



Natriuretic Peptides for the Diagnosis and Prognosis of Heart Failure

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Royalties: UpToDate

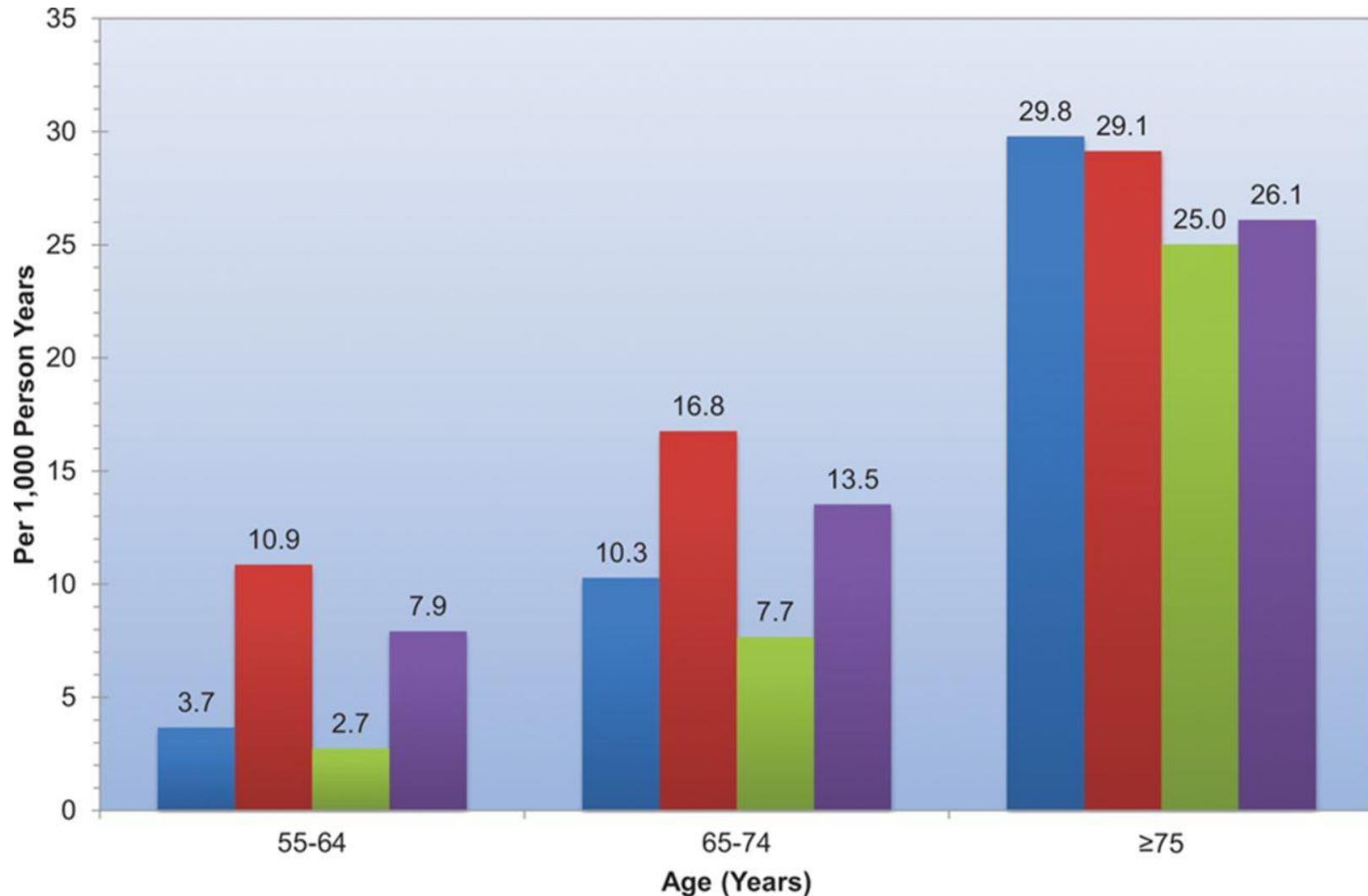
Learning Objectives

- Explain the signs and symptoms of HF
- Discuss the optimal diagnostic thresholds for NT-proBNP to diagnose HF
- Explain the prognostic implications of an elevated natriuretic peptide level with or without a diagnosis of HF
- Identify potential confounders whether they be medical comorbidities or treatments for HF that may influence natriuretic peptides and recognize if these might impact the threshold to diagnose HF

The Role for Natriuretic Peptides in Cardiovascular Disease

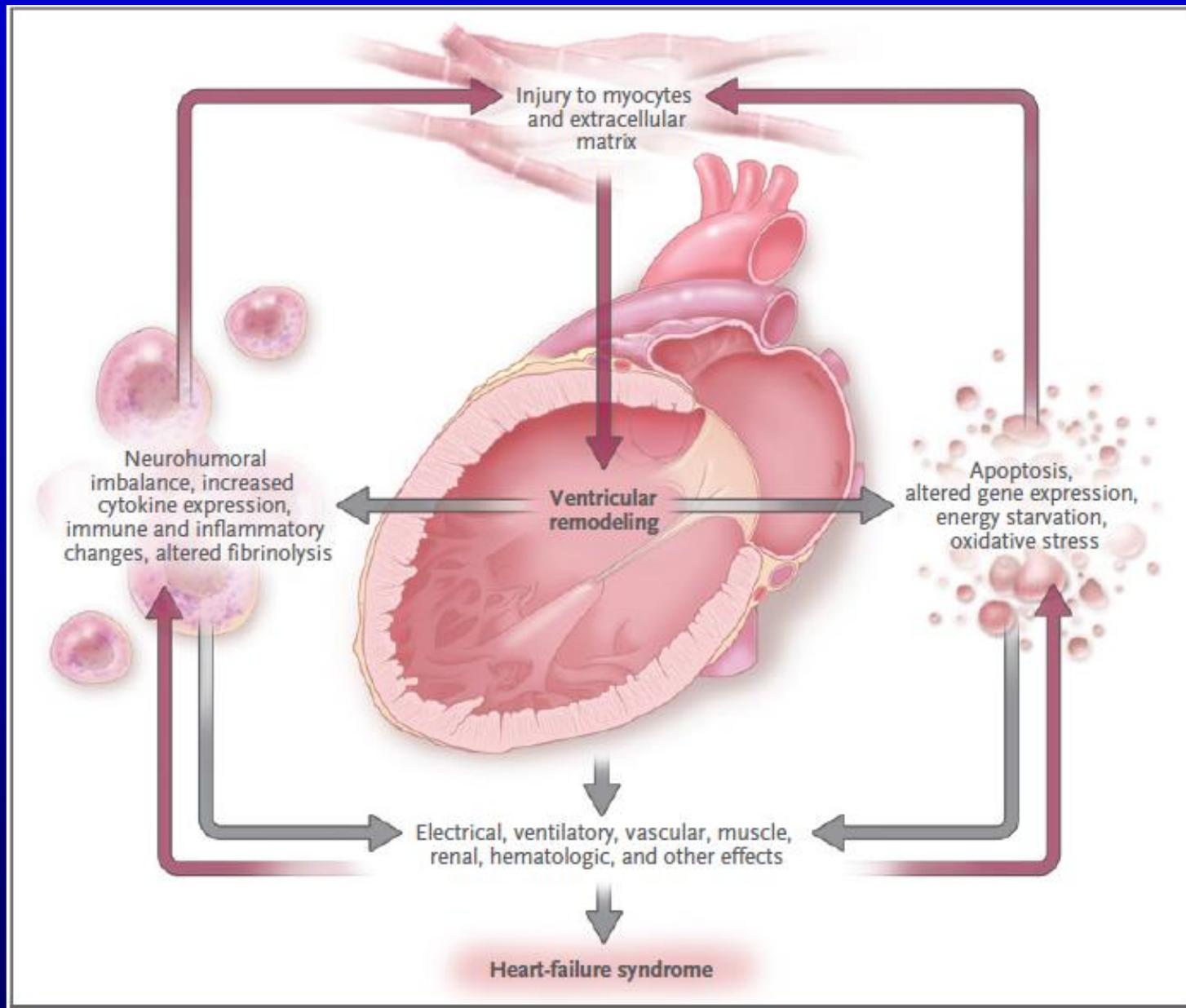
- Review of acute decompensated heart failure
 - Epidemiology
 - Pathophysiology
 - Clinical presentation
- Diagnosis of heart failure in patients presenting with dyspnea
 - ICON Reloaded
 - Considerations in patients with known heart failure
- Determining prognosis with natriuretic peptides

First acute decompensated heart failure annual event rates



■ White Men ■ Black Men ■ White Women ■ Black Women
(per 1000 from ARIC community surveillance [2005–2011])

Pathophysiology of Systolic Heart Failure



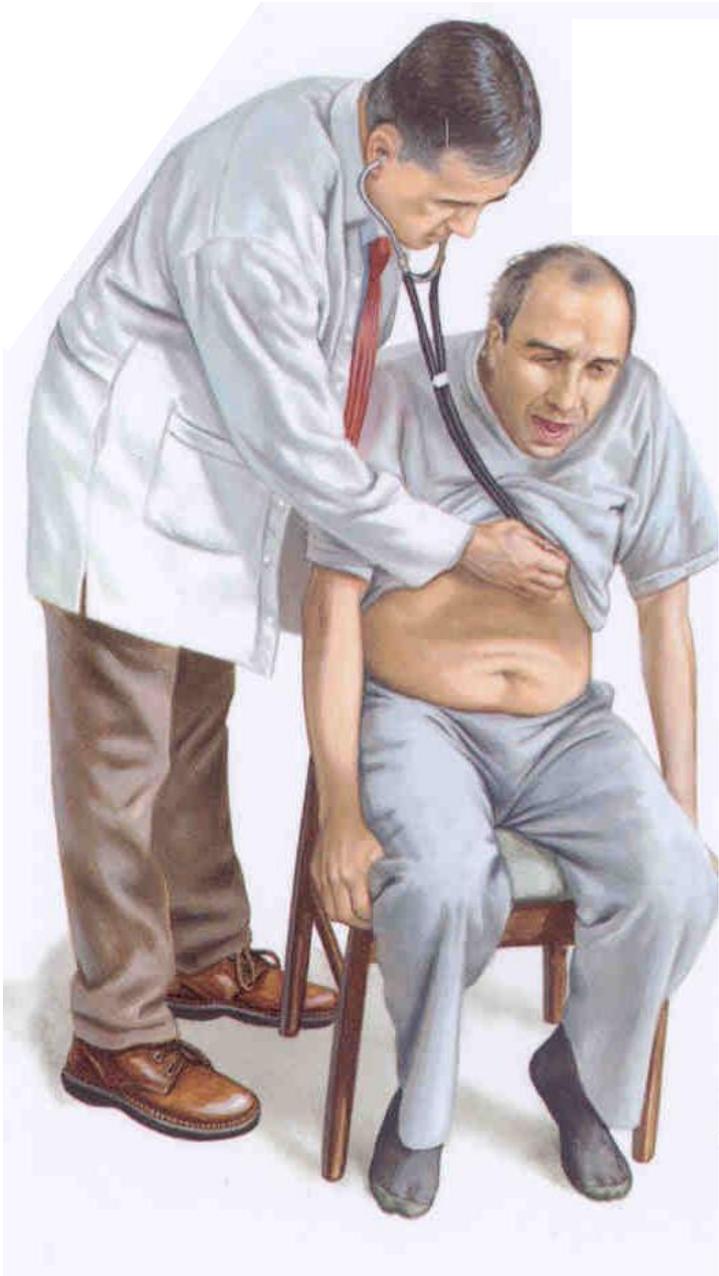
A New Cough



Case Presentation

- 73 year male with 10 days of cough productive of yellow-green phlegm.
- 1-2 days of increased dyspnea with exertion, and now at rest. At baseline he could climb a flight of stairs and walk several blocks
- Positive for orthopnea, and paroxysmal nocturnal dyspnea.
- No fever or chills, chest pain, diaphoresis or nausea.
- Past history:
 - CABG and MI 10 years ago
 - HTN, diabetes and hyperlipidemia

Physical Findings



Case Presentation

- Pulse 92 beats/min and regular
- Blood pressure 121/74 mm Hg
- There is jugular venous distension
- Lateral displacement of the cardiac apical beat on the left side of the chest
- Edema of the lower limbs
- The lung examination is normal

Criteria for Heart Failure

Table 1. Criteria of CHF.*

MAJOR CRITERIA

Paroxysmal nocturnal dyspnea or orthopnea
Neck-vein distention
Rales
Cardiomegaly
Acute pulmonary edema
S₃ gallop
Increased venous pressure \rightarrow 16 cm of water
Circulation time \geq 25 sec
Hepatojugular reflux

MINOR CRITERIA

Ankle edema
Night cough
Dyspnea on exertion
Hepatomegaly
Pleural effusion
Vital capacity \downarrow $\frac{1}{3}$ from maximum
Tachycardia (rate of \geq 120/min)

MAJOR OR MINOR CRITERION

Weight loss \geq 4.5 kg in 5 days in response to treatment

*For establishing a definite diagnosis of congestive heart failure in this study, 2 major or 1 major & 2 minor criteria had to be present concurrently.



Normal Chest X-ray

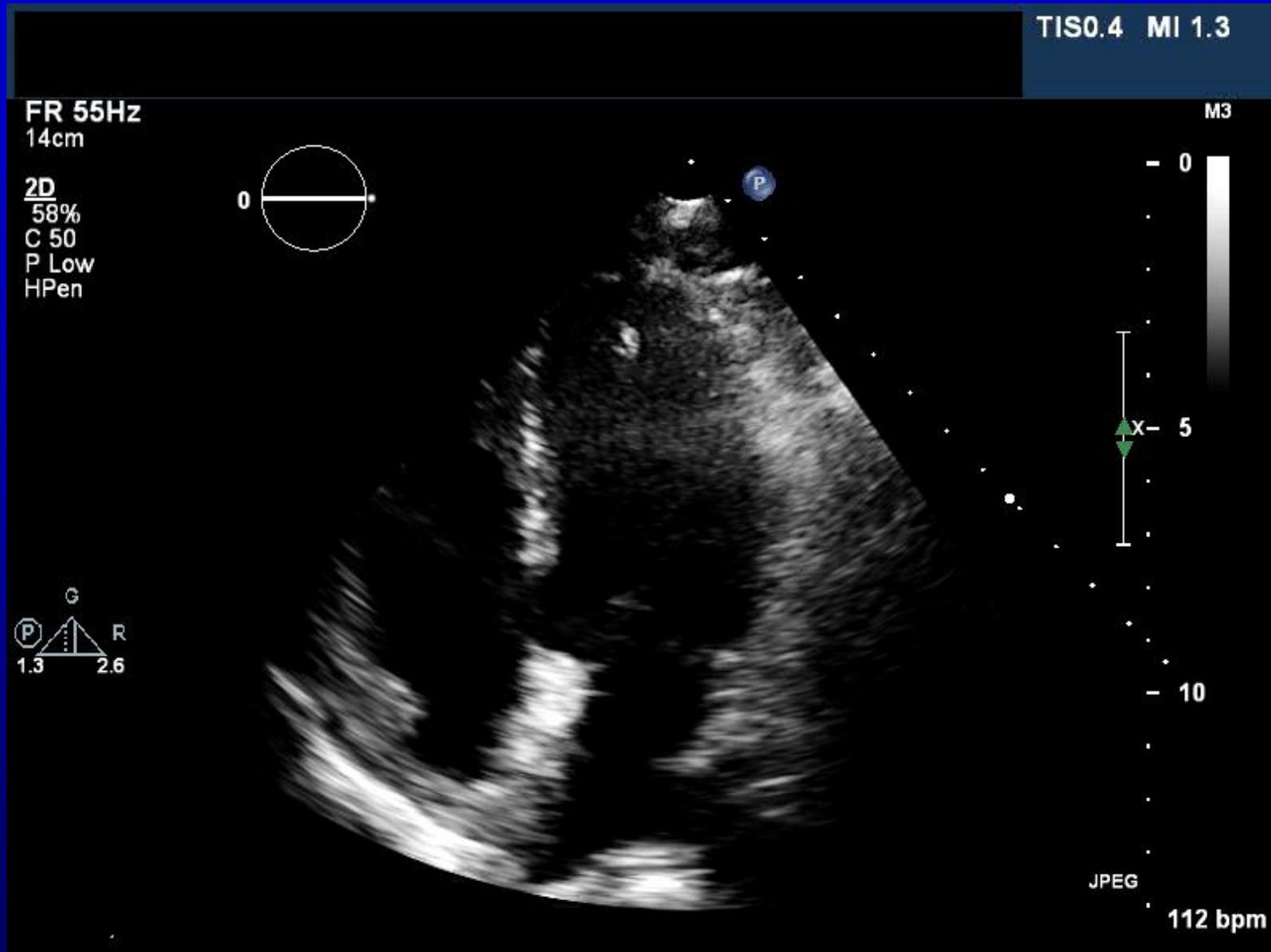


Case Presentation

Chest X-ray



Normal echocardiogram



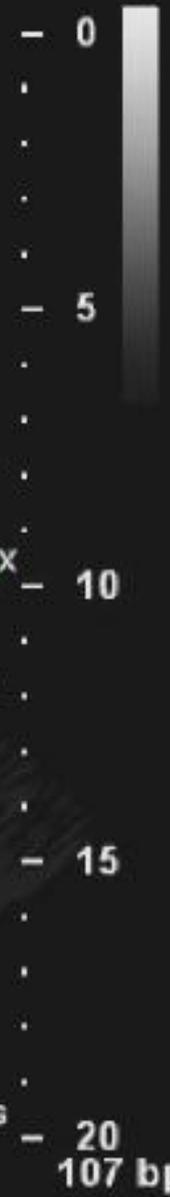
PHILIPS

TISO.8 MI 1.4
ECHO

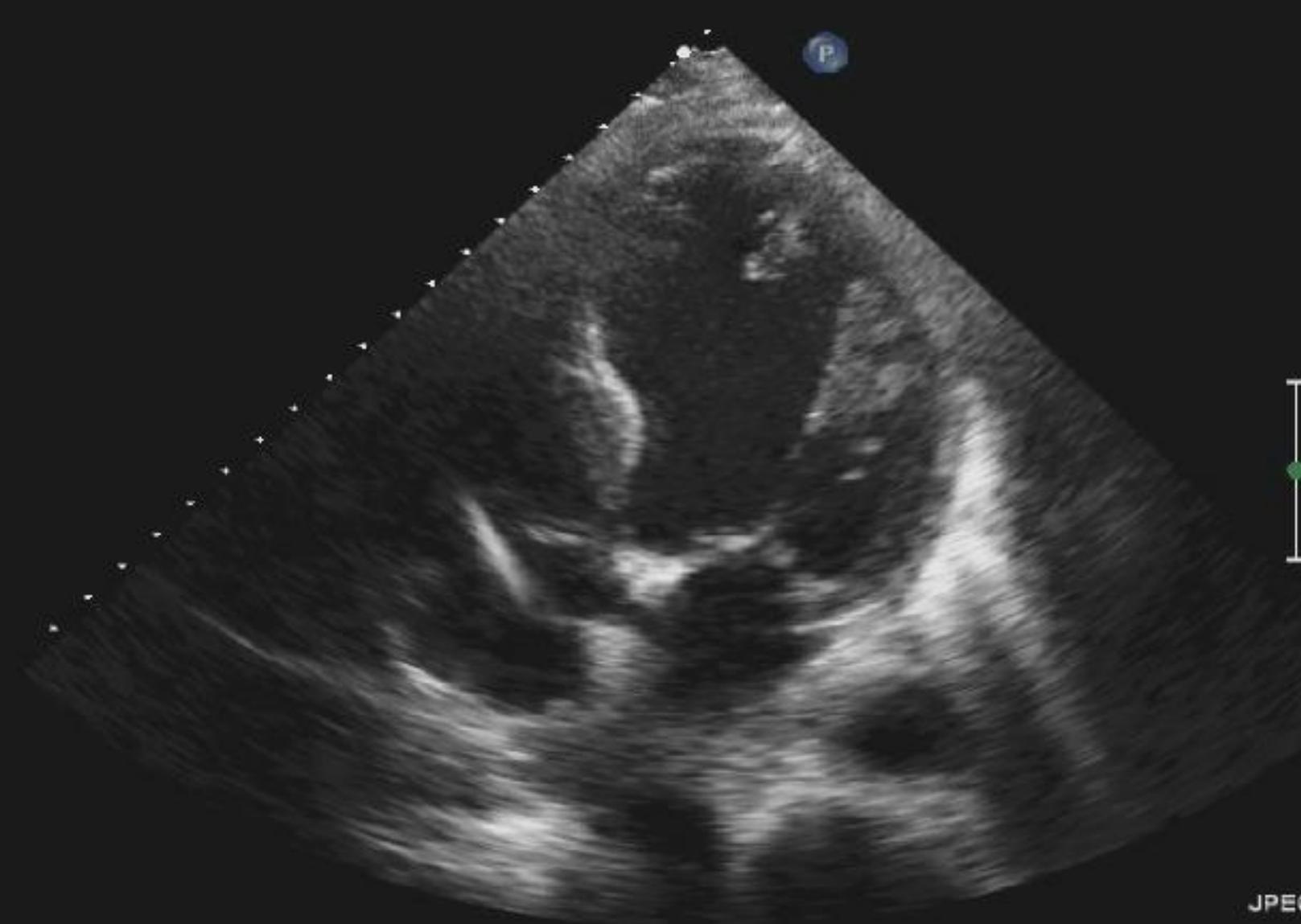
FR 48Hz
20cm

2D
73%
C 50
P Low
HGen

M3



JPEG
107 bpm



The Role for Natriuretic Peptides in Cardiovascular Disease

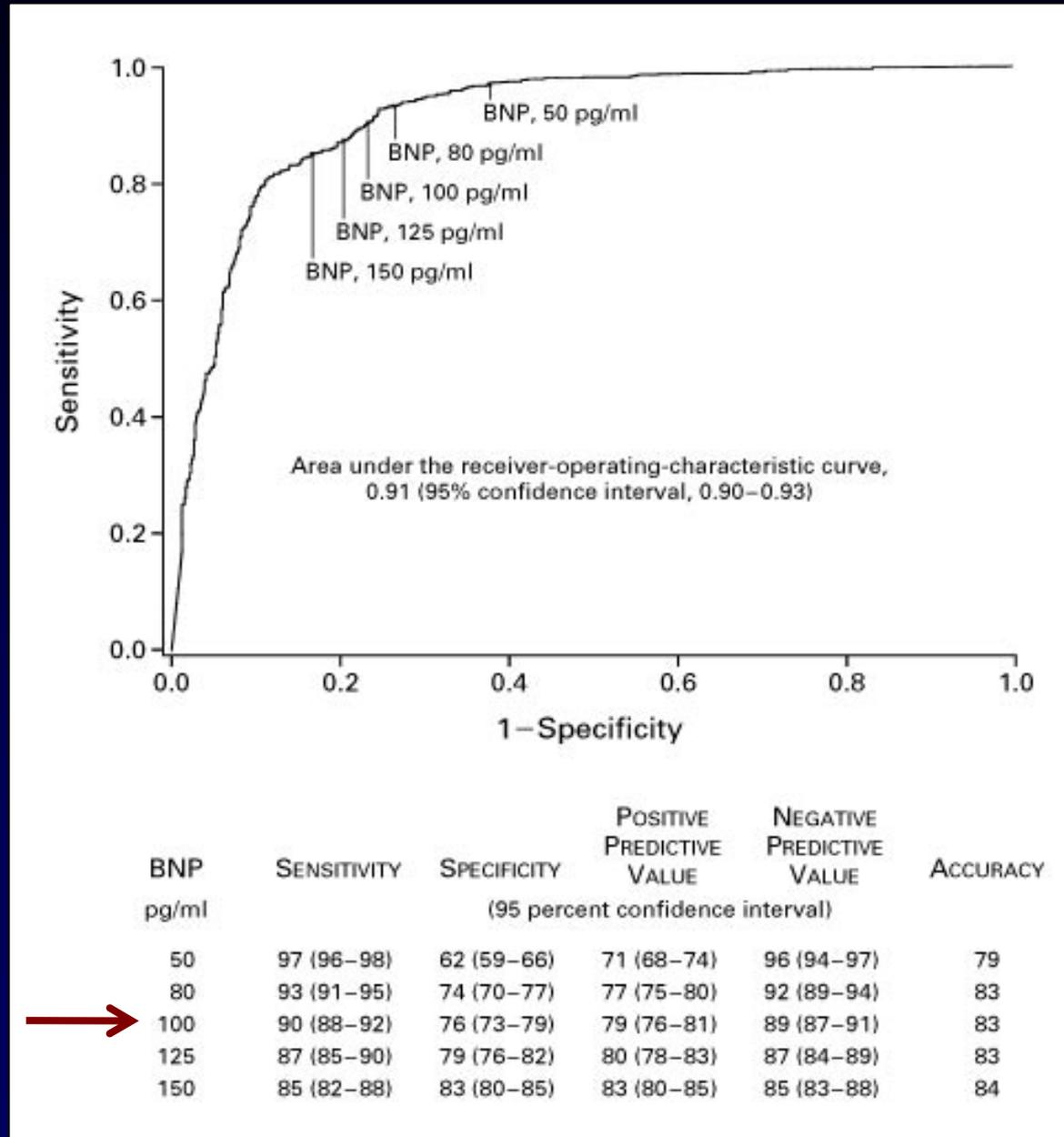
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Poll Question #1

How is NT-proBNP best used to diagnose acute heart failure?

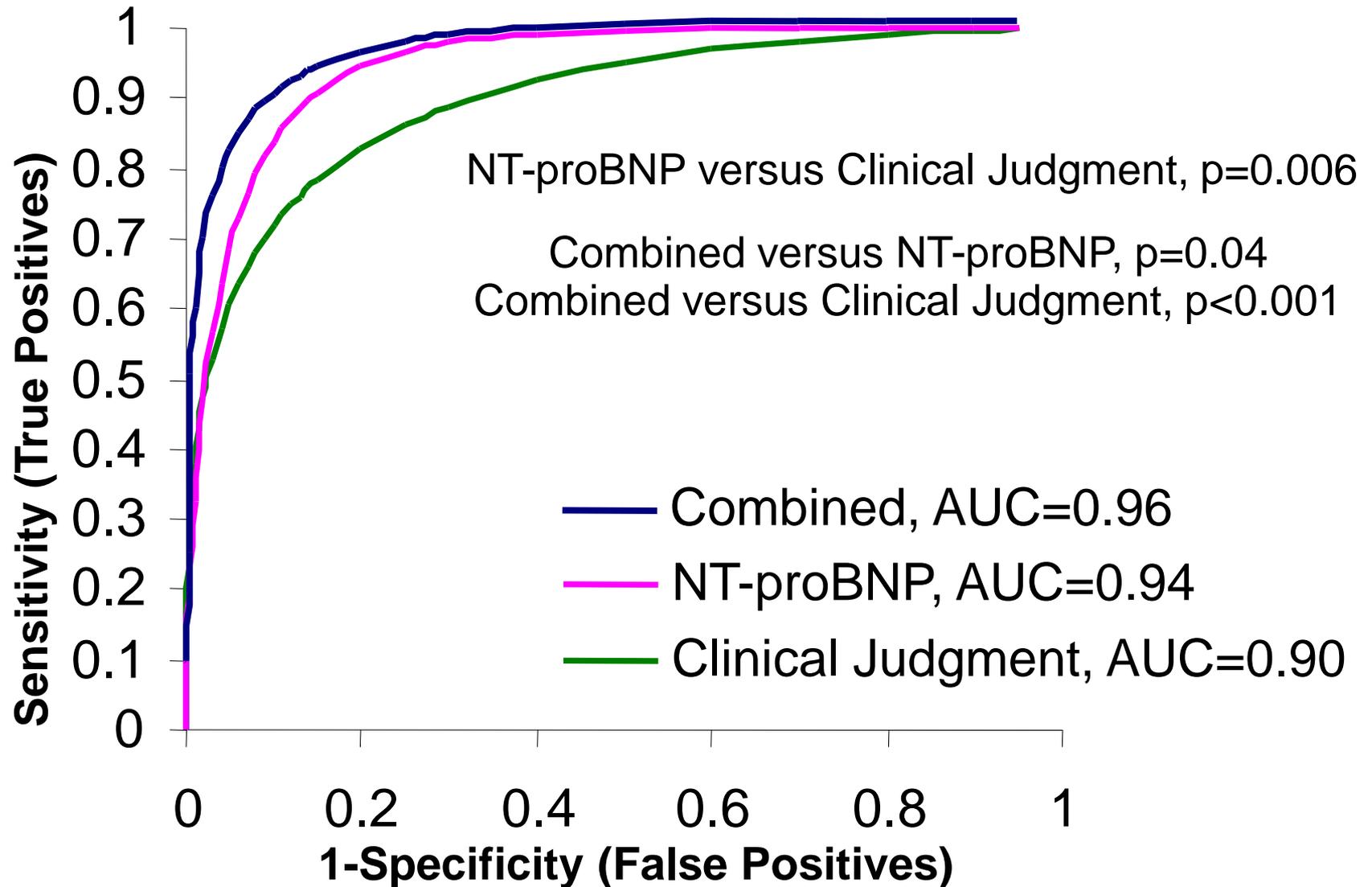
- a) Single cut-off for all patients being presenting with dyspnea (shortness of breath) of uncertain etiology
- b) Age specific cut-offs to “rule-in” heart failure and a single cut-off to “rule-out” Heart failure
- c) Gender specific cut-offs to “rule-in” and “rule-out” heart failure
- d) Renal function specific cut-offs (i.e. above and below an eGFR of 60 mL/min/1.73m²) to “rule-in” and “rule-out” heart failure

Receiver-Operating-Characteristic Curve for Various Cutoff Levels of BNP in Differentiating between Dyspnea Due to Heart Failure or Due to Other Causes

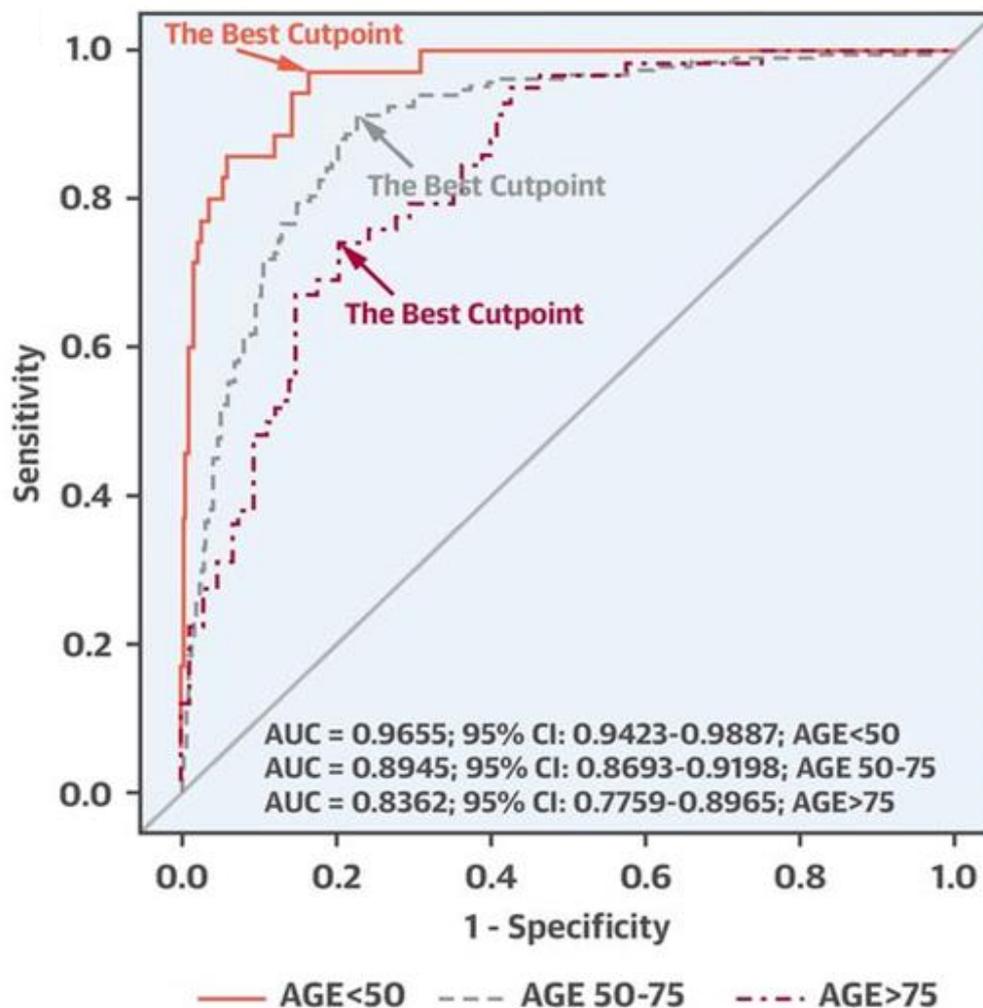




Results: Primary Endpoint



NT-proBNP for diagnosis of acute heart failure in patients with shortness of breath (ICON-RELOADED)

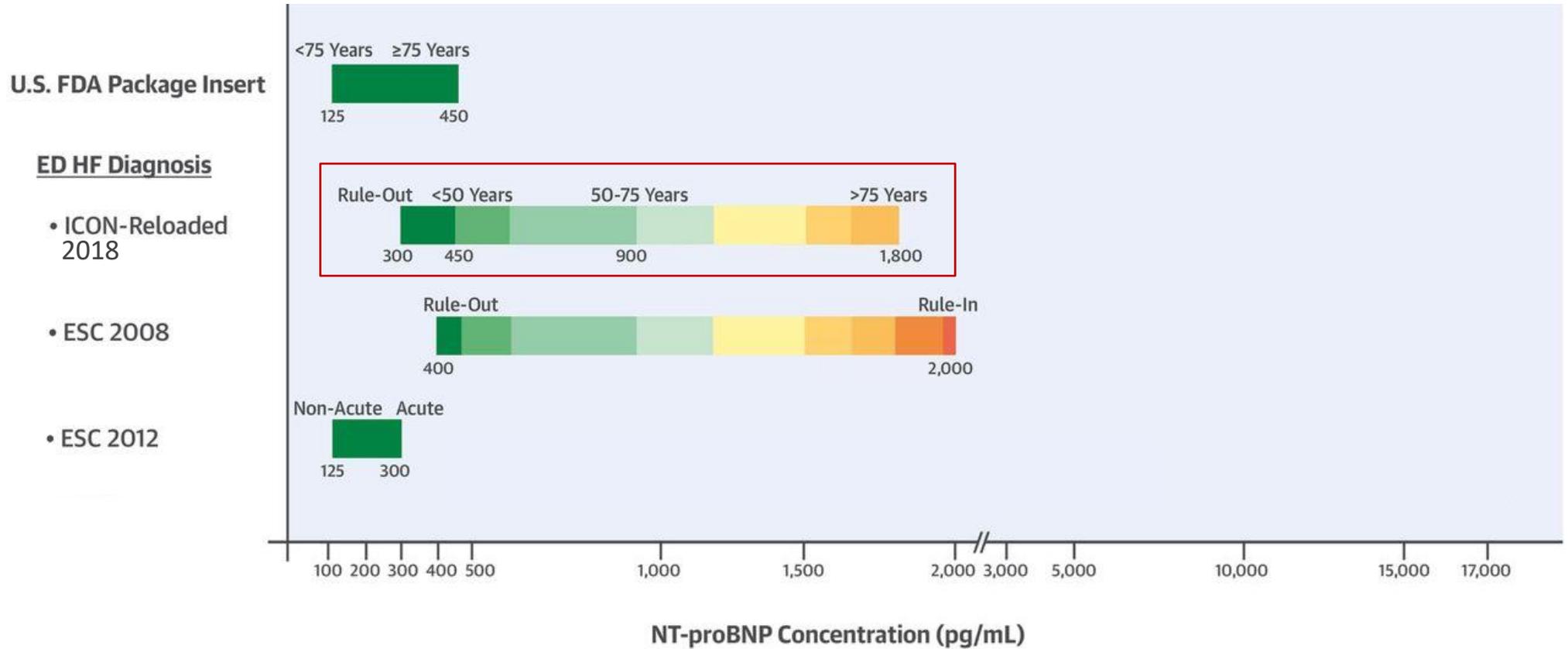


	AUC	p Value for Difference in AUC
1.73 m ²	0.872	0.12
1.73 m ²	0.907	

	Age <50	Age 50-75	Age ≥75
Sensitivity	97.1% (95% CI 91.6%-100.0%)	91.3% (95% CI 87.2%-95.4%)	74.1% (95% CI 62.9%-85.4%)
Specificity	83.6% (95% CI 80.1%-87.1%)	77.0% (95% CI 73.8%-80.3%)	79.6% (95% CI 72.0%-87.2%)
PPV	32.7% (95% CI 28.0%-37.7%)	53.0% (95% CI 49.3%-56.7%)	66.2% (95% CI 56.6%-74.5%)
NPV	99.7% (95% CI 98.1%-100.0%)	96.9% (95% CI 95.1%-98.0%)	85.1% (95% CI 78.6%-90.0%)
Accuracy	84.6% (95% CI 81.3%-87.9%)	80.2% (95% CI 77.5%-82.9%)	77.7% (95% CI 71.4%-84.0%)

Diagnostic threshold for acute heart failure with NT-proBNP

Diagnostic Recommendations Heterogeneity



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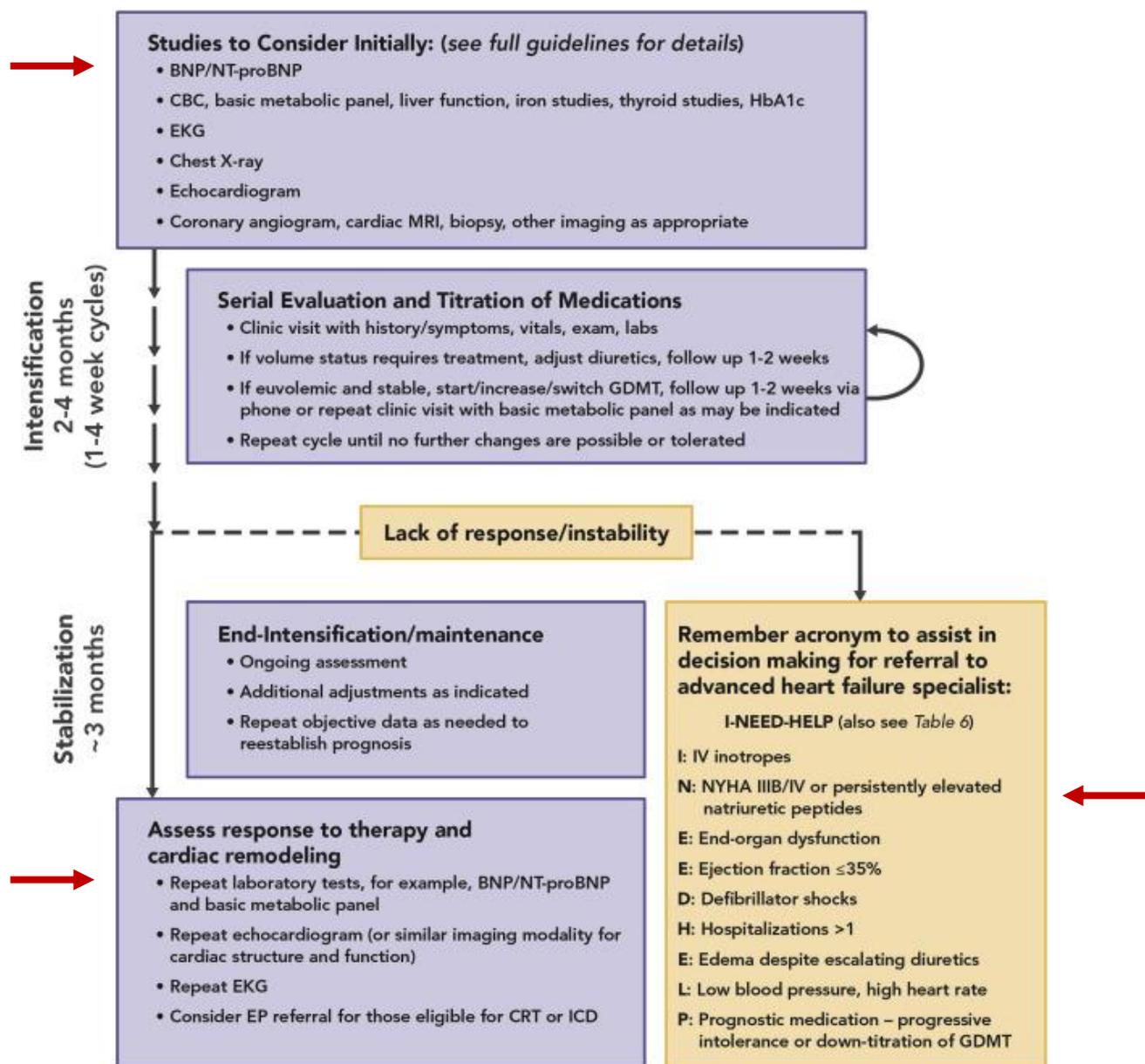
Poll Question #2

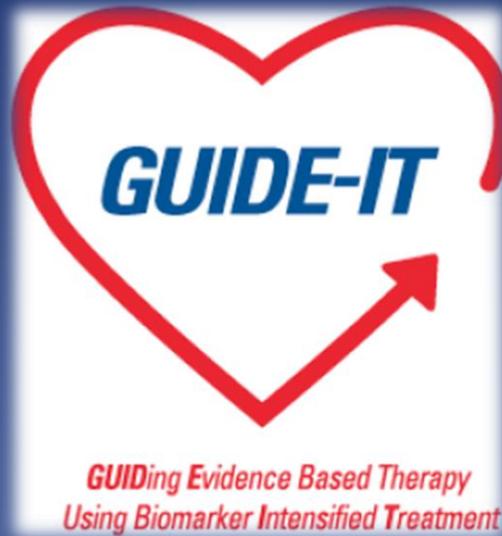
For outpatients with heart failure are their special considerations for BNP and NT-proBNP interpretation?

- a) Expect levels of both BNP and NT-proBNP to be always elevated and therefore can't be used to diagnose to determine if heart failure exacerbation is a cause of worsening shortness of breath
- b) BNP and NT-proBNP levels can change in the opposite direction depending on the type of medical therapy limiting the use of BNP for the diagnosis of a heart failure exacerbation
- c) Knowing a baseline level of BNP or NT-proBNP in a stable outpatient with heart failure is recommended
- d) Following serial NT-proBNP levels could be an effective way of determining if patients are on optimal medical treatment to prevent hospitalizations and death

ACC Expert Consensus Decision Pathway for HF Treatment

The role of BNP/NT-proBNP testing in outpatients



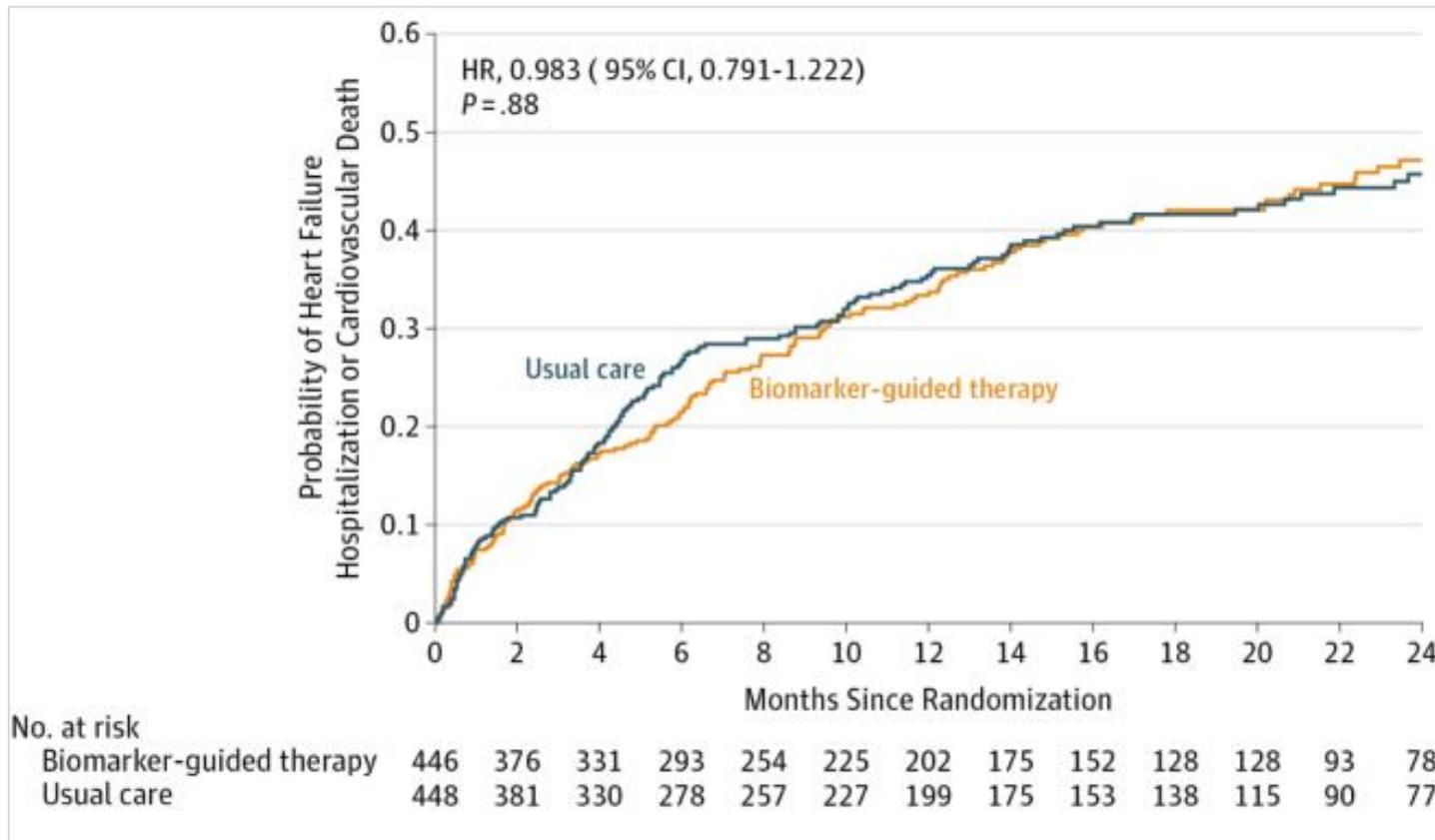


Primary Hypothesis of NIH GUIDE-IT trial

- In high risk heart failure patients with LV systolic dysfunction, a strategy of titrating medical therapy based on minimizing natriuretic peptide levels will be superior to usual care with regard to the composite endpoint of heart failure hospitalizations or CV mortality

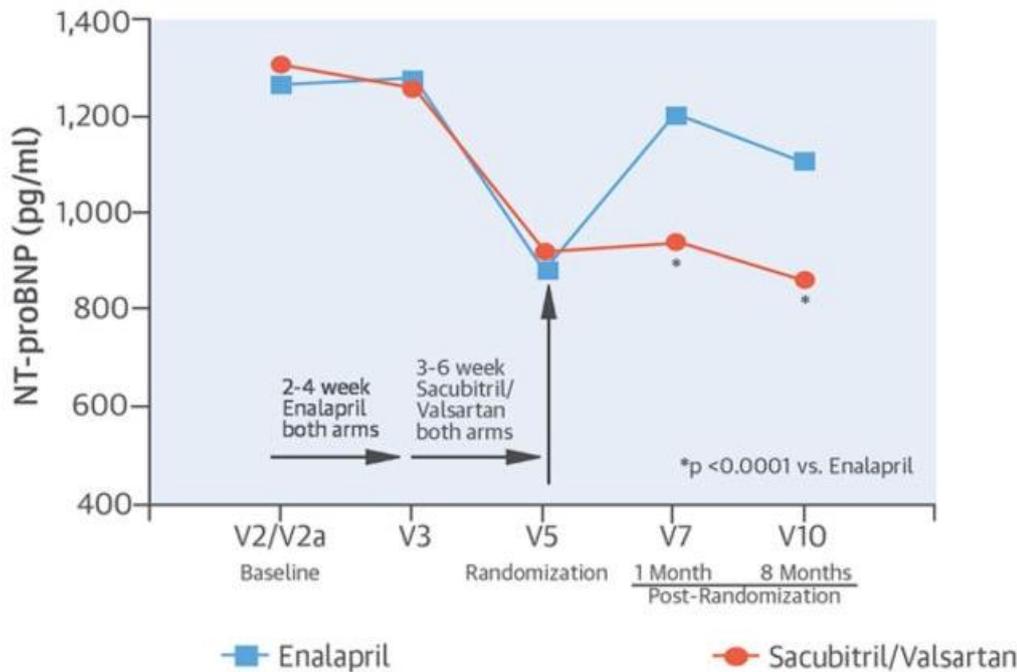
GUIDE-IT Primary Endpoint

First HF Hospitalization or Cardiovascular Death

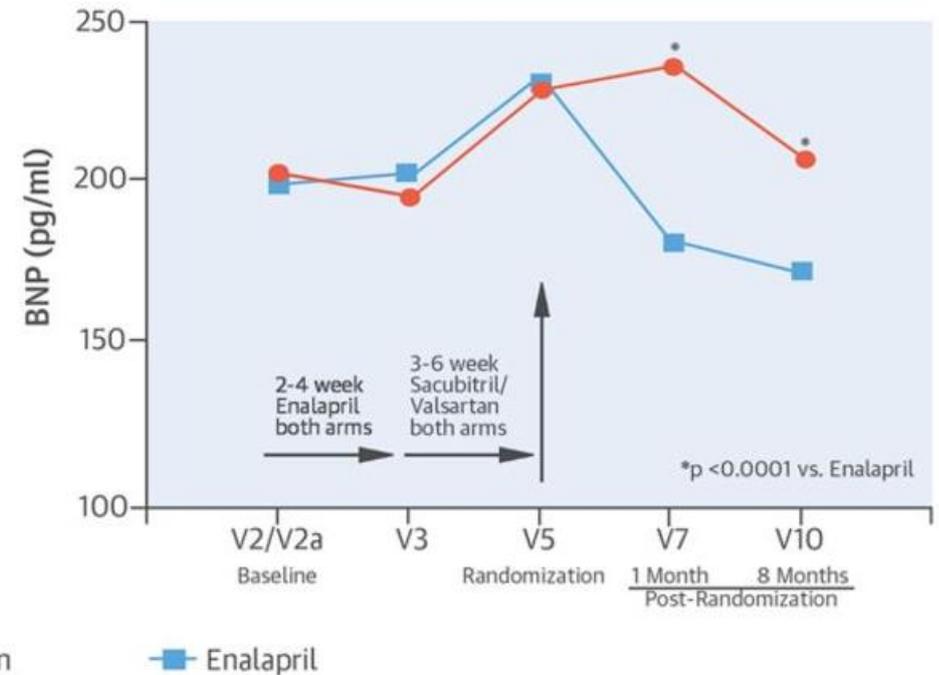


Changes in NT-proBNP and BNP Patients With HF treated with Sacubitril/Valsartan (Entresto) PARIDIGM-HF

B. Change in NT-proBNP: Effects of Treatment



C. Change in BNP: Effects of Treatment

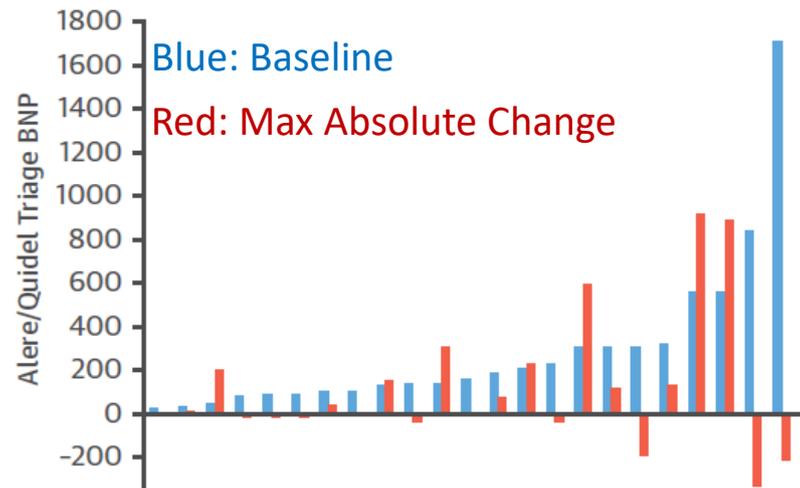


Never Simple!

Changes in BNP level after starting Entresto can depend on the patient and the assay

TABLE 4 Percent Change in Various Biomarker Concentrations as a Function Of Maximum Achieved Dose of Sacubitril/Valsartan

Final Visit Biomarker (% Change) vs. Maximum Dose	None (n = 2)	Sacubitril/Valsartan 24/26 mg (n = 5)	Sacubitril/Valsartan 49/51 mg (n = 9)	Sacubitril/Valsartan 97/103 mg (n = 7)	p Value
Abbott Architect BNP	-1 (-32 to +166)	-36 (-71 to +28)	+39 (-20 to +104)	-22 (-37 to +134)	0.38
Alere/Quidel Triage BNP	+36 (-28 to +110)	-14 (-28 to +12)	+39 (-0 to +158)	-11 (-18 to +165)	0.16
Siemens Centaur BNP	+15 (-16 to +224)	-11 (-20 to +29)	+41 (+9 to +118)	+9 (-23 to +161)	0.64
Roche NT-proBNP	-13 (-52 to +31)	-25 (-35 to 0)	+5 (-19 to +22)	-21 (-54 to +12)	0.69



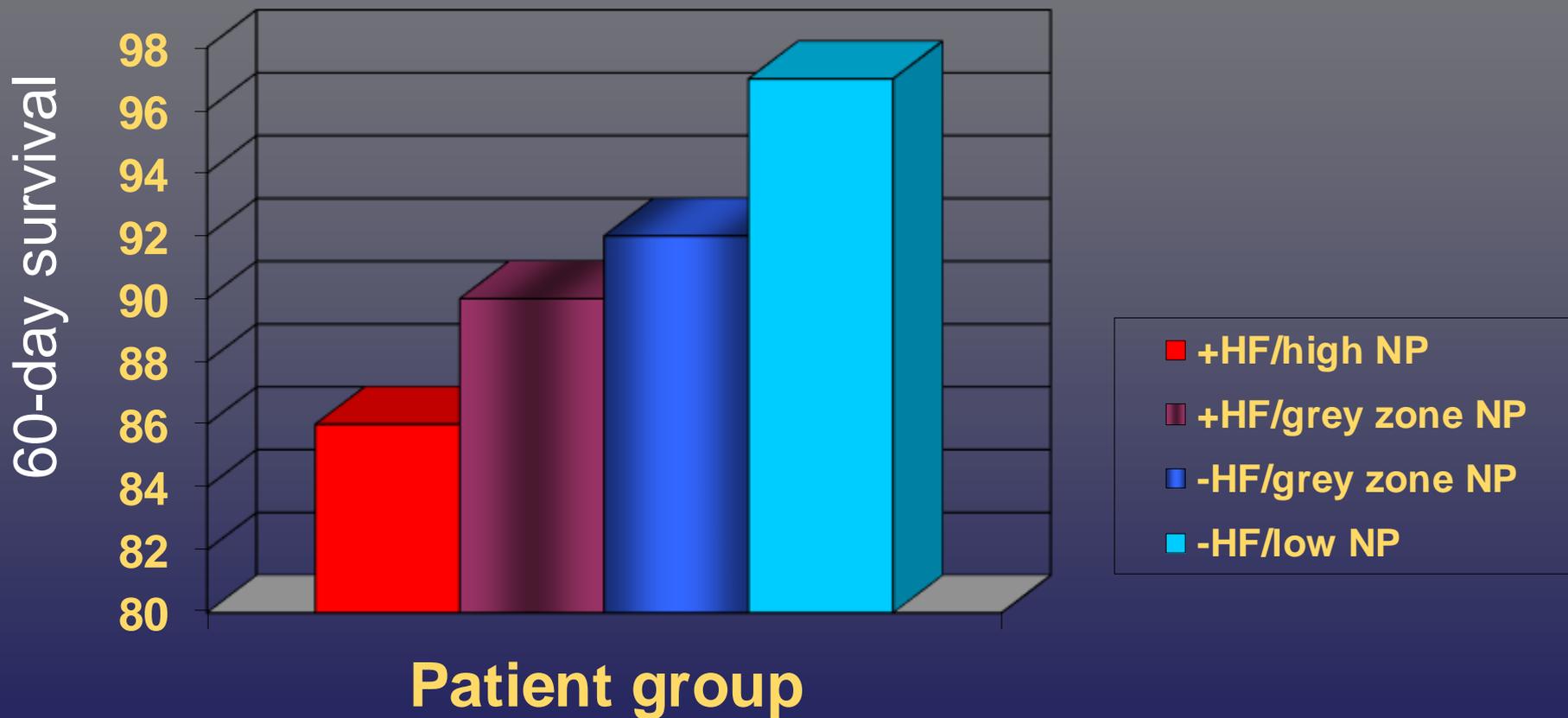
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Prognosis for the dyspnea patient

Diagnosis, NT-proBNP and the

“grey zone”

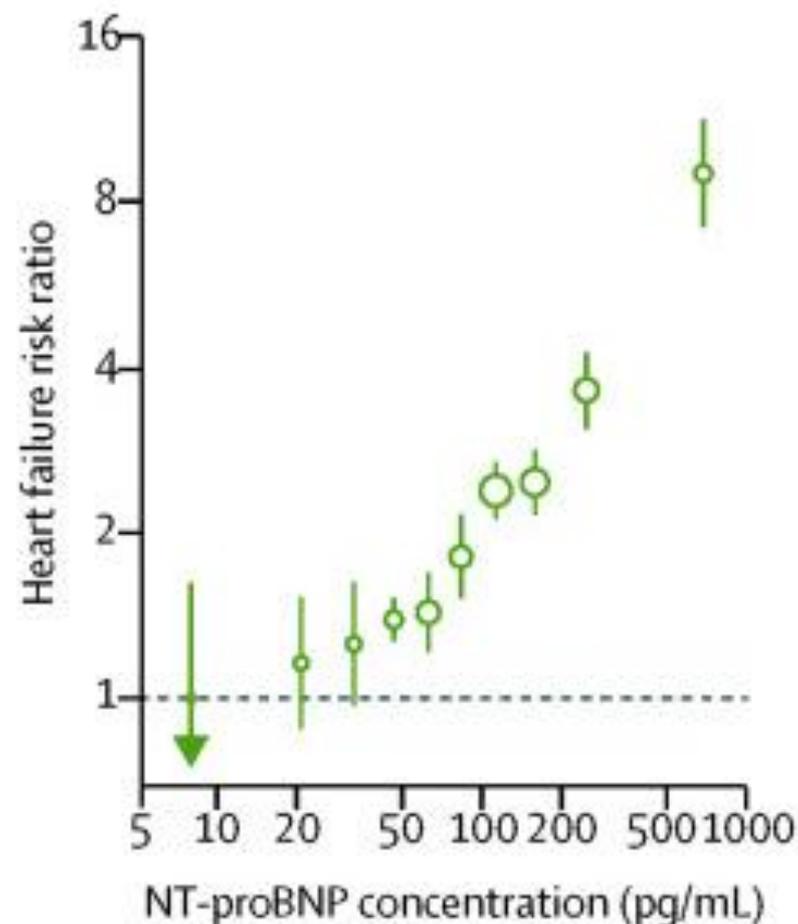


“Grey Zone” NT-proBNP is between 300 pg/ml and age adjusted rule-in cut-off

Natriuretic peptides and integrated risk assessment for HF

An individual-participant-data meta-analysis of 16 general population cohorts without HF to predict future incident HF

- Risk ratio = top third/bottom third
- Median follow-up 7.8 years
- 2212 incident heart failure outcomes



Role of Natriuretic Peptides in CVD

Conclusions

- NT-proBNP now has clearly defined values based on age for the diagnosis of HF in patients presenting with shortness-of-breath with possible HF
- NT-proBNP can assist with prognosis and can be repeated in the ambulatory setting to gauge the need for referral to a HF specialist