



Natriuretikus peptidek a sürgősségi Diagnosztikában

Siófok, 2017 november 9

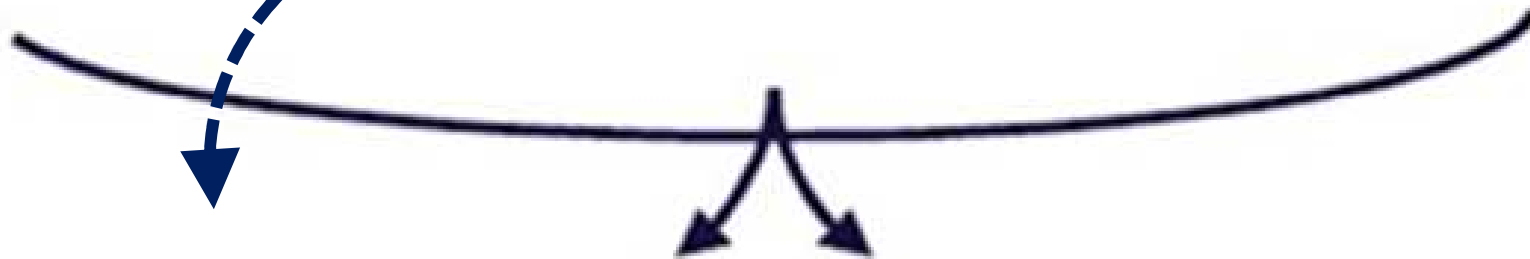
Dr. Rudas László

**↑ Ventricular Wall
Stress (Myocyte Stretch)**

Pre-Pro-BNP₁₋₁₃₄



Pro-BNP₁₋₁₀₈



**N-terminal
Pro-BNP₁₋₇₆**

BNP₇₇₋₁₀₈

BNP Versus NTproBNP

	BNP	NTproBNP
Amino acids	32	76
Molecular weight (kd)	3.5	8.5
Half-life (min)	22	60–120
Clearance		
Primary mechanism	Neutral endopeptidase	Renal
Clearance receptor	NPR-C	Renal
Hemodialysis	No	No
Correlation with GFR	<p>Passzív vese kiválasztás megegyező az NT-proBNP és a BNP esetében, megközelítően 15%–20%</p>	
Biologically active	Yes	No

Stabilabb paraméter!

Daniels LB J Am Coll Cardiol 2007; 50:2357-2368.

Szívelégtelenségen kívüli NP emelkedéssel járó állapotok:

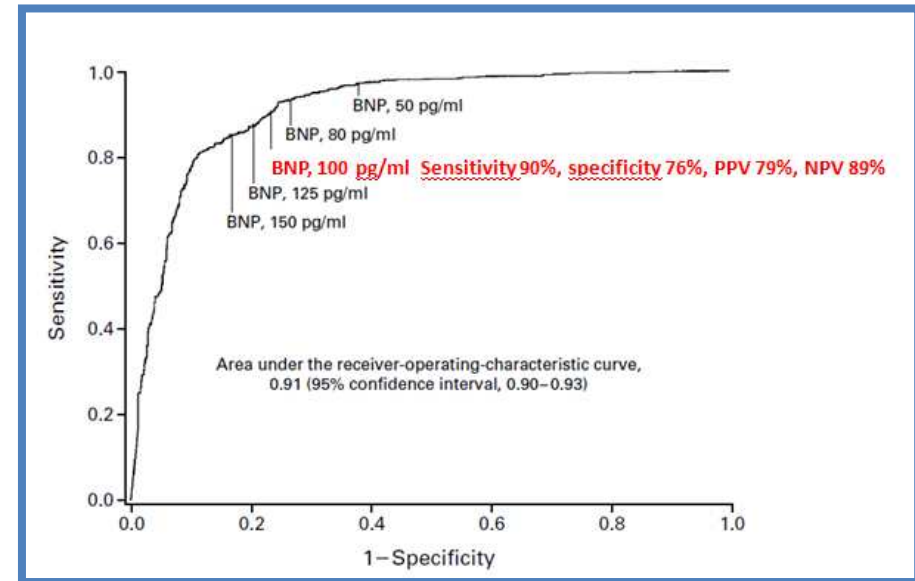
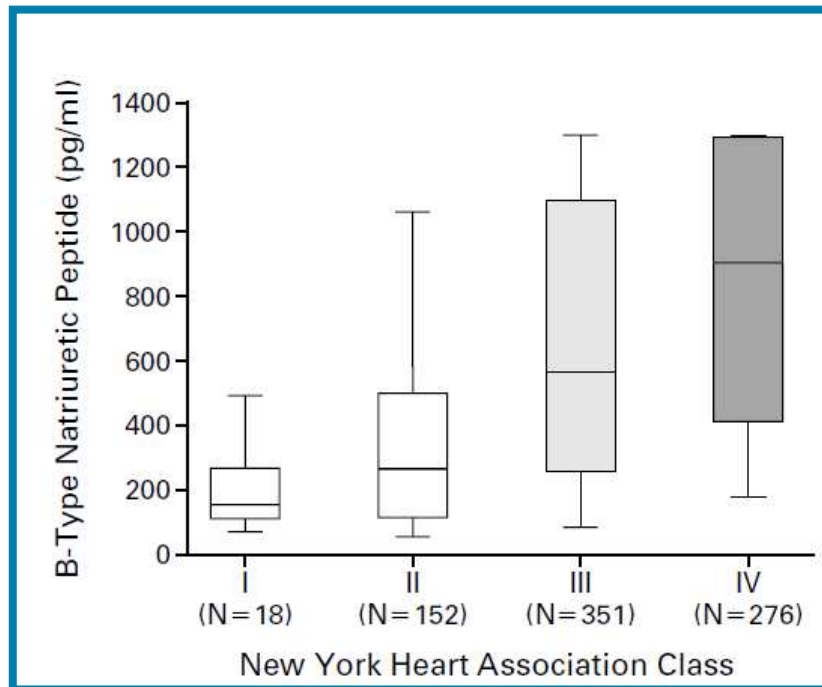
- bal kamra hipertrófia
- tachikardia
- jobb szívfél túlterhelés
- szívizom isémia
- hypoxemia
- veseelégtelenség
- májzsugorodás
- idős életkor
- infekció, szepszis, égési sérülés, toxikus ártalom
- OSA

Relatív alacsony BNP szintekkel járó állapotok:

- „flash tüdőödéma”
- obezitás
- perikardiális tamponád, konstrikcio

Az első nagy NP
diagnosztikus vizsgálatok
sürgősségi osztályokon

Rapid BNP mérés a sürgősségi szívelégtelenség diagnosztikában

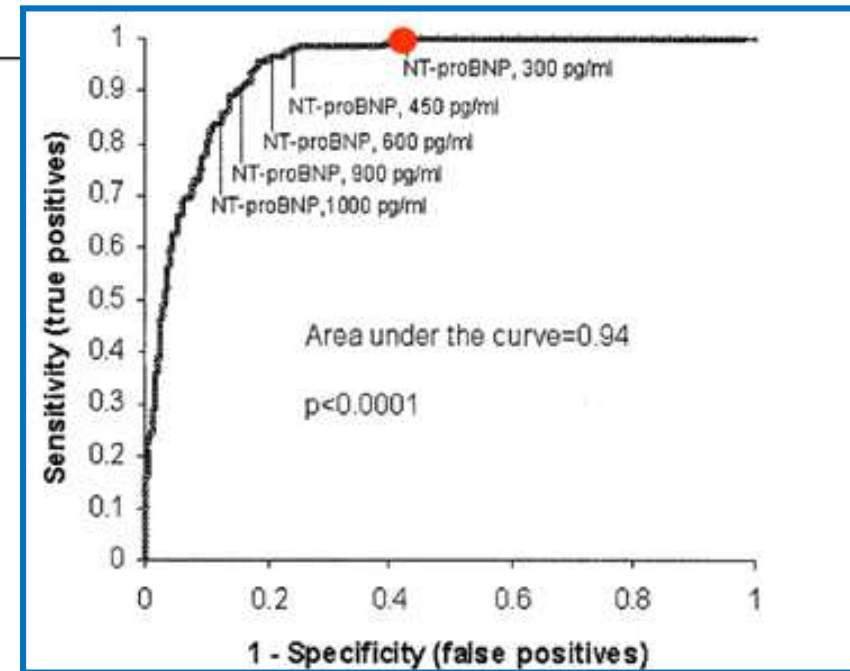
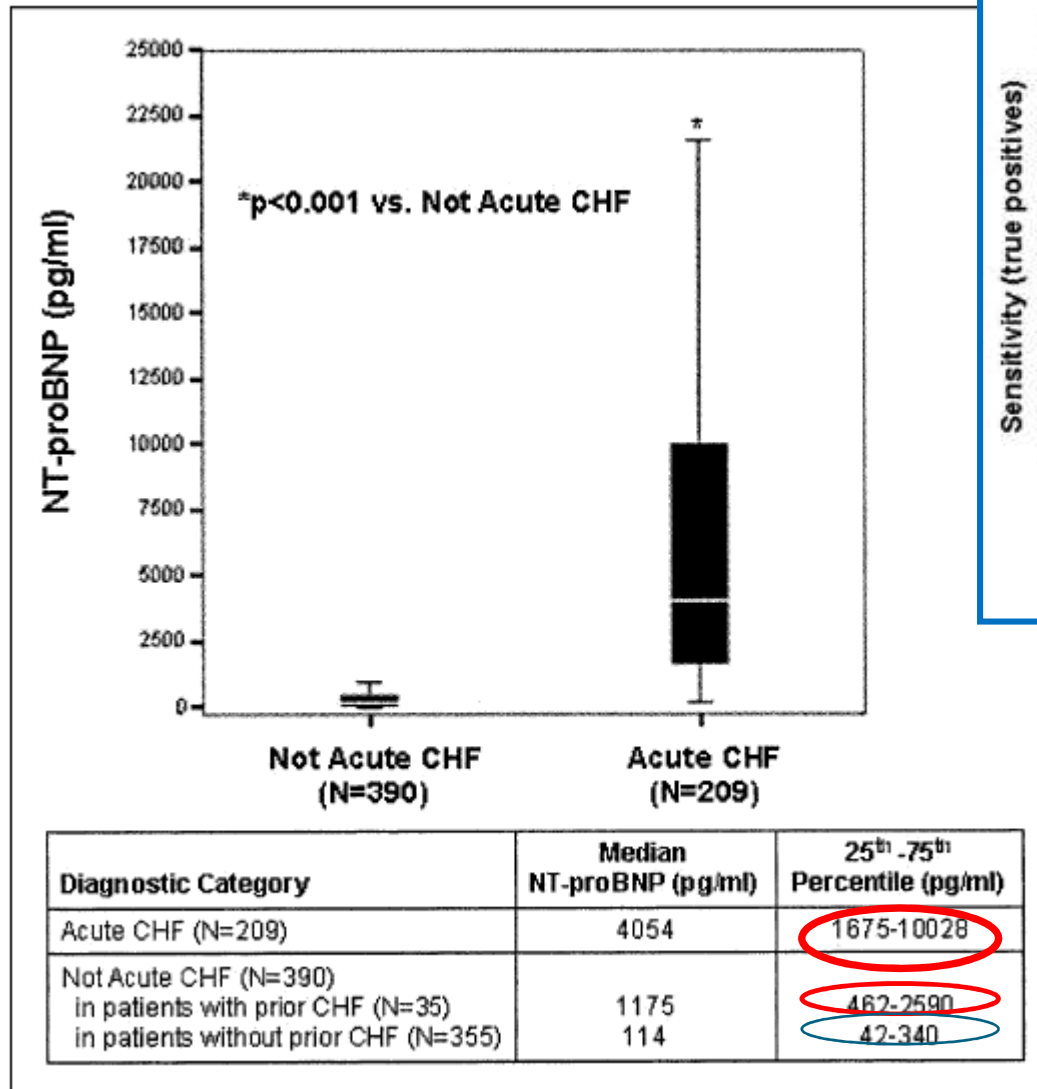


MULTIPLE LOGISTIC-REGRESSION ANALYSIS OF FACTORS USED FOR DIFFERENTIATING BETWEEN PATIENTS WITH AND THOSE WITHOUT CONGESTIVE HEART FAILURE.

PREDICTOR	P VALUE	ODDS RATIO (95% CI)*
Age	0.04	1.02 (1.00-1.03)
History of congestive heart failure	<0.001	11.08 (6.55-18.77)
History of myocardial infarction	<0.001	2.72 (1.63-4.54)
Rales	<0.001	2.24 (1.41-3.58)
Cephalization of vessels	<0.001	10.69 (5.32-21.47)
Edema	<0.001	2.88 (1.81-4.57)
Jugular venous distention	0.04	1.87 (1.04-3.36)
<u>B-type natriuretic peptide ≥ 100 pg/ml</u>	<0.001	<u>29.60 (17.75-49.37)</u>

Maisel AS . N Engl J Med 2002;347:161-167.

N Terminális Po-BNP mérés a sürgősségi osztályon (PRIDE study)



További megállapítás:
- erős életkorfüggés

BNP-t vagy NT pro-BNP-t
használjunk?

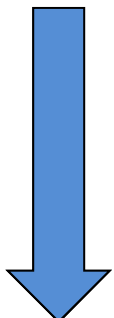
Egy új gyógyszer közbeszól

**Endogenous
vasoactive peptides**

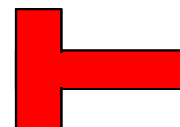
(natriuretic peptides, adrenomedullin,
bradykinin, substance P,
calcitonin gene-related peptide)



- Neurohormonal activation
- Vascular tone
- Cardiac fibrosis,
hypertrophy
- Sodium retention



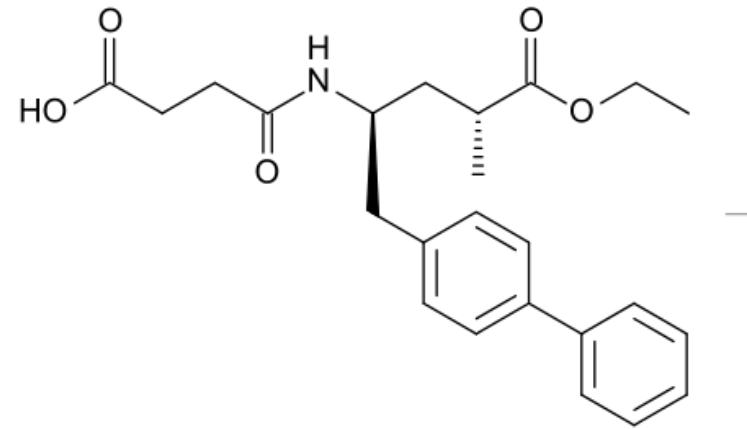
Neprilysin



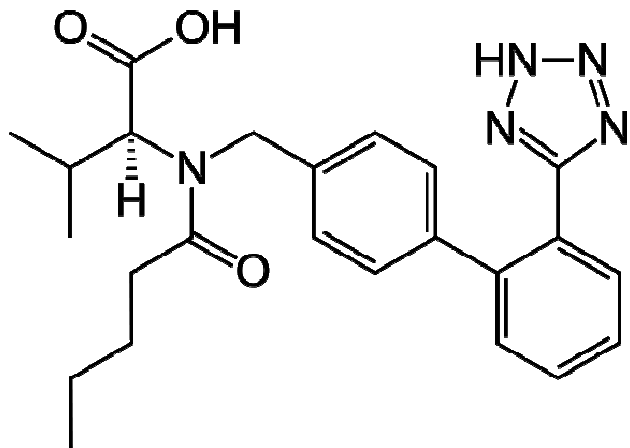
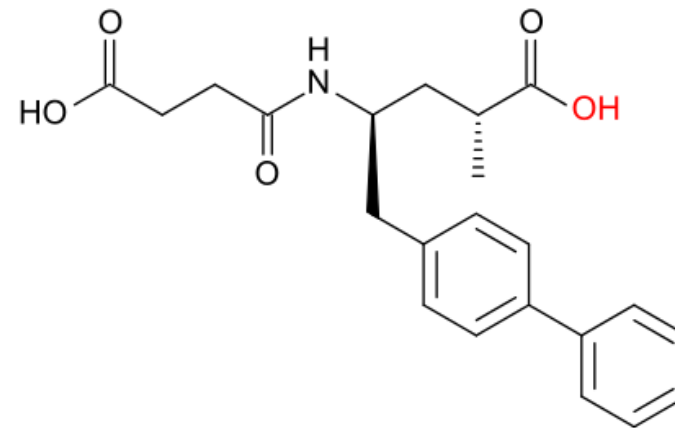
**Neprilysin
inhibition**

Inactive metabolites

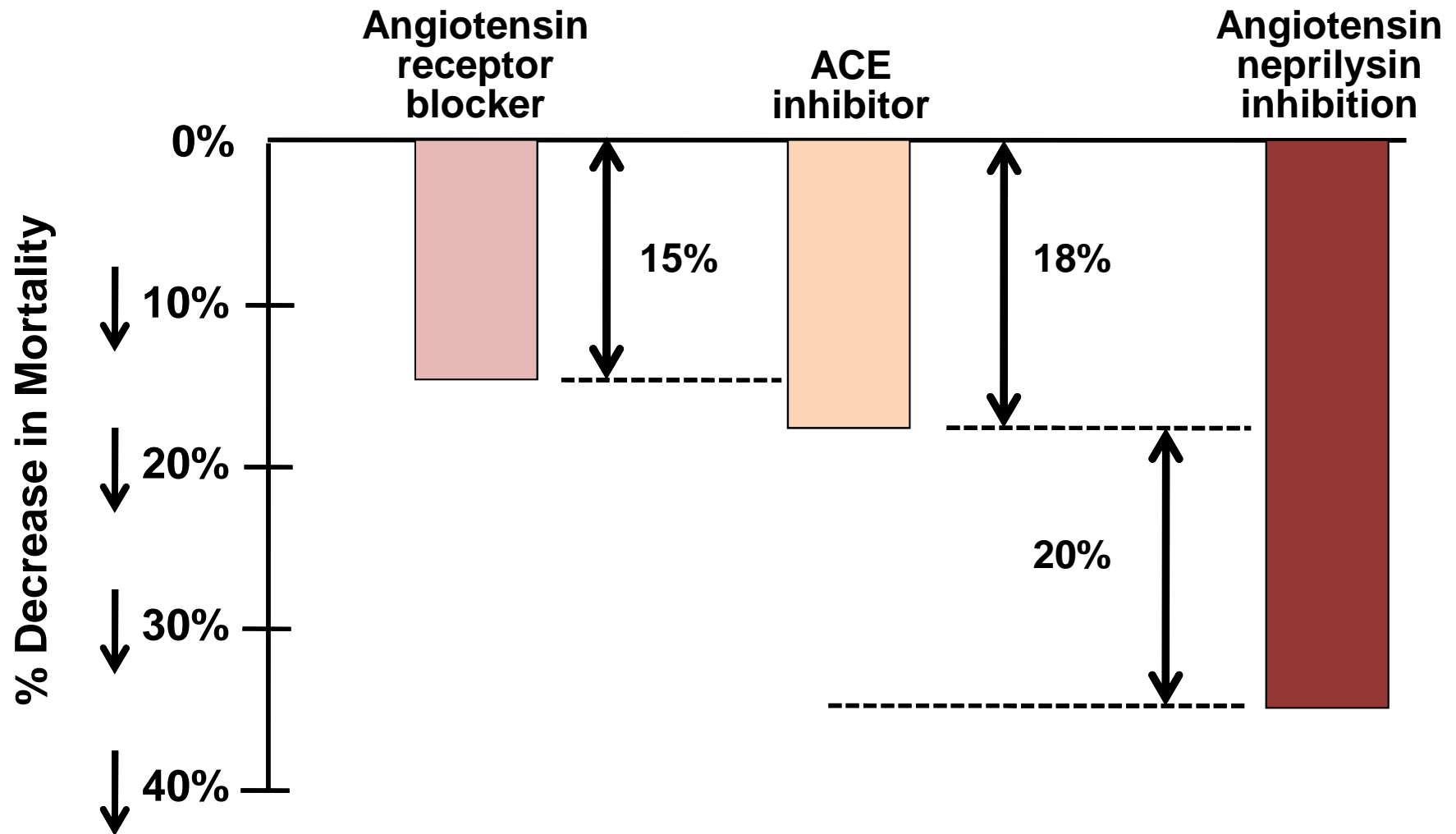
Sacubitril is a „pro-drog”



ARNI

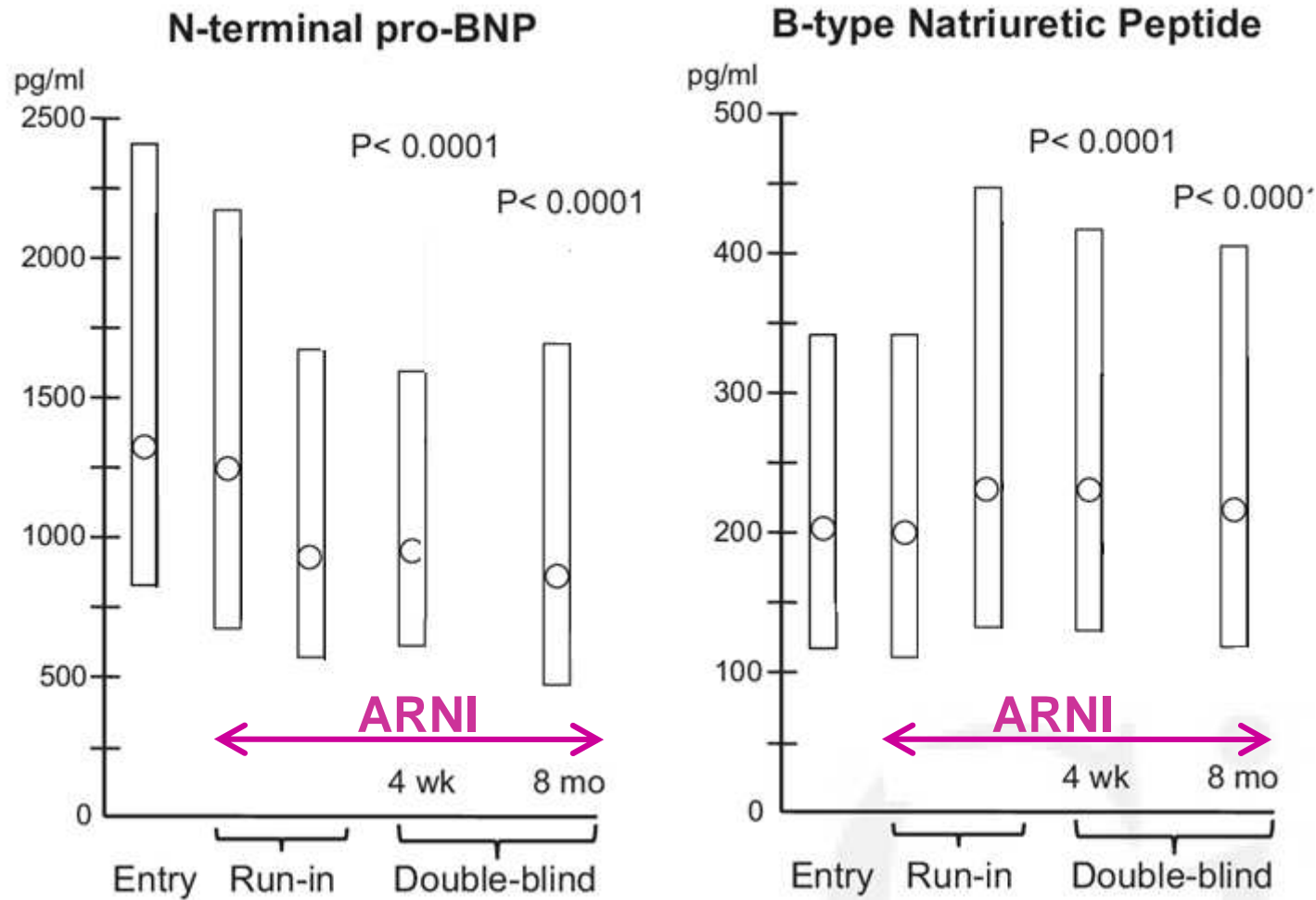


Valsartan.



A PARADIGM-HF vizsgálat alapján

A PARADIGM-HF vizsgálat tanulságai



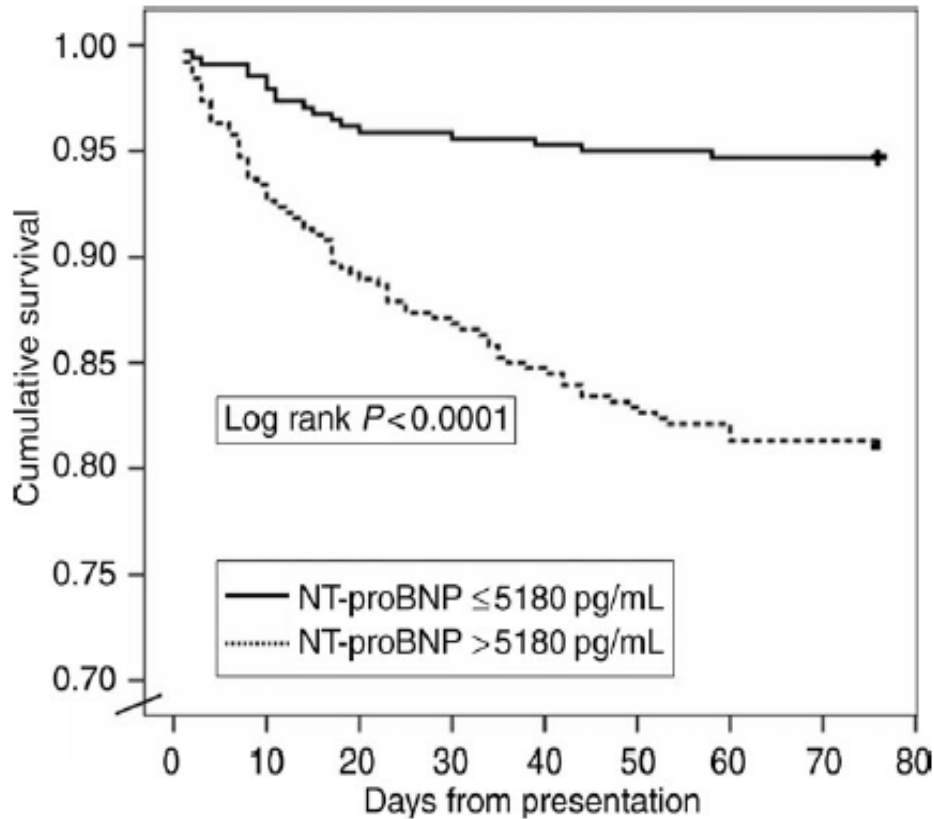
Packer M et al., 2015; Circulation, DOI: 10.1161/CIRCULATIONAHA.114.013748

Határértékek:

-SBO gyorsdiagnosztika?

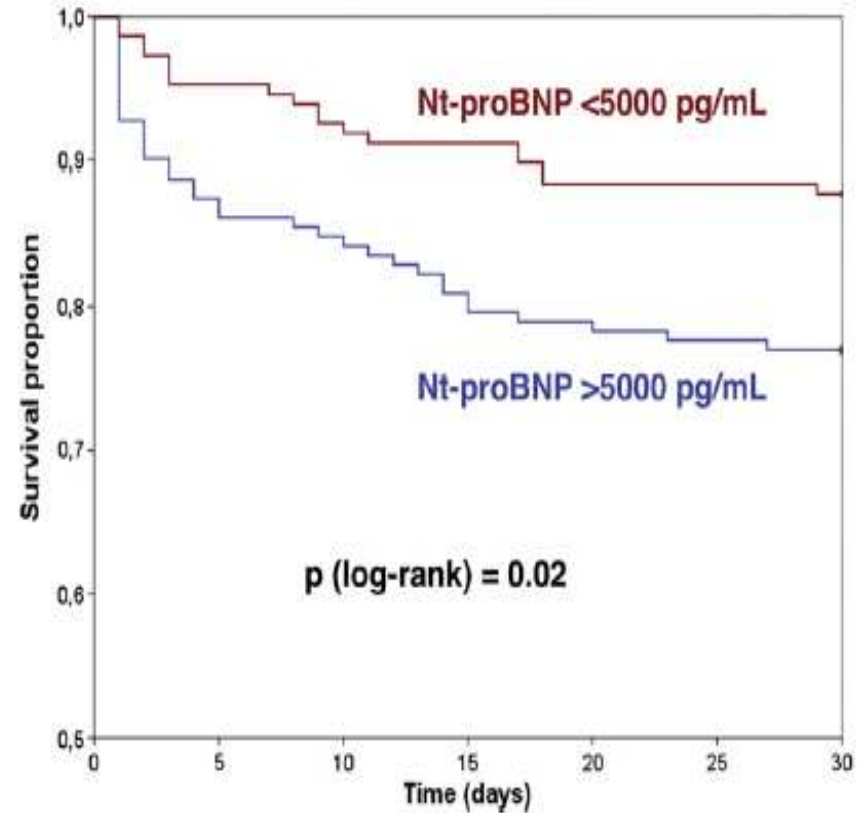
-Rövid távú prognózis?

Rövid távú prognózis
(international pooled analysis
of 1256 patients)



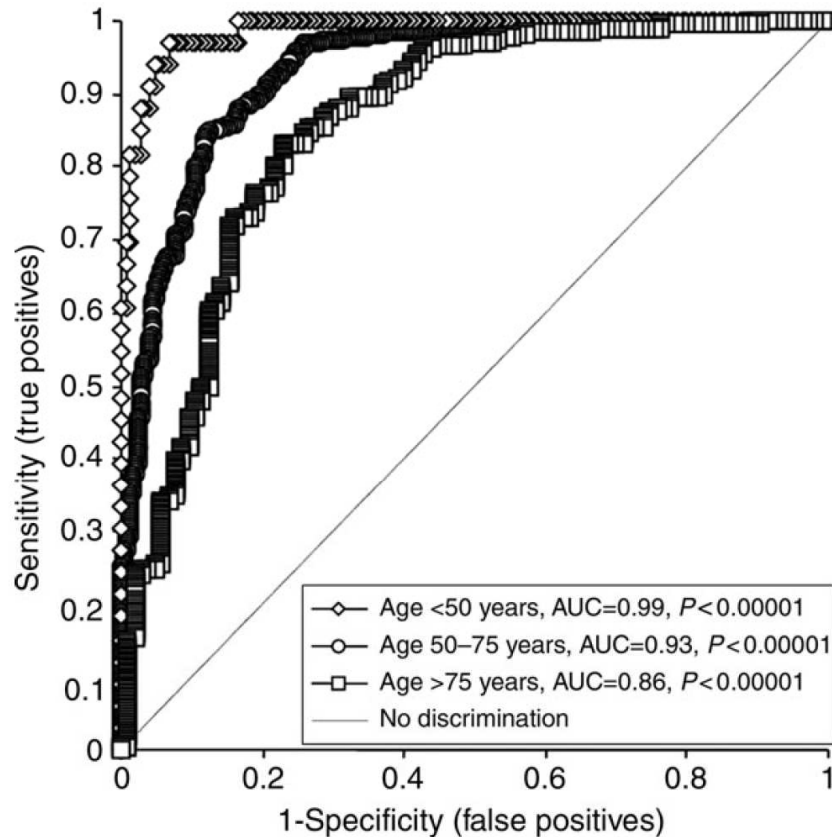
Januzzi JL
European Heart Journal
(2006) 27, 330–337.

Rövid távú prognózis
(single site, retrospective review
of 322 adult patients)



M. Marchetti et al.
Am J Emerg Medi
(2017) 35 :444–447

NT-proBNP testing for diagnosis and short-term prognosis in acute destabilized heart failure. An international pooled analysis of 1256 patients (ICON study)



Az életkor
és
a ROC görbék

ROC curves for NT-proBNP-based diagnosis of acute HF across three age groups. As depicted, NT-proBNP had high AUC in each age group.

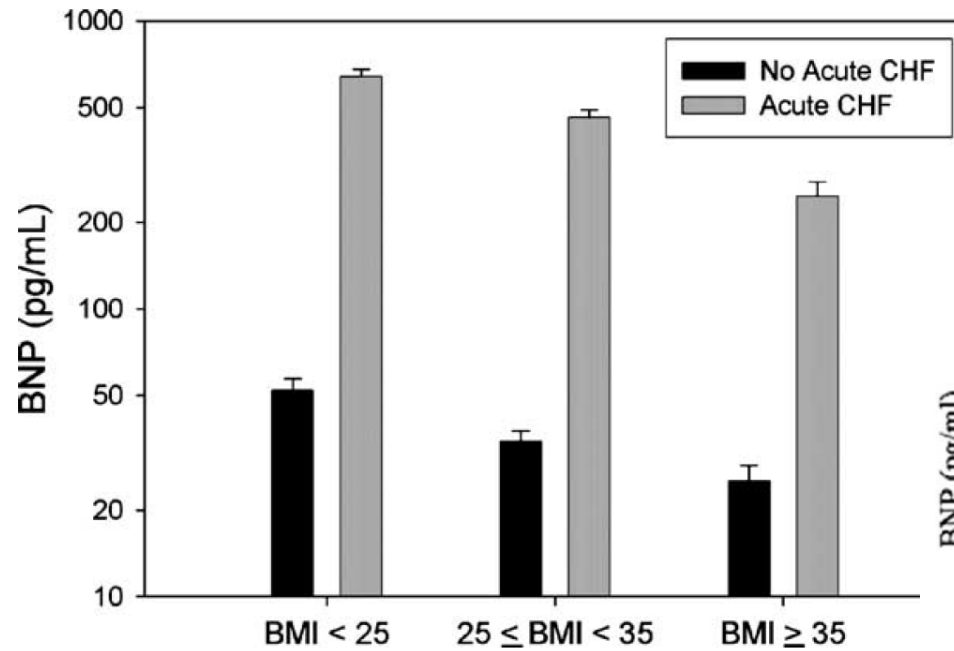
Januzzi JL *European Heart Journal* (2006) 27, 330–337.

NT-proBNP testing for diagnosis and short-term prognosis in acute destabilized heart failure. an international pooled analysis of 1256 patients

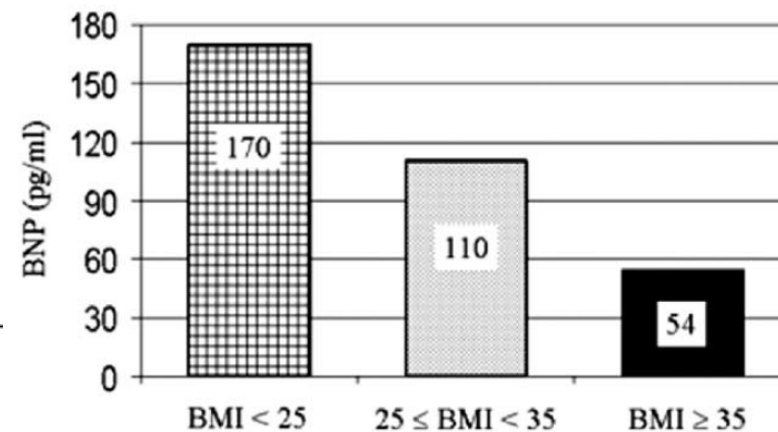
Optimal NT-proBNP cut-points for the diagnosis or exclusion of acute HF among dyspnoeic patients					
Category	Optimal cut-point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Confirmatory ('rule in') cut-points					
<50 years (<i>n</i> = 184)	450 pg/mL	97	93	76	99
50–75 years (<i>n</i> = 537)	900 pg/mL	90	82	83	88
>75 years (<i>n</i> = 535)	1800 pg/mL	85	73	92	55
Exclusionary ('rule out') cut-point					
All patients (<i>n</i> = 1256)	300 pg/mL	99	60	77	98

Januzzi JL *European Heart Journal* (2006) 27, 330–337.

A BNP szint alakulása obezitás és szívelégtelenség szövődésekor (a BNP study alvizsgálatában)



Határértékek 90%-os szenzitivitásnál



-Szupprimált kardiális endokrin funkció

-Felgyórsult NP clearance

Suggested natriuretic peptide cutoff values for acute decompensated heart failure

	ACEP recommendation	CKD	BMI >35kg/m²
Exclude			
BNP	<100	<200	54
NTproBNP	<300	<300	
Identify			
BNP	>500		
NTproBNP			
<50 years	>450	>1,200	
50–75 years	>900	>4,502	
>75 years	>1,800		

NT-proBNP:

Költségeffektivitás

a sürgősségi gyakorlatban

NT pro-BNP teszt a Rotterdami **Erasmus egyetem** sürgősségi osztályán a szívelégtelenség diagnózisában, hatása a költségekre, (2004-6; n=500)

End points	NT-proBNP group, n = 236	Control group, n = 241	P
ED admission (min)			
Median	170	172	.12*
IQR	120-220	130-235	
Overall time to discharge (d)			
Median	1.9	3.9	.04*
IQR	0.12-8.4	0.16-11.0	
Hospitalization			
No. of patients (%)	147 (62)	162 (67)	.26†
Duration of hospitalization			
Median	7.8	8.1	.48*
IQR	4.8-13.9	4.4-15.6	
Admission to intensive care			
No. of patients (%)	38 (16)	38 (16)	.92†
In-hospital mortality			
No. patients (%)	14 (6)	15 (6)	.89†
30-d mortality			
No. of patients (%)	15 (6)	18 (8)	.26†
30-d readmission			
No. of patients (%)	7 (3)	12 (5)	.18†

*Mann-Whitney U test.

† χ^2 test.

Rutten JHW Am Heart J 2008;156:71-7.)

Az NT-proBNP költségeffektivitása a sürgősségi osztályon a PRIDE vizsgálat alapján

Variable	Standard Clinical Assessment	NT-pro-BNP-Guided Assessment	Relative Change, NT-pro-BNP-Guided Assessment vs Standard Assessment
Base-case analysis			
Direct medical costs due to hospitalizations and echocardiograms	\$5,032	\$4,558	9.4% reduction
Risk for SAE (Serious Adverse Events)	0.258	0.254	1.6% reduction
Probability of correct CHF diagnosis	0.967	0.957	1.0% reduction
Proportion of true-positive CHF cases	0.320	0.328	2.5% increase
Proportion of true-negative non-CHF cases	0.647	0.629	2.8% reduction
No. of echocardiograms	0.251	0.105	58.0% reduction
No. of initial hospitalizations after ED	0.778	0.677	13.0% reduction
Average length of stay (d)	4.41	3.88	12.0% reduction
Sensitivity analysis			
Postdischarge mortality risk during follow-up	0.0288	0.0285	1.0% reduction

Siebert U Am J Cardiol 2006;98:800–805)

Az NT-proBNP költségeffektivitása a sürgősségi osztályon a PRIDE vizsgálat alapján

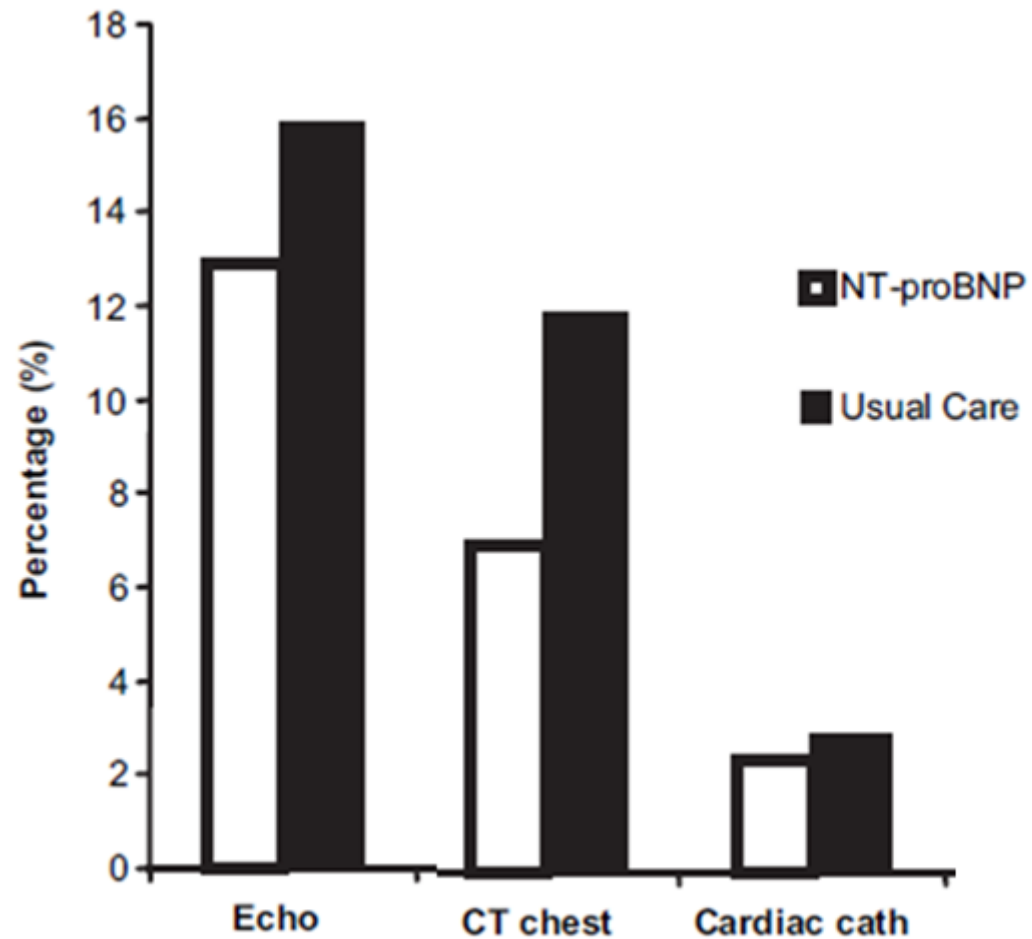
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NT pro-BNP teszt haszna kanadai sürgősségi osztályokon a szívelégtelenség megítélésében (**IMPROVE-CHF vizsgálat**)

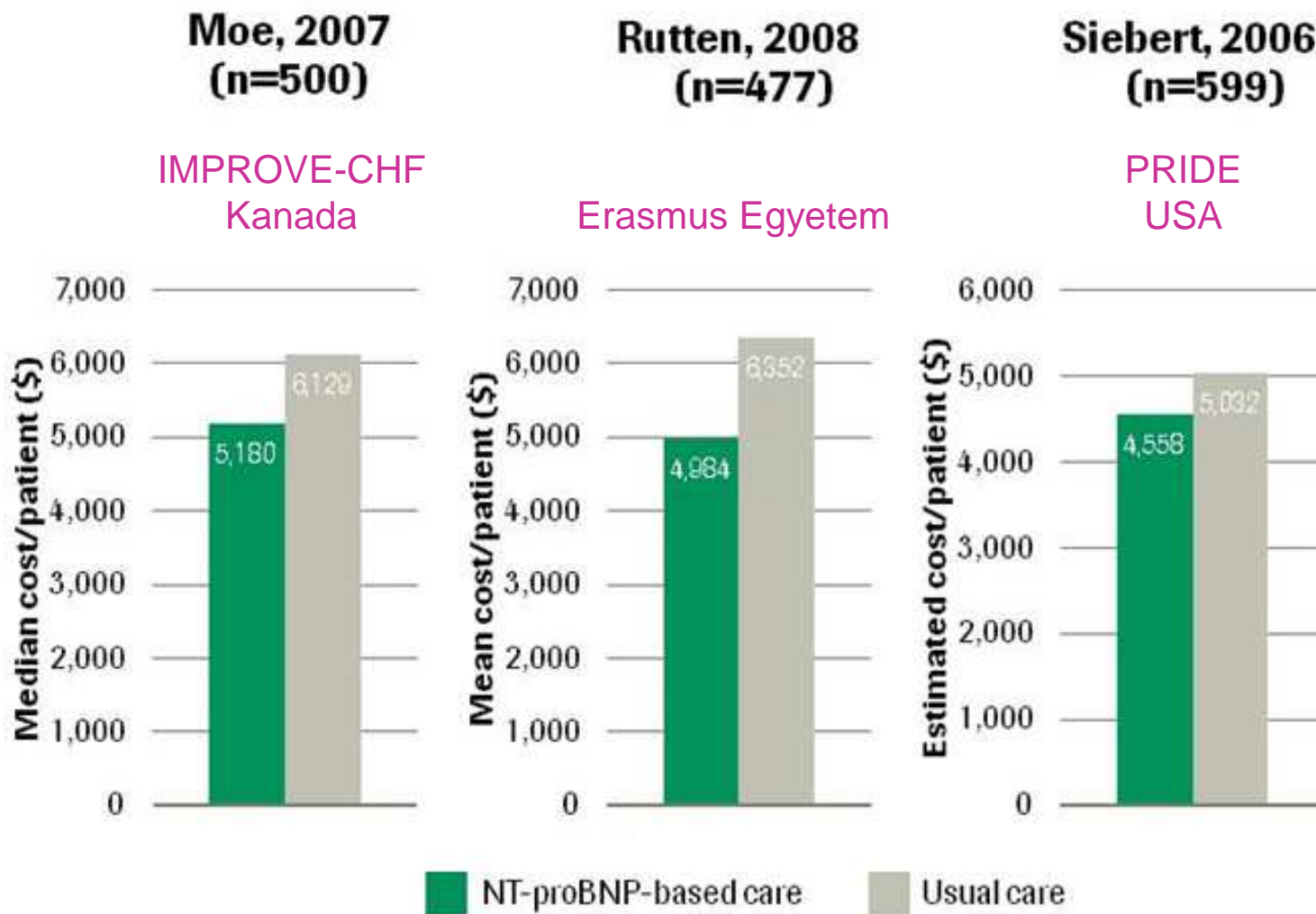
	NT-proBNP (n=105)	Usual Care (n=114)	P*
Duration of ED visit, median (Q1 to Q3), h	<u>5.4 (3.8 to 7.7)</u>	7.5 (4.8 to 9.3)	0.0028†
Duration of ICU stay, median (Q1 to Q3), d	8 (3 to 12)	5.5 (3 to 10)	0.6737†
Initial hospitalization from ED, n (%)	<u>62 (59)</u>	70 (61)	0.7219
Hospital LOS, median (Q1 to Q3), d	6 (4 to 11)	7 (4 to 14)	0.5174†
In-hospital mortality, n (%)	4 (3.8)	3 (2.6)	0.6205
Deaths by 60 d, n (%)‡	5 (5.0)	6 (5.4)	0.8814
Patients rehospitalized by 60 d, n (%)	7 (11.3)	6 (8.6)	0.6008

NT pro-BNP teszt haszna kanadai sürgősségi osztályokon a szívelégtelenség megítélésében (**IMPROVE-CHF vizsgálat**)



Moe GW et al., Circulation 2007;115:3103-3110,

Költségek alakulása a sürgősségi osztályon nehézlégzéssel jelentkező betegek estén



A tesztek helye
napjaink vezérfonalaiban

2016 ESC Guidelines for the diagnosis and treatment of heart failure



Recommendations regarding applied diagnostic measurements

Recommendations	Class ^a	Level ^b	Ref ^c
Upon presentation a measurement of plasma natriuretic peptide level (BNP, NT-proBNP or MR-proANP) is recommended in all patients with acute dyspnoea and suspected AHF to help in the differentiation of AHF from non-cardiac causes of acute dyspnoea.	I	A	31–534
At admission in all patients presenting with suspected AHF, the following diagnostic tests are recommended:			
a. 12-lead ECG;	I	C	
b. chest X-ray to assess signs of pulmonary congestion and detect other cardiac or non-cardiac diseases that may cause or contribute to the patient's symptoms;	I	C	
c. the following laboratory assessments in the blood: cardiac troponins, BUN (or urea), creatinine, electrolytes (sodium, potassium), glucose, complete blood count, liver function tests and TSH.	I	C	
Echocardiography is recommended immediately in haemodynamically unstable AHF patients and within 48 hours when cardiac structure and function are either not known or may have changed since previous studies.	I	C	

AHF = acute heart failure; BNP = B-type natriuretic peptide; BUN = blood urea nitrogen; ECG = electrocardiogram; MR-proANP = mid-regional pro A-type natriuretic peptide; NT-proBNP = N-terminal pro-B type natriuretic peptide; TSH = thyroid-stimulating hormone

^aClass of recommendation.

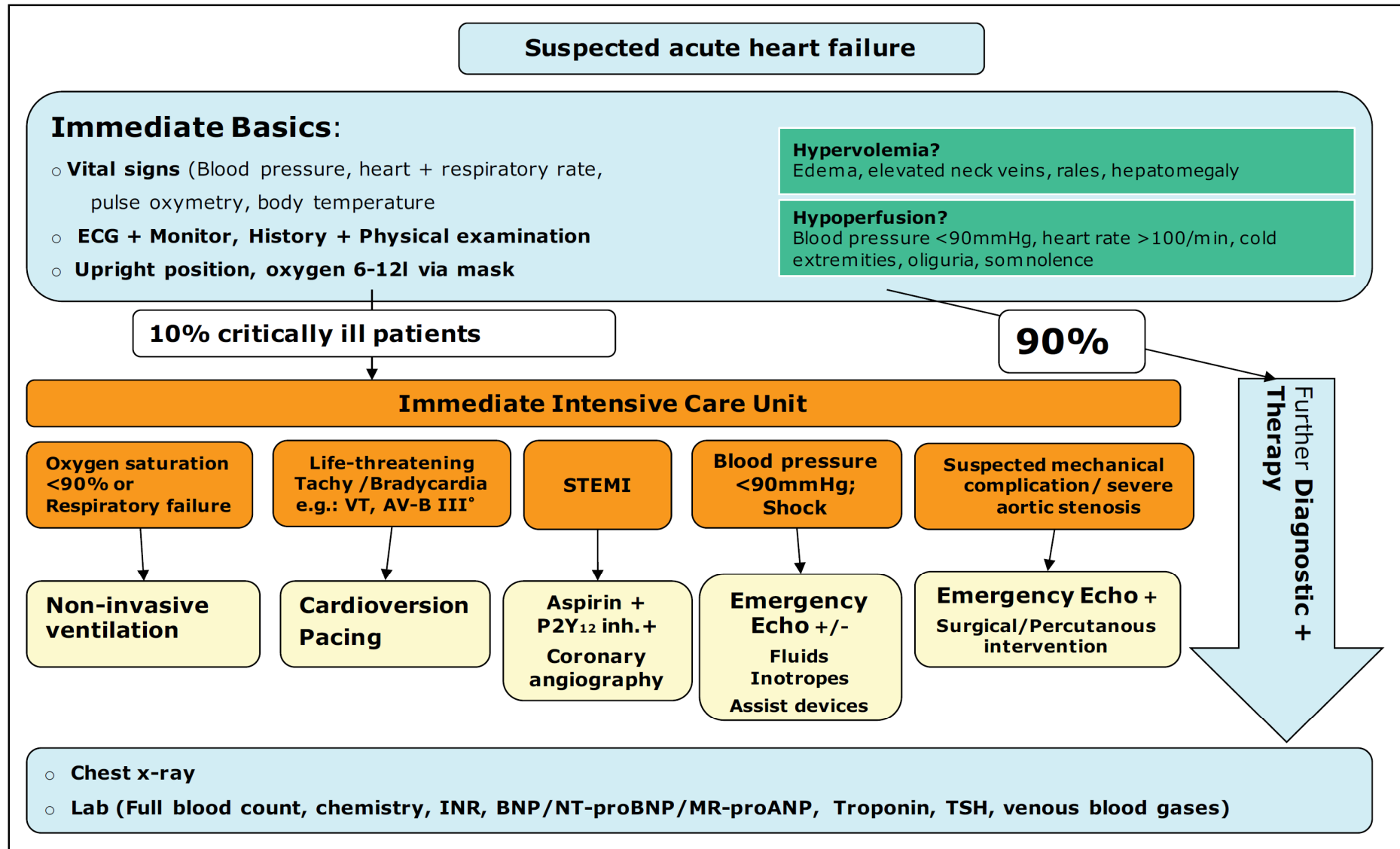
^bLevel of evidence.

^cReference(s) supporting recommendations.

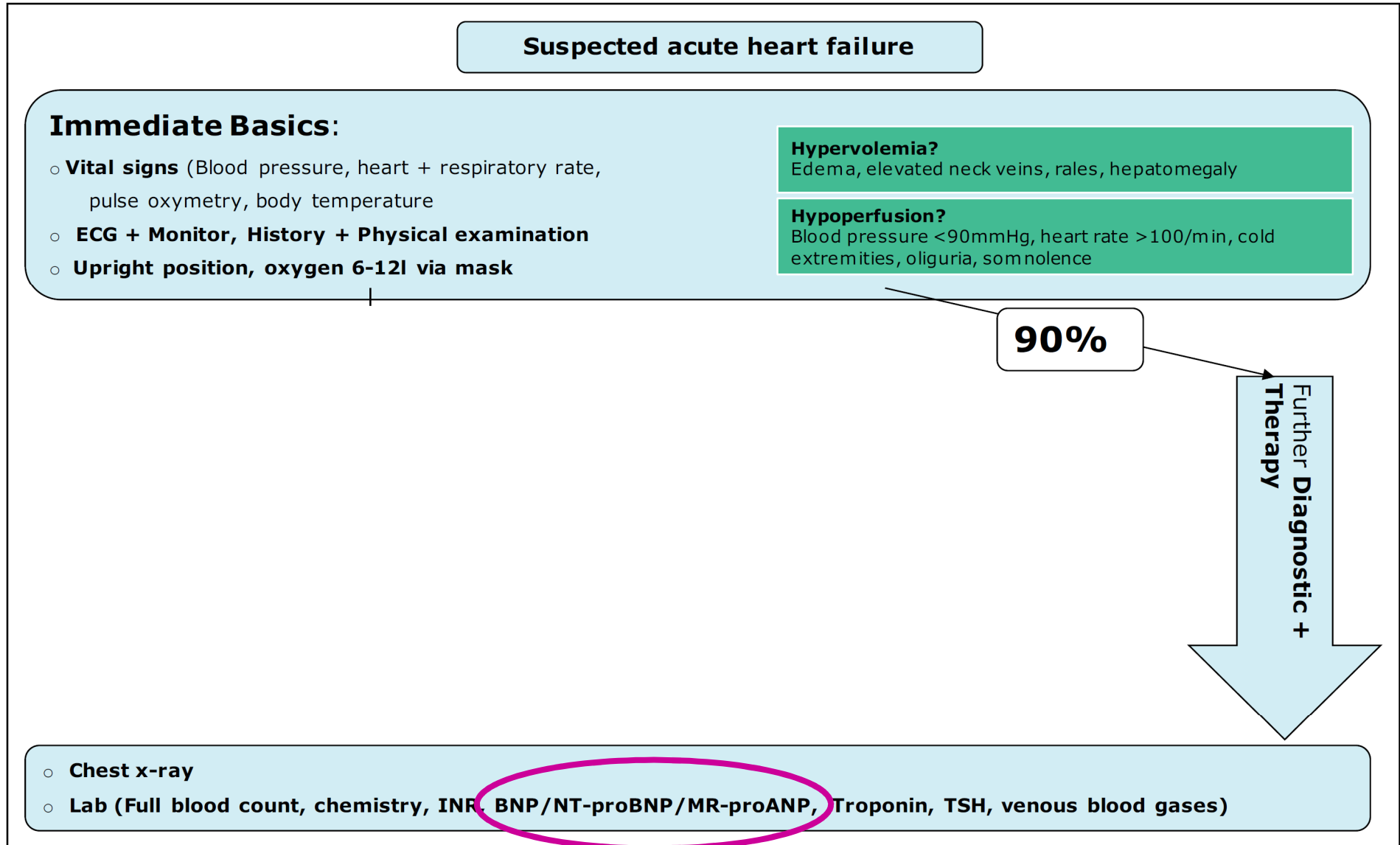
Ponikowski P et al. European Heart Journal doi:10.1093/eurheartj/ehw128

European Society of Cardiology-Acute Cardiovascular Care Association

Position paper on acute heart failure 2017



European Society of Cardiology-Acute Cardiovascular Care Association Position paper on acute heart failure 2017



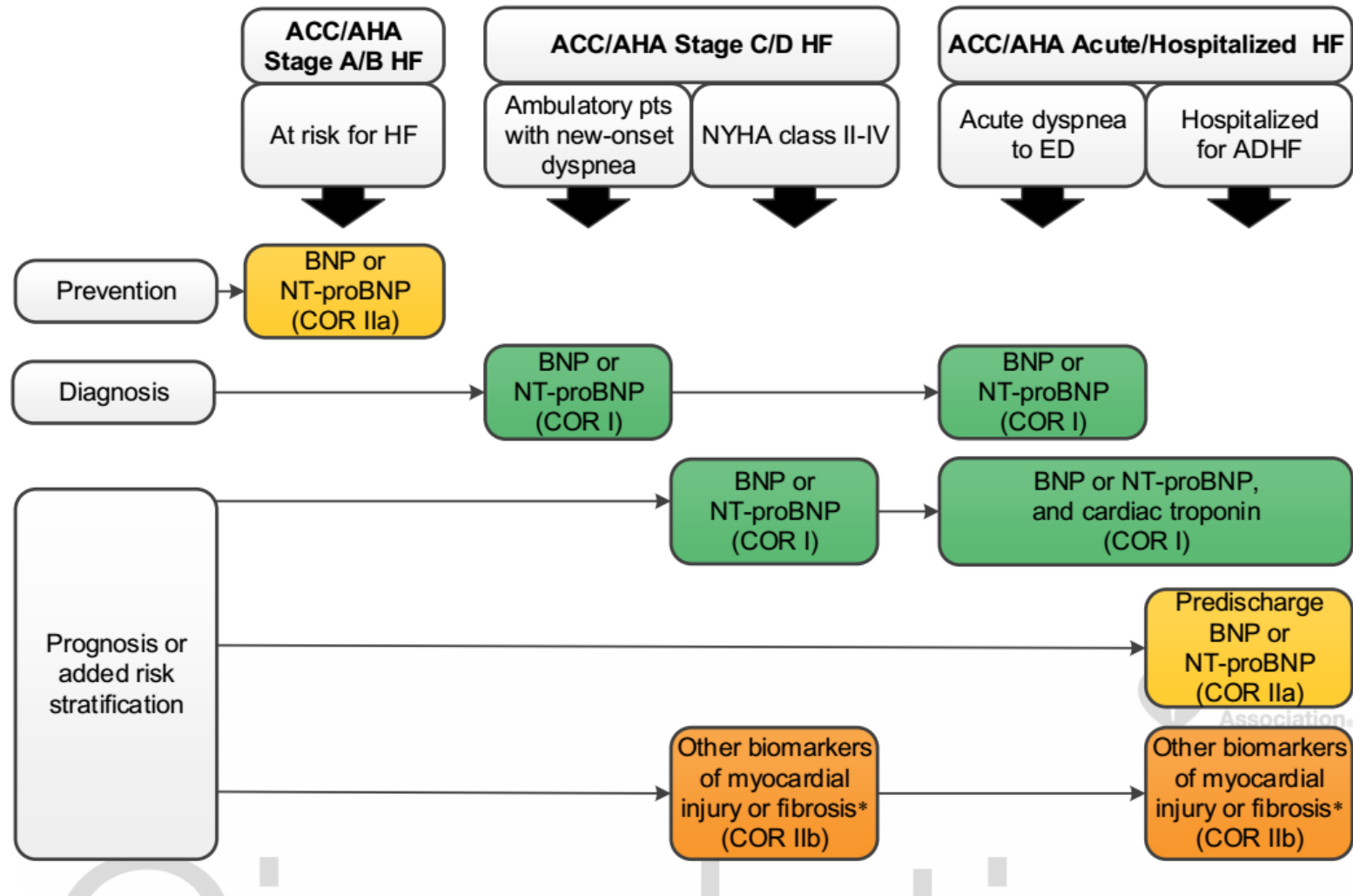
2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

Biomarkers: Recommendation for Diagnosis		
COR	LOE	Recommendation
I	A	In patients presenting with dyspnea, measurement of natriuretic peptide biomarkers is useful to support a diagnosis or exclusion of HF
<p>Natriuretic peptide biomarker testing in the setting of chronic ambulatory HF provides incremental diagnostic value to clinical judgment, especially when the etiology of dyspnea is unclear .</p> <p>In emergency settings, natriuretic peptide biomarker levels usually have higher sensitivity than specificity and may be more useful for ruling out than ruling in HF</p>		

Yancy CW et al., Circulation. 2017; DOI: 10.1161/CIR.0000000000000509

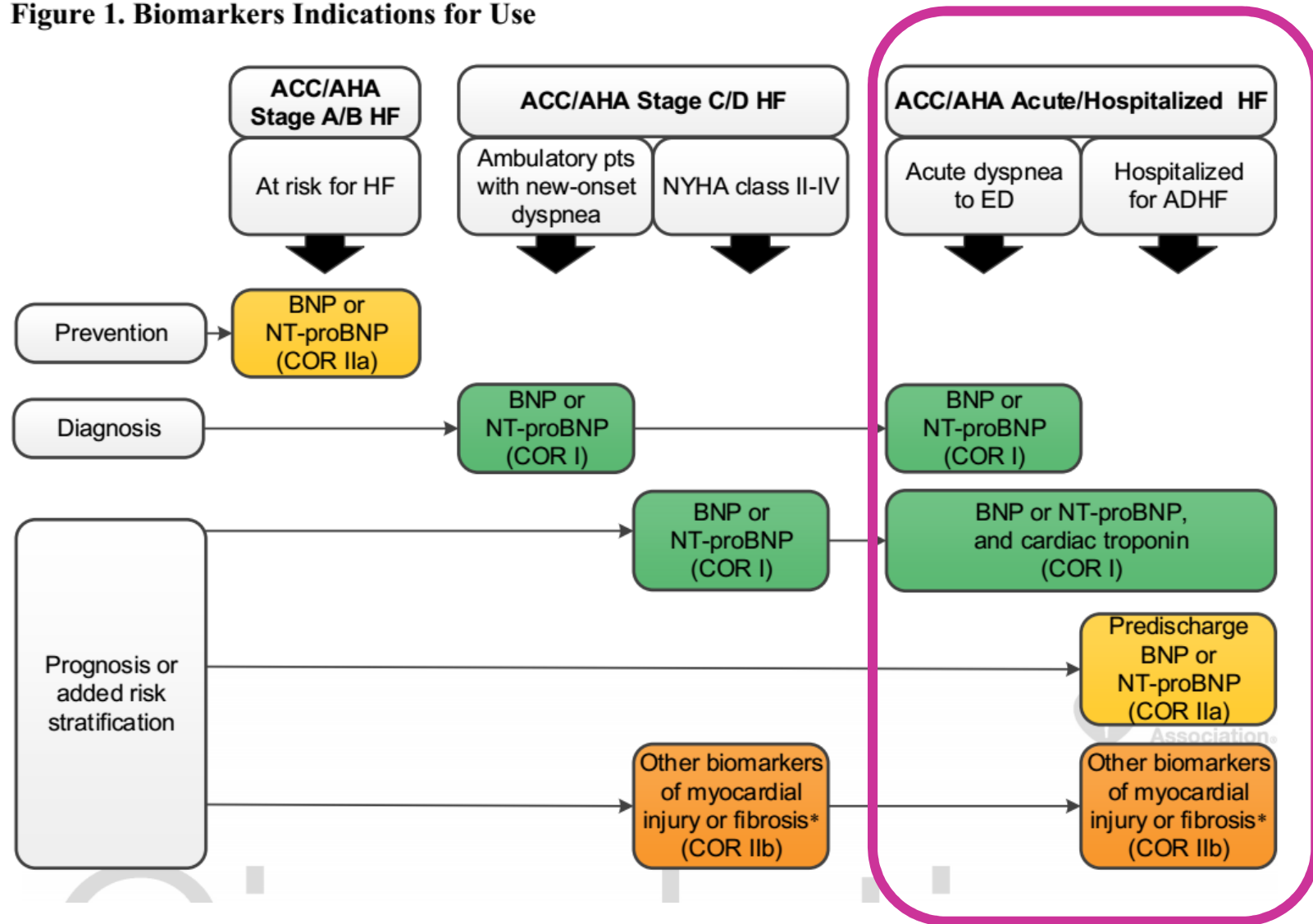
2017 ACC/AHA/HFSA HF Guideline

Figure 1. Biomarkers Indications for Use



2017 ACC/AHA/HFSA HF Guideline

Figure 1. Biomarkers Indications for Use



Köszönöm a figyelmet!