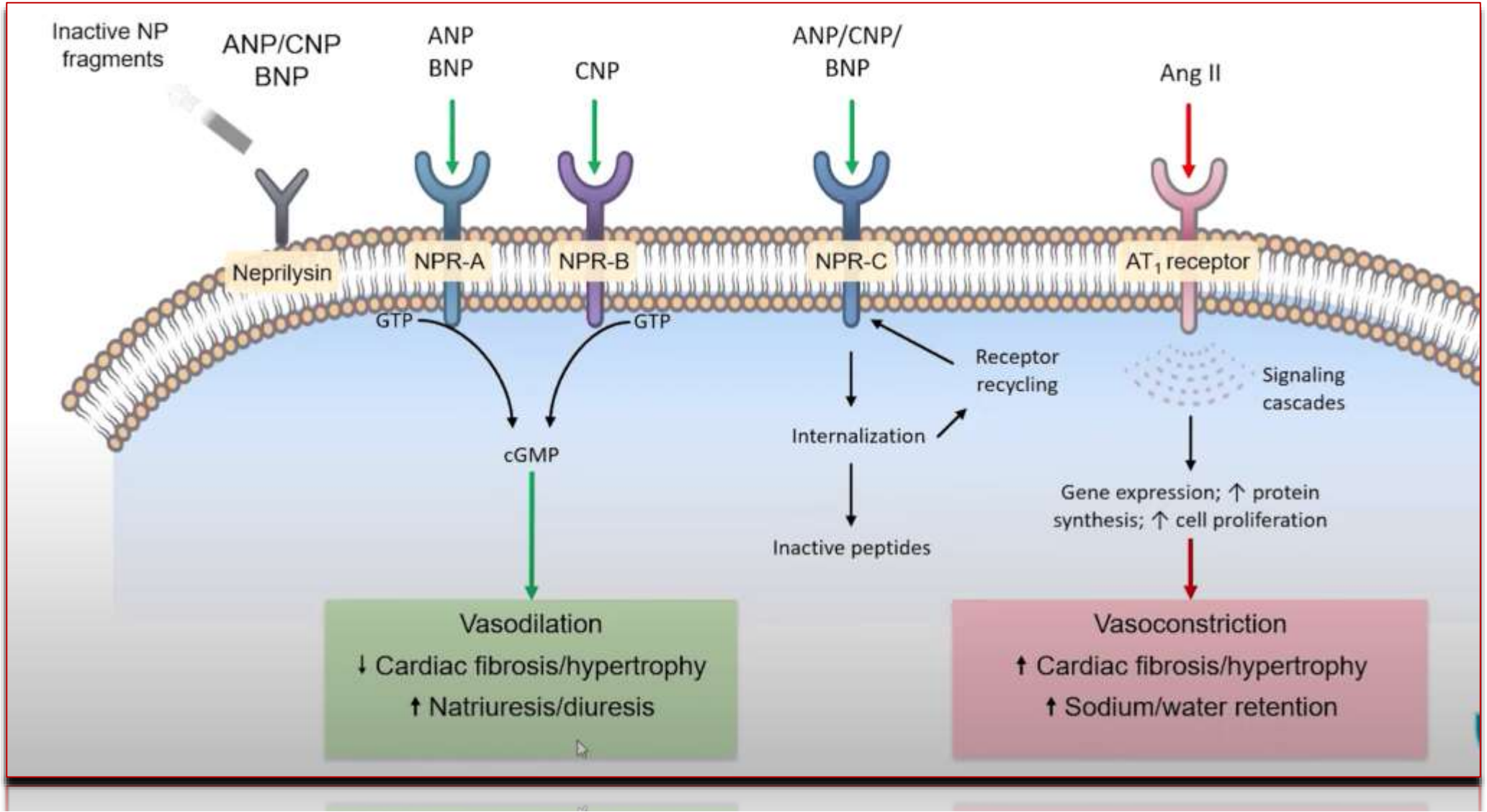
2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC

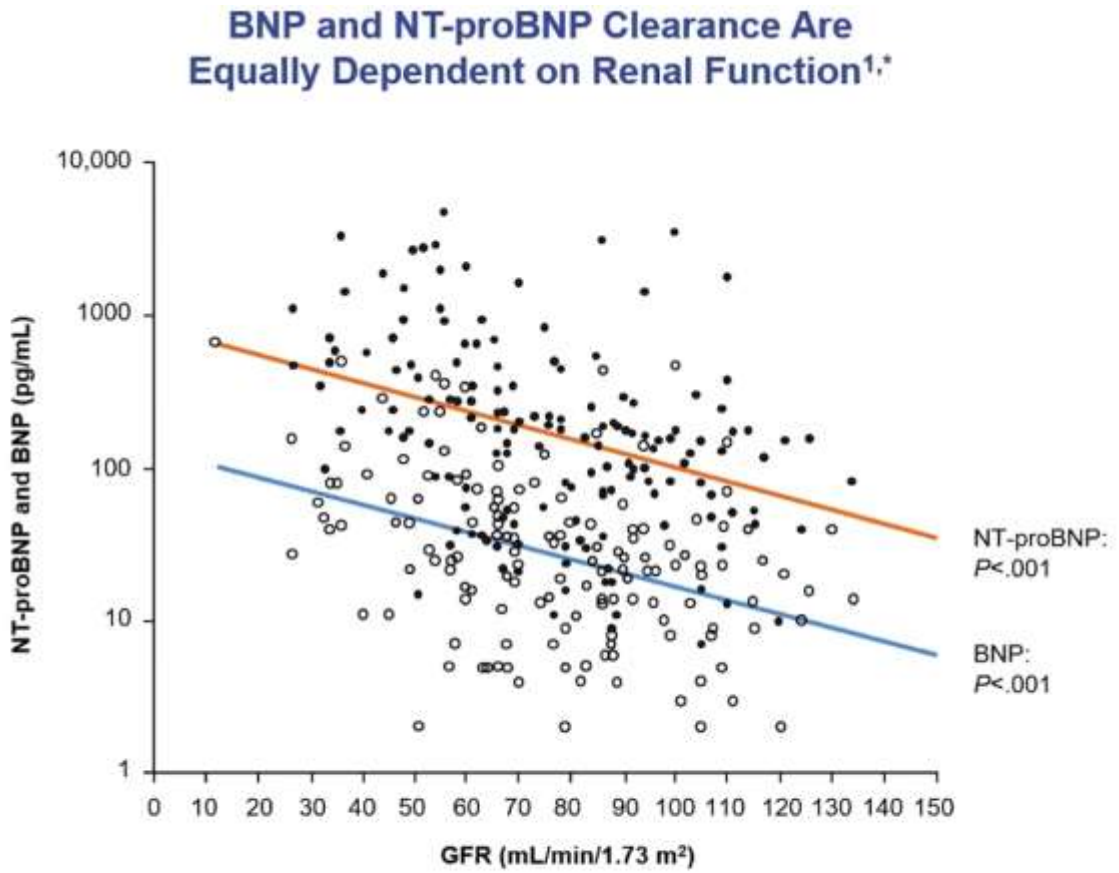

NPPB gene
Regulated by stretch, hormones, cytokines and hypoxia
ProBNP1-108
Furin/corin
H2N
1
10
70
76
77
108
COOH
NT-proBNP
(non-biologically active biomarker)
BNP
(biologically active)
Neprilysin sites
Of degradation
BNP degraded products
pGC-A receptor
cGMP

NPs oppose the RAAS



natriuretic peptide clearance

- BNP[1]
  - NPR
  - Renal excretion
  - Neprilysin
- NT-proBNP[1,2]
  - Less well understood
  - Renal excretion partially responsible



BNP, B-type natriuretic peptide; GFR, glomerular filtration rate; NPR, natriuretic peptide receptor; NT-proBNP, N-terminal pro-brain natriuretic peptide.
*In patients with hypertension (N=165) undergoing renal arteriography with invasive renal plasma flow measurements and echocardiography.
1. van Kimmenade RRJ et al. *J Am Coll Cardiol.* 2009;53:884-890. 2. Palmer SC et al. *Eur J Heart Fail.* 2009;11:832-839.

cardiac correlates for NP values

- Left ventricle
  - Systolic function
  - Diastolic function
  - Chamber size
  - Wall thickness
- Right ventricle
  - Systolic function
  - Chamber size
- Atria
  - Size
- Valves
  - AS, AI
  - MR, MS
  - TR, TS
- Filling pressures
  - Pulmonary
  - Left ventricle, left atrial
- Coronary ischemia
- Heart rhythm
- Aortic capacitance

clinical correlates of elevated NPs

Selected Potential Causes of Elevated Natriuretic Peptide Levels

Cardiac
HF, including RV syndromes
Acute coronary syndromes
Heart muscle disease, including LVH
Valvular heart disease
Pericardial disease
Atrial fibrillation
Myocarditis
Cardiac surgery
Cardioversion
Toxic-metabolic myocardial insults, including cancer chemotherapy
Noncardiac
Advancing age
Anemia
Renal failure
Pulmonary: obstructive sleep apnea, severe pneumonia
Pulmonary hypertension
Critical illness
Bacterial sepsis
Severe burns

NPs in clinical practice guidelines

Indication	Class	LOE
NPs for diagnosis[1-3]	I	A
NPs for prognosis[1-3]	I	A
NPs for predischarge risk assessment[1-3]	IIa	B-NR
NPs to prevent HF onset[1-3]	IIa	B-R
NPs to guide HF therapy[4]	IIa	B

JACC Journal of the American College of Cardiology

Circulation Journal of the American Heart Association

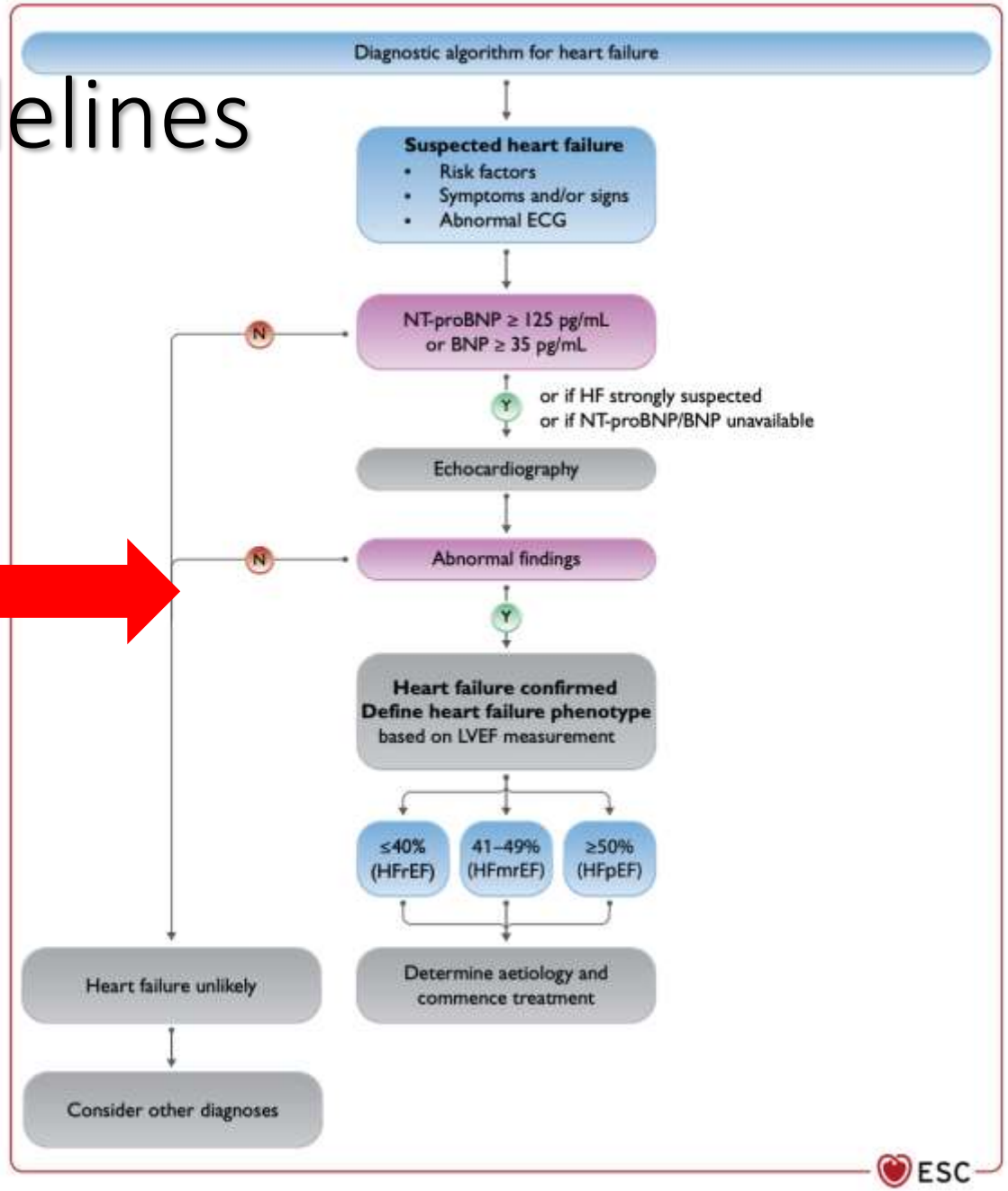
Journal of Cardiac Failure

doi: 10.1016/j.jacc.2017.04.025. Epub 2017 Apr 28.

NPs in clinical practice guidelines

- Plasma concentrations of NPs are recommended as initial diagnostic tests in patients with symptoms suggestive of HF to rule out the diagnosis.

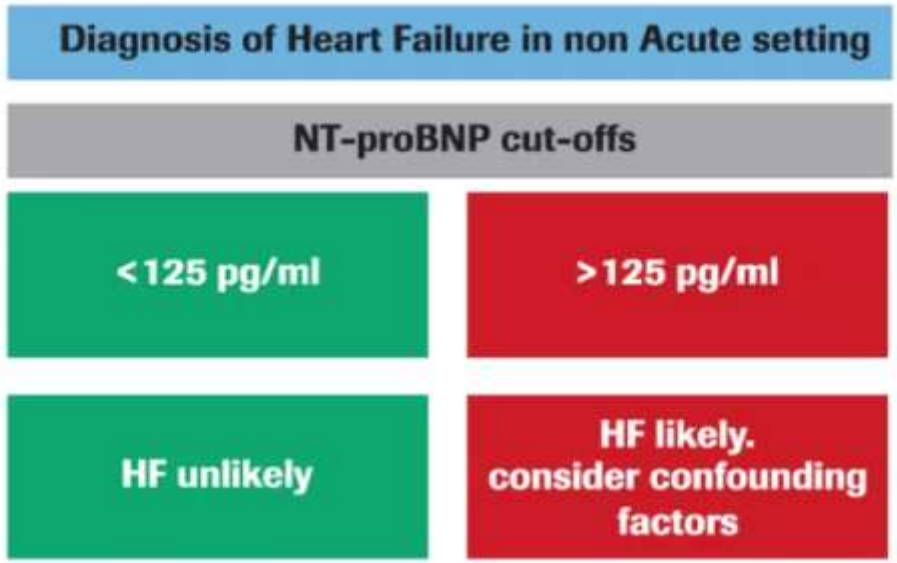
- Elevated concentrations support a diagnosis of HF, are useful for prognostication and may guide further cardiac investigation.



Recommended diagnostic tests in all patients with suspected chronic heart failure

Recommendations	Class[a]	Level[b]
BNP/NT-proBNP[c]	I	B
12-lead ECG	I	C
Transthoracic echocardiography	I	C
Chest radiography (X-ray)	I	C
Routine blood tests for comorbidities, including full blood count, urea and electrolytes, thyroid function, fasting glucose and HbA1c, lipids, iron status (TSAT and ferritin)	I	C

BNP = B-type natriuretic peptide; ECG = electrocardiogram; HbA1c = glycated haemoglobin; NT-proBNP = N-terminal pro-B-type natriuretic peptide; TSAT = transferrin saturation.
[a]Class of recommendation.
[b]Level of evidence.
[c]References are listed in section 4.2 for this item.



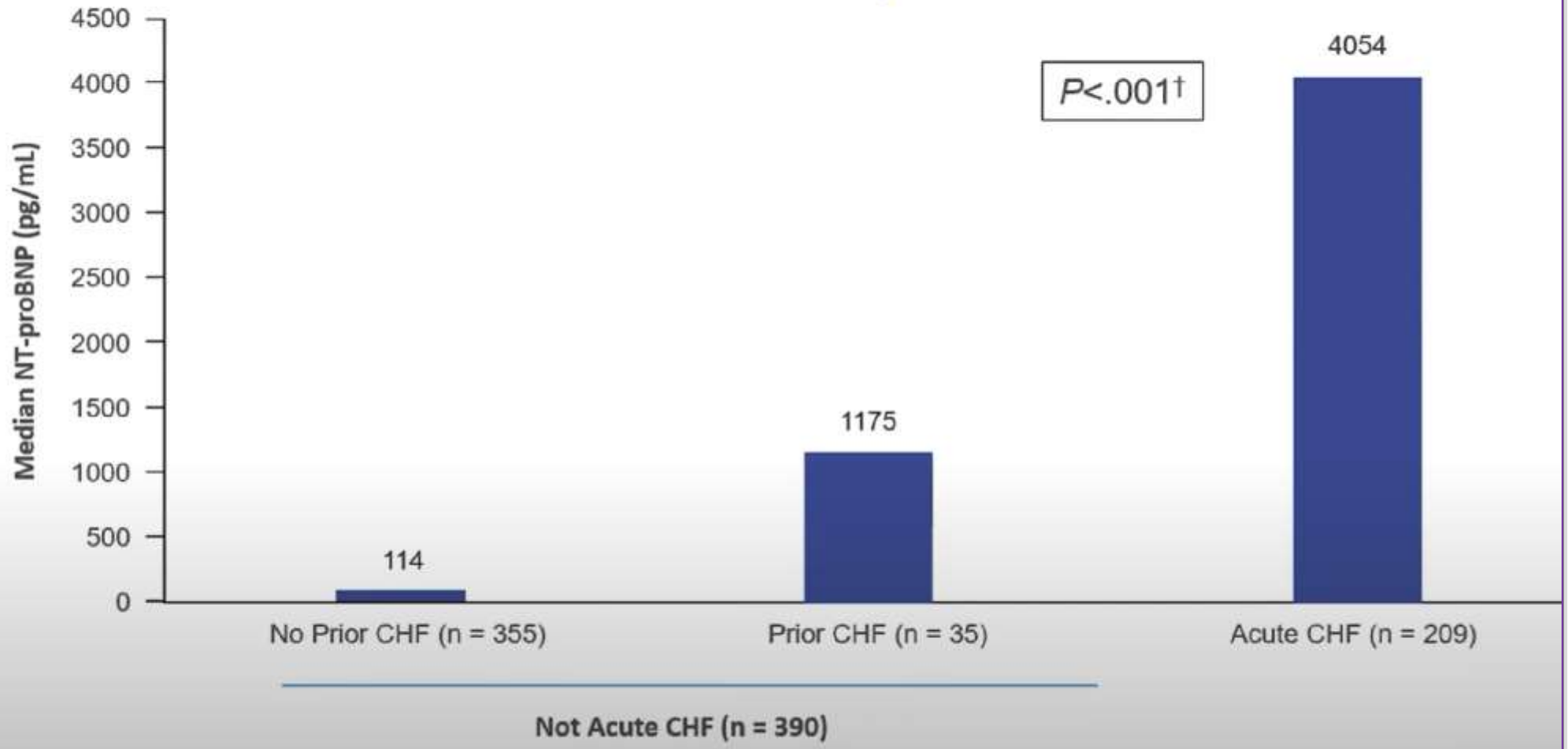
Setting	Natriuretic peptide value	Interpretation
Non-acute setting	BNP <35 pg/mL or NT-proBNP <125 pg/mL	HF is unlikely
Acute setting	BNP <100 pg/mL or NT pro-BNP <300 pg/mL	HF is unlikely
	BNP >500 pg/mL or NT pro-BNP >450 pg/mL (in patients <50 years) NT pro-BNP >900 pg/mL (in patients 50 to 75 years) NT pro-BNP >1,800 pg/mL (in patients >75) years)	HF is likely

BNP=B-type natriuretic peptide; HF=heart failure; NT pro-BNP=N-terminal pro B-type natriuretic peptide

Cut-off values and interpretation of natriuretic peptide in patients with suspected HF in non-acute and acute setting

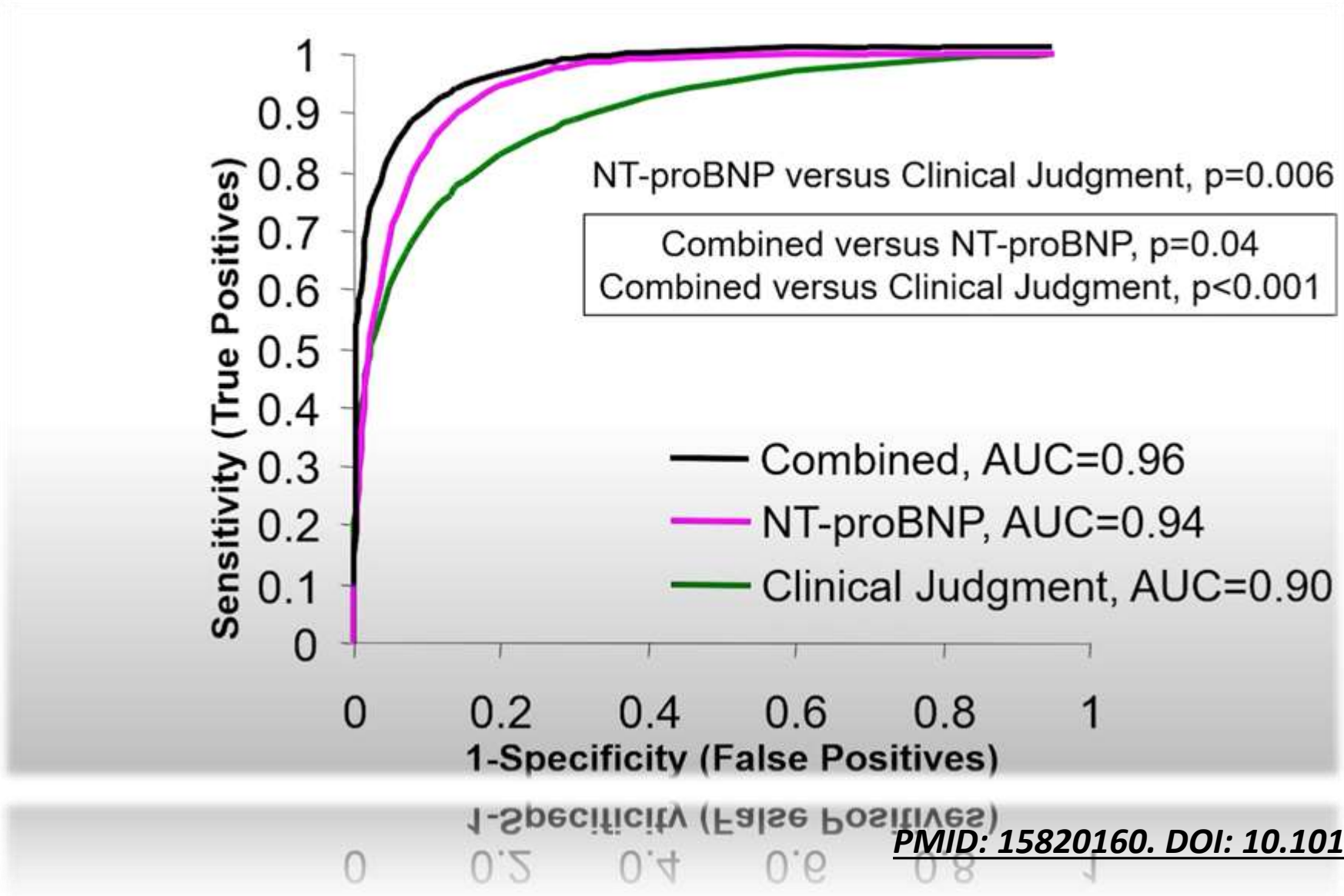
European Heart Journal (2021) 42, 35993726 ESC GUIDELINES doi:10.1093/eurheartj/ehab368

NT-proBNP Levels Were Elevated in Patients With Acute HF in the PRIDE Study*



CHF, congestive heart failure; PRIDE, N-Terminal Pro-BNP Investigation of Dyspnea in the Emergency Department.
*Patients (N = 599) were consenting adults ≥21 years of age presenting to the emergency department of the Massachusetts General Hospital with complain of dyspnea. †*P* value represents the comparison of acute CHF with patients with not-acute CHF.
Januzzi JL Jr et al. *Am J Cardiol.* 2005;95:948-954.

PRIDE study



PMID: 15820160. DOI: 10.1016/j.amjcard.2004.12.032

NT pro BNP: utility in outpatient dyspnea

History
Physical examination

Measure NT-proBNP

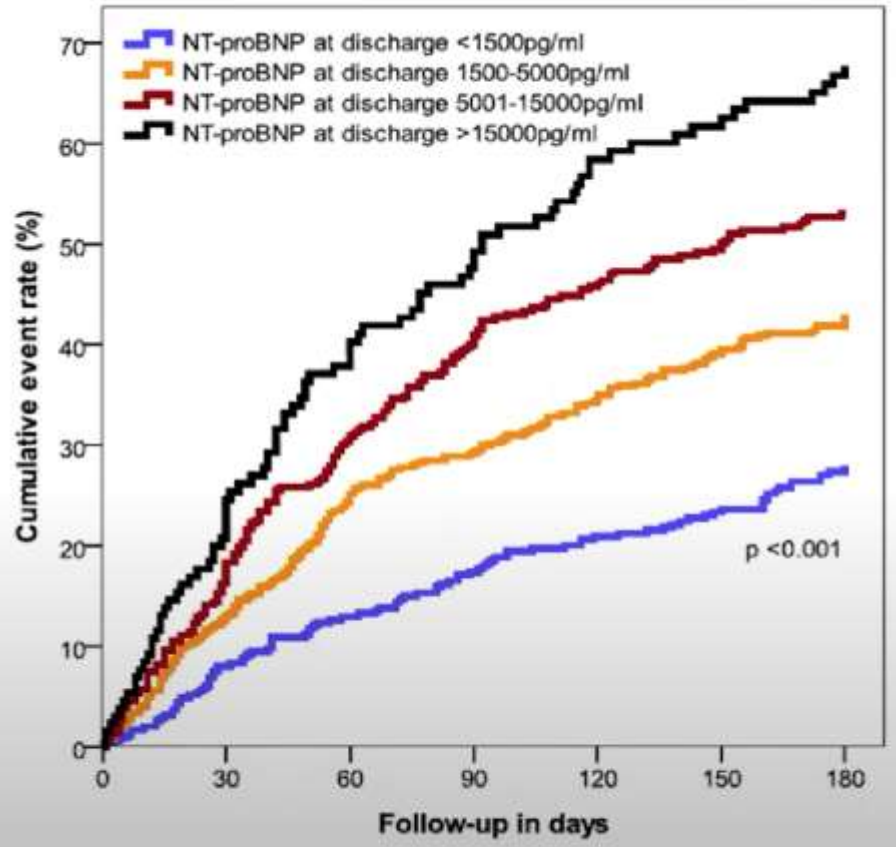
NT-proBNP <125 pg/mL?

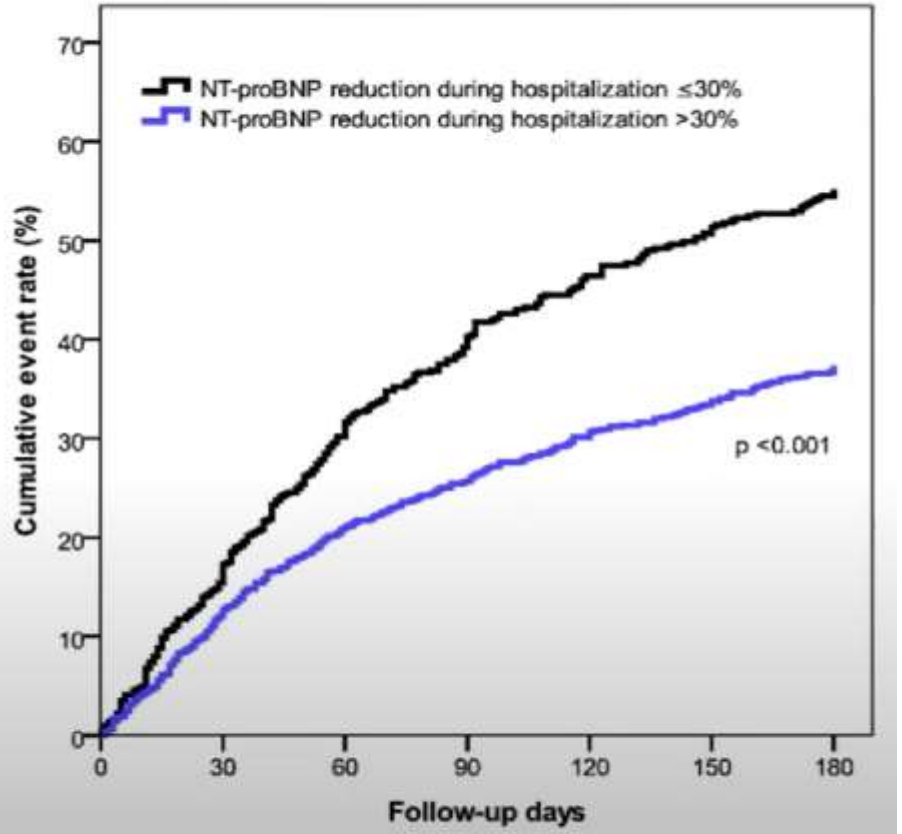
HF unlikely:
Seek alternative diagnosis

NT-proBNP ≥125 pg/mL?

HF possible:
Cardiac work up

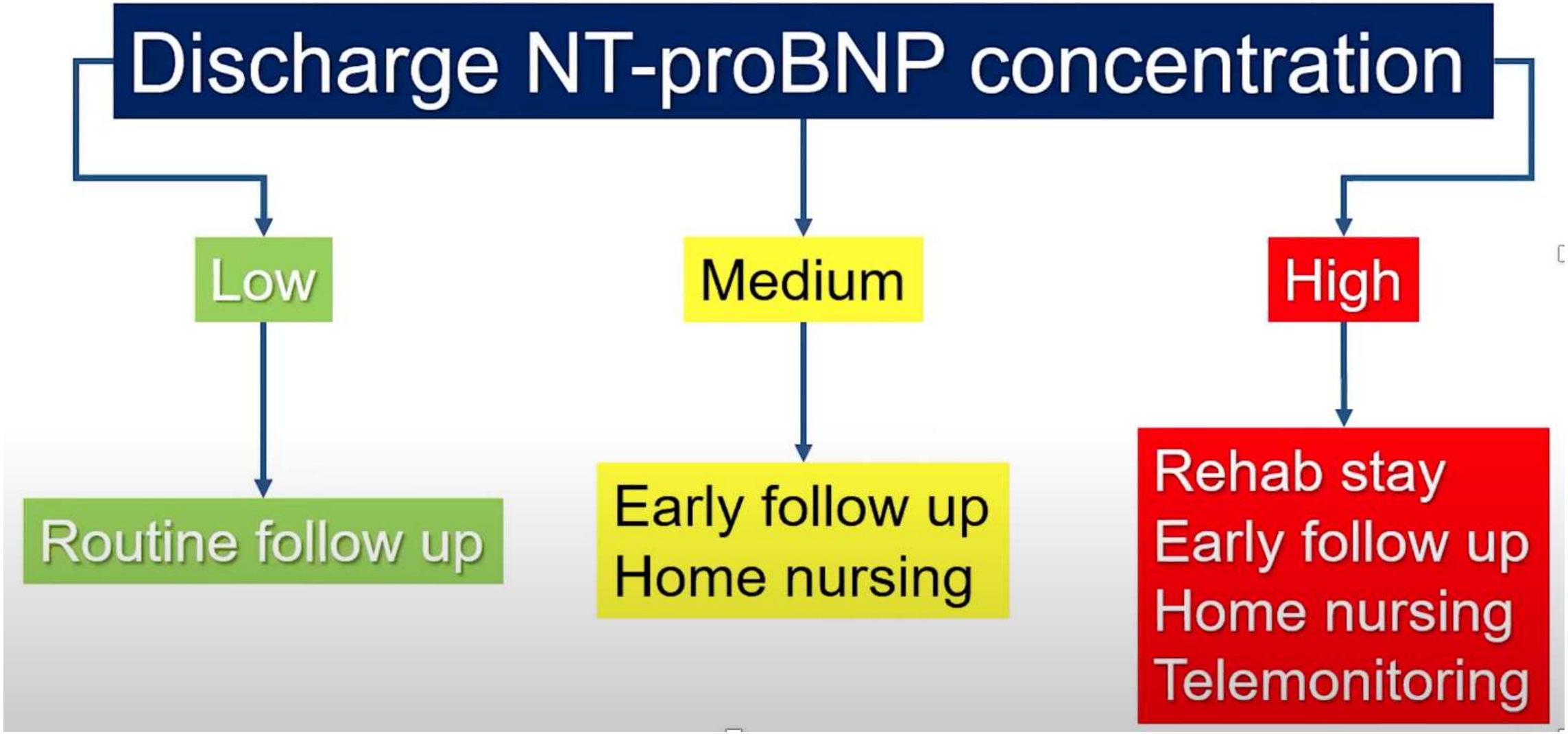
NT –proBNP and prognosis after ADHF treatment





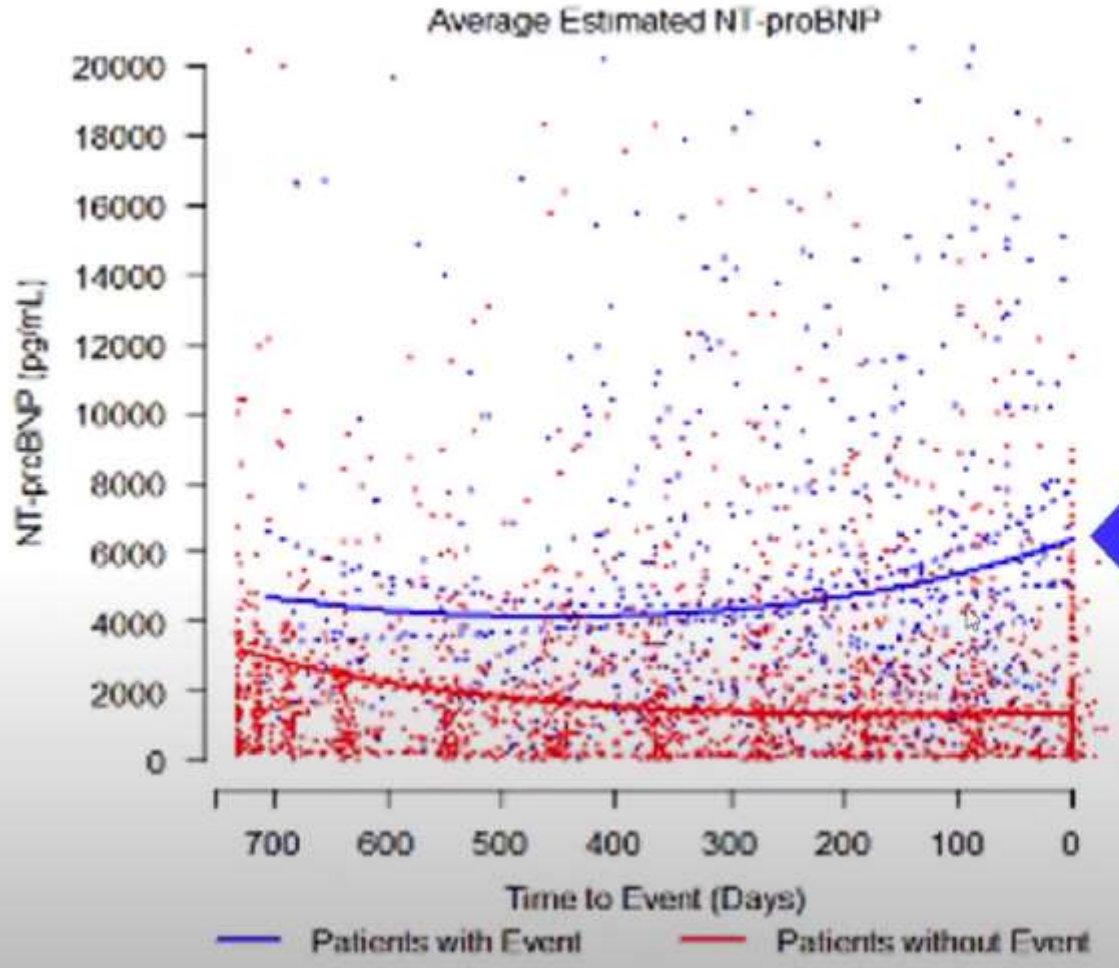
Salah, et al, Heart, 2014

Individualized care based on discharge NT-proBNP



bridge from hospital to home

When does NT-pro BNP rise relative to events ?

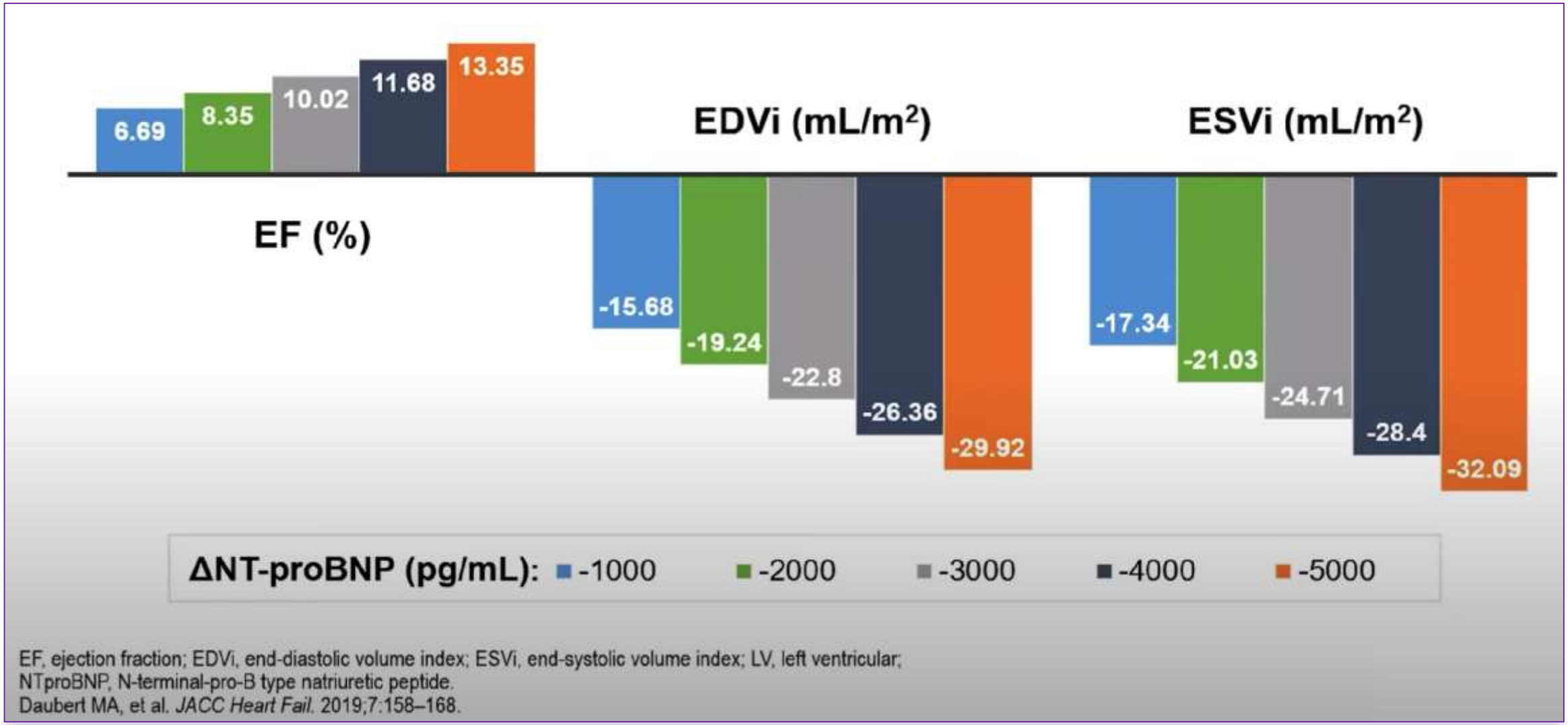


Serial results of NT-proBNP differed considerably among study participants with and without events (CV death/HF hospitalization)

Event happens here

Fuery M et al in preparation

change in LV structure and function at 1 year by NT-pro BNP reduction



EF, ejection fraction; EDVi, end-diastolic volume index; ESVi, end-systolic volume index; LV, left ventricular; NTproBNP, N-terminal-pro-B type natriuretic peptide.
Daubert MA, et al. *JACC Heart Fail.* 2019;7:158–168.

operationalizing NP monitoring to enhance clinical dicision-making chronic HF

- **Hospital to home**: In recently decompensated patients, measure 1 2 weeks after discharge (office or home).
- **Outpatients**: measure every 3 months
  - Facilitates GDMT decision making (removal of diuretic after GDMT)
  - Stable concentrations <1000 pg/mL (NT-proBNP) or <100 pg/mL (BNP): imaging and other testing may be reasonably deferred
  - Elevated/rising concentrations: repeat imaging, further evaluations, review medication/lifestyle program and adjust as appropriate
  - **Markedly elevated concentrations**: Consider transplant referral, consider diagnoses associated with “unexpectedly elevated” NP (amyloidosis).

HF, heart failure; NT-pro-BNP, N-terminal pro-B type natriuretic peptide.
Yancy CW, et al. *J Am Coll Cardiol*. 2018;71:201–230.

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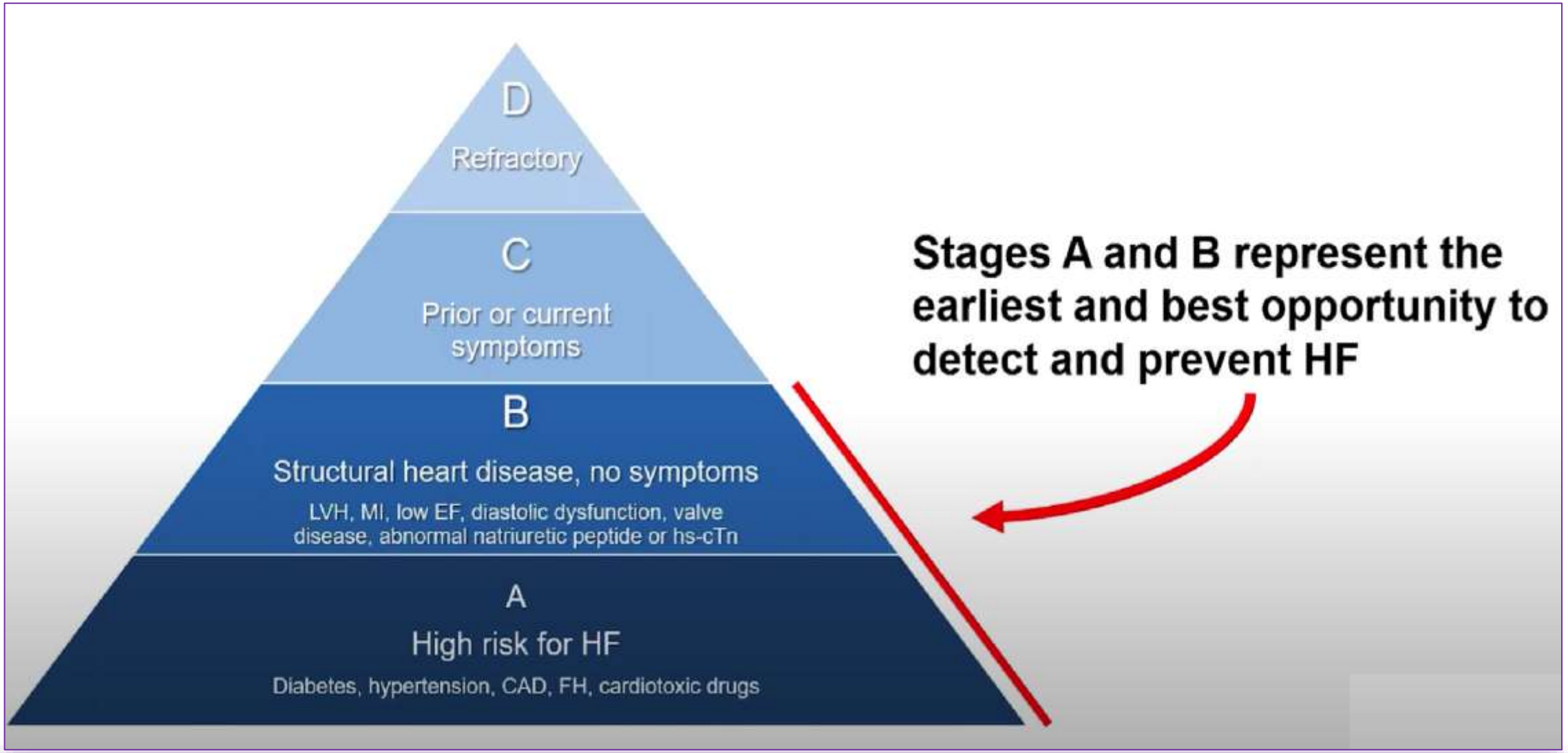
UDHF stages of heart failure

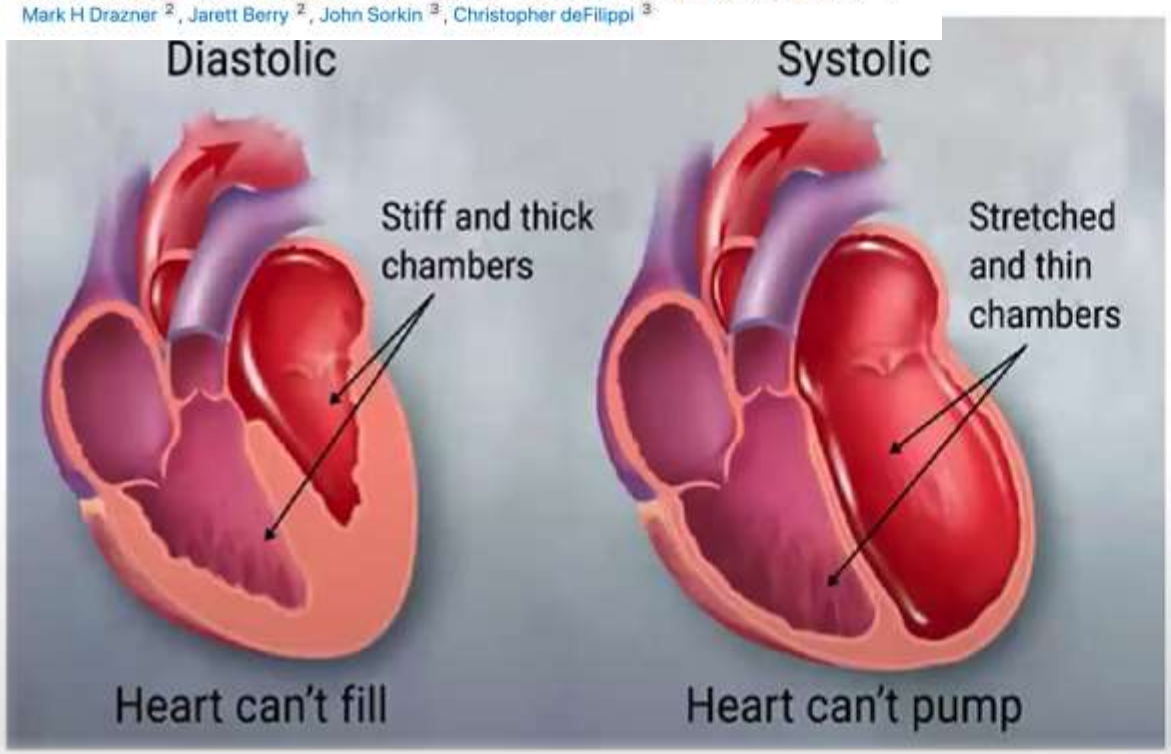


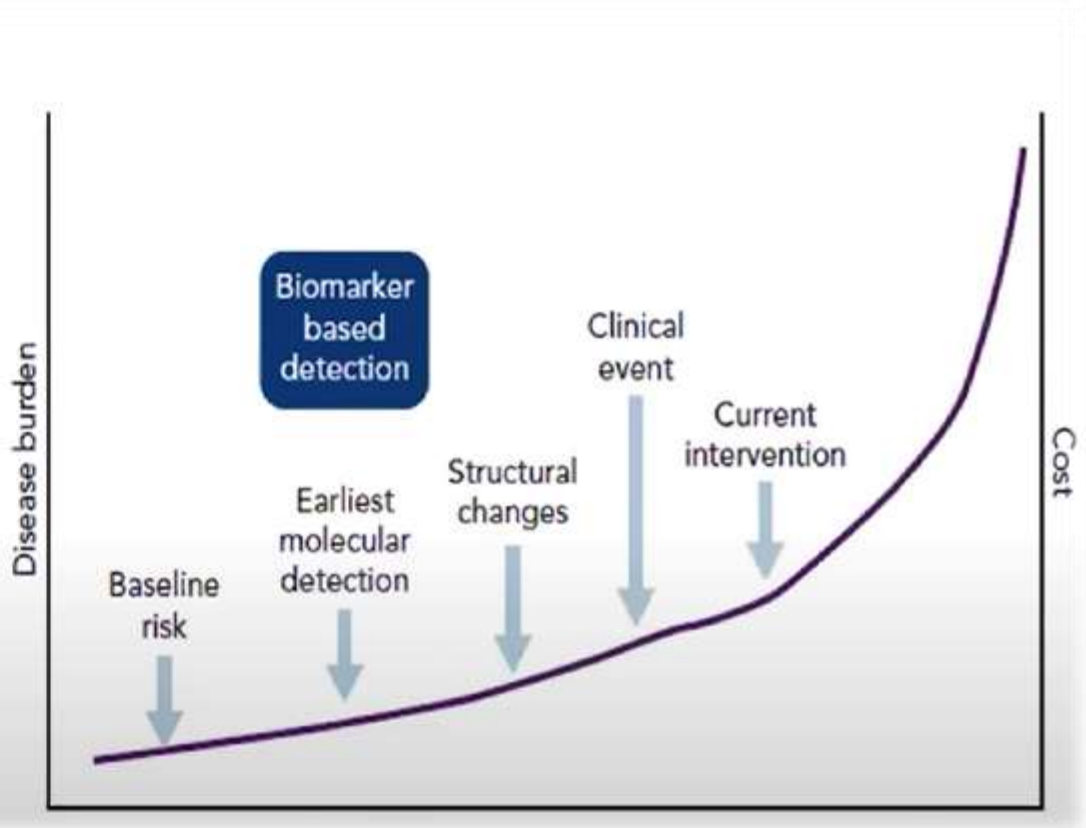
Stage B heart failure and biomarkers for early detection

Observational Study > JACC Heart Fail. 2015 Jun;3(6):445-455.
doi: 10.1016/j.jchf.2014.12.018. Epub 2015 May 14.

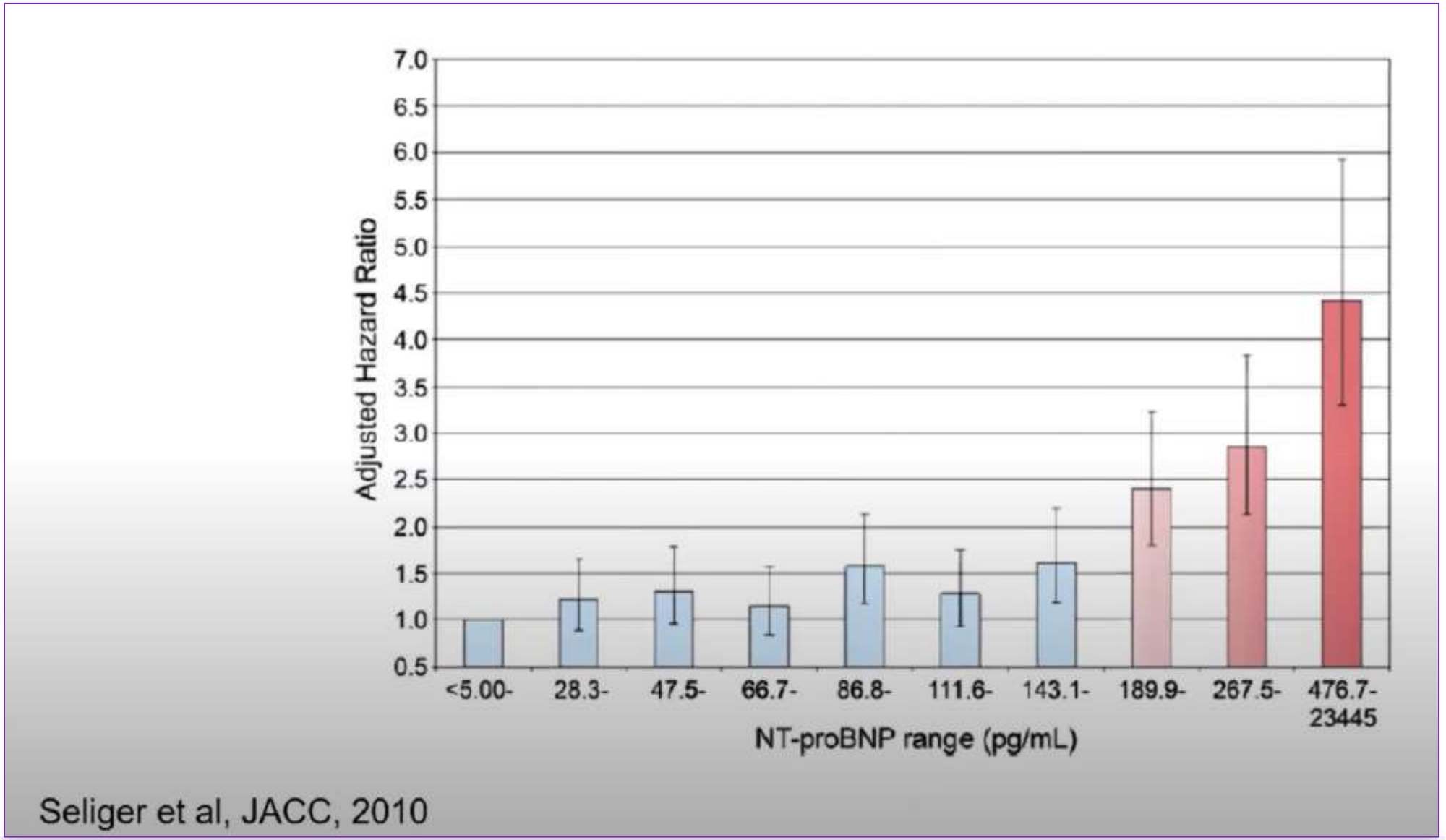
Older Adults, "Malignant" Left Ventricular Hypertrophy, and Associated Cardiac-Specific Biomarker Phenotypes to Identify the Differential Risk of New-Onset Reduced Versus Preserved Ejection Fraction Heart Failure: CHS (Cardiovascular Health Study)

Stephen L Seliger [1], James de Lemos [2], Ian J Neeland [2], Robert Christenson [3], John Gottdiener [3], Mark H Drazner [2], Jarett Berry [2], John Sorkin [3], Christopher deFilippi [3]



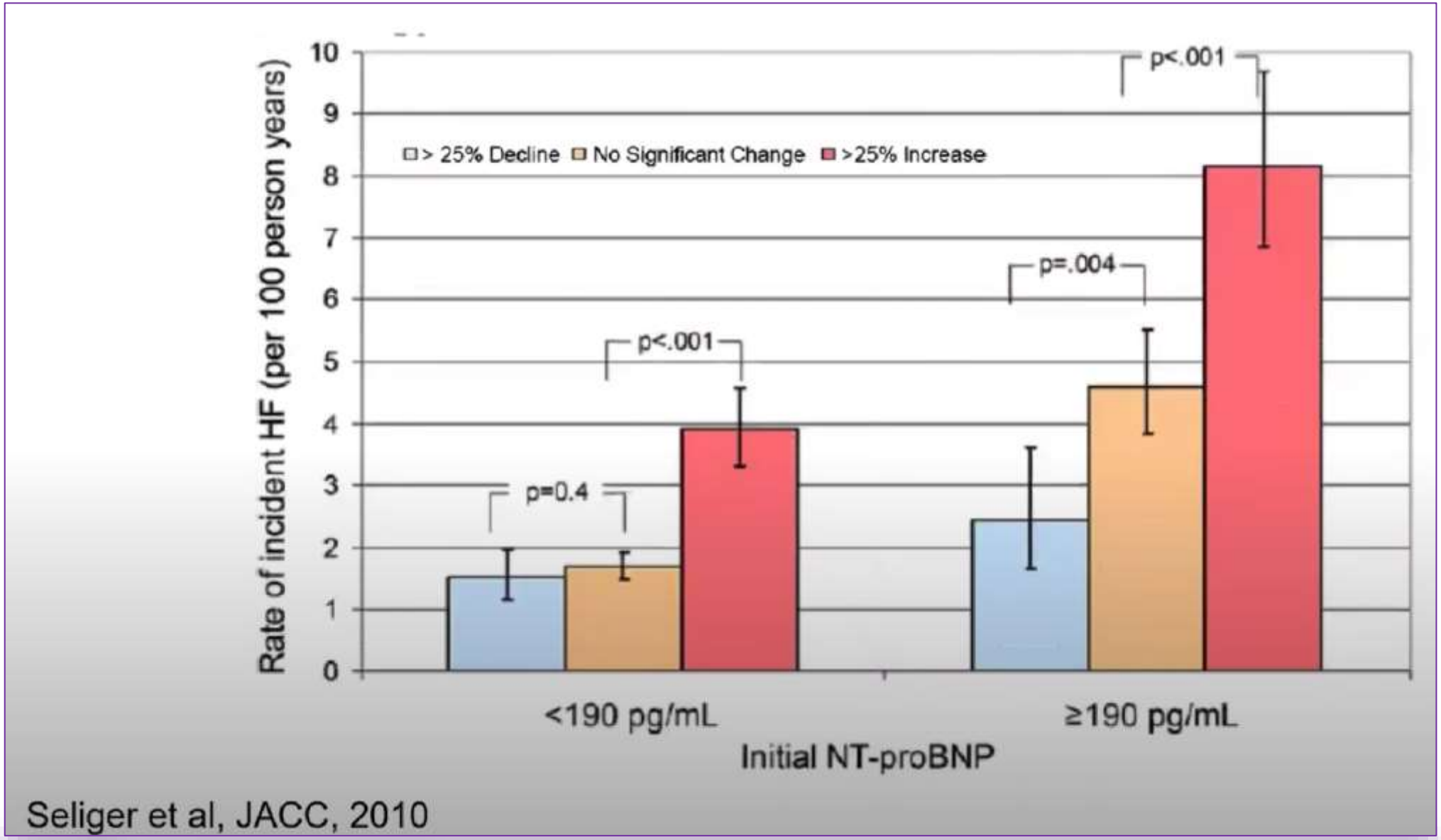


NT-proBNP and prognosis in stage A HF



Seliger et al, JACC, 2010

NT-proBNP and prognosis in stage A HF



Seliger et al, JACC, 2010

conclusion &
take home message

- Over the past 20 years, NT pro BNP has evolved (evrimleşmek) from a curiosity to an essential tool in the daily monitoring of individuals with suspected heart failure.

- NPs are the main tool not only in diagnosing heart failure, but in evaluating the effectiveness of our treatment and determining the patient's prognosis.

- It is also important in the early diagnosis of heart failure and in the management of patients with unexplained dyspnea.