



DOKUZ EYLÜL UNIVERSITY

Kardiyolog gözüyle Acil'de NT-proBNP testi

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Natriuretic Peptides in Clinical Practice

This work is an initiative of Heart Failure Working Group of Turkish Society of Cardiology

Natriuretic Peptides in Clinical Practice
Yüksel Çavuşoğlu; Eskişehir-Turkey

Natriuretic Peptides in Heart Failure
Hakan Altay; Istanbul-Turkey

Natriuretic Peptides in the Diagnosis of Heart Failure and New Diagnostic Algorithms
Tolga Sinan Güvenç; Alberta-Canada

Natriuretic Peptides in the Diagnosis of Heart Failure with Preserved and Mid-Range Ejection Fraction
Özlem Yıldırım Türk; Istanbul-Turkey

Conditions Causing Natriuretic Peptide Elevation Other Than Heart Failure
Tamer Sayın; Ankara-Turkey

Natriuretic Peptides in the Identification of Heart Failure Prognosis and Risks
Mehmet Birhan Yılmaz; Izmir-Turkey

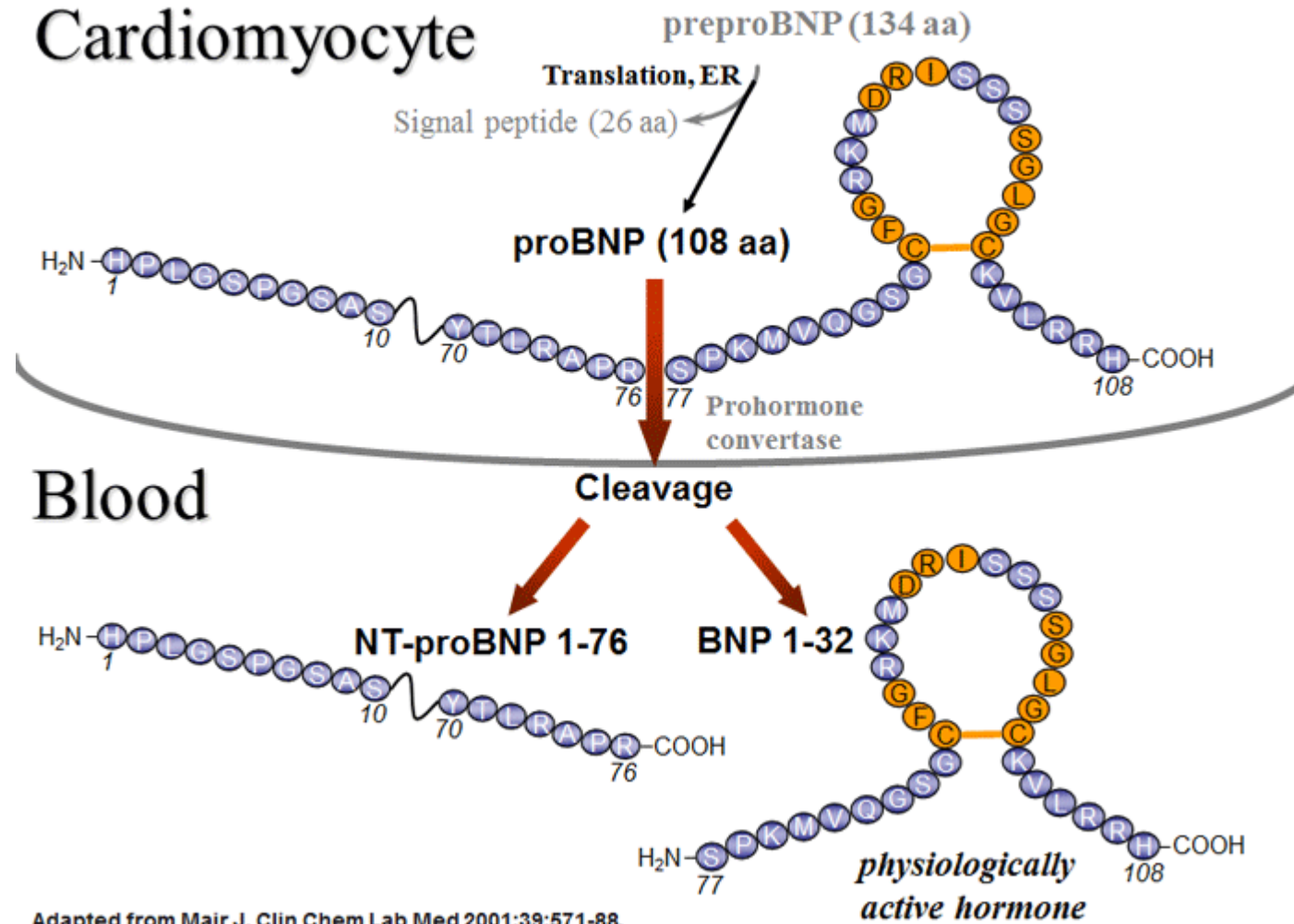
- Natriüretik Peptit: Kardiyak duvar gerilimine sekonder salınan hormon

NP	ANP	BNP	NT-proBNP	CNP
Structure	28-amino-acid peptide	32-amino-acid peptide	76-amino-acid peptide	22-amino-acid peptide
Site of synthesis	Atrium	Ventricle	Ventricle	Vessel endothelium
Signal	Atrial distension	Ventricular wall stress (volume load)	Ventricular wall stress (volume load)	Cytokines (IL-1,TNF), endothelium-dependent agonist (Ach)
Main physiological action	Natriuresis Vasodilation RAAS and SNS suppression Antifibrotic Anti-hypertrophic	Natriuresis Vasodilation RAAS and SNS suppression Antifibrotic	Inactive	Vasodilation? Antifibrotic? Anti-hypertrophic? Anti-inflammatory? Anti-thrombotic?
Receptor	NPR-A	NPR-A	-	NPR-B
Secondary messenger	Guanylate cyclase/cGMP	Guanylate cyclase/cGMP	-	Guanylate cyclase/cGMP
Clearance	NPR-C NEP breakdown	NPR-C NEP breakdown	Passively by skeletal muscle, liver and kidneys	NPR-C NEP breakdown

Ach: acetylcholine; ANP: atrial natriuretic peptide; BNP: Brain natriuretic peptide; CNP: C-type natriuretic peptide; cGMP: cyclic guanylate monophosphate; IL-1: interleukin-1; NEP: neutral endopeptidase; NP: natriuretic peptide; NPR: natriuretic peptide receptor; RAAS: renin-angiotensin-aldosterone system; SNS: sympathetic nervous system; TNF: tumor necrosis factor

FIGURE 1

Cardiomyocyte



Adapted from Mair J, Clin Chem Lab Med 2001;39:571-88.

NT-proBNP vs BNP

Comparative biological characteristics of NT-proBNP and BNP^{1,2}

NT-proBNP	BNP
Hormonally inactive	Hormonally active
76 amino acids	32 amino acids
Half life: 60–120 mins	Half-life: 20 mins
Higher plasma levels, cumulative concentrations reflect whole cardiac situation	Lower plasma levels, depend on the patient's situation at the moment
Up to 3 days stable at room temperature	Less stable than NT-proBNP
No interference by therapeutics	Interference by therapy with BNP or degradation inhibitors or NPs

Renal extraction ratio is equivalent for both BNP and NT-proBNP and is only about 15–20%^{3,4,5}

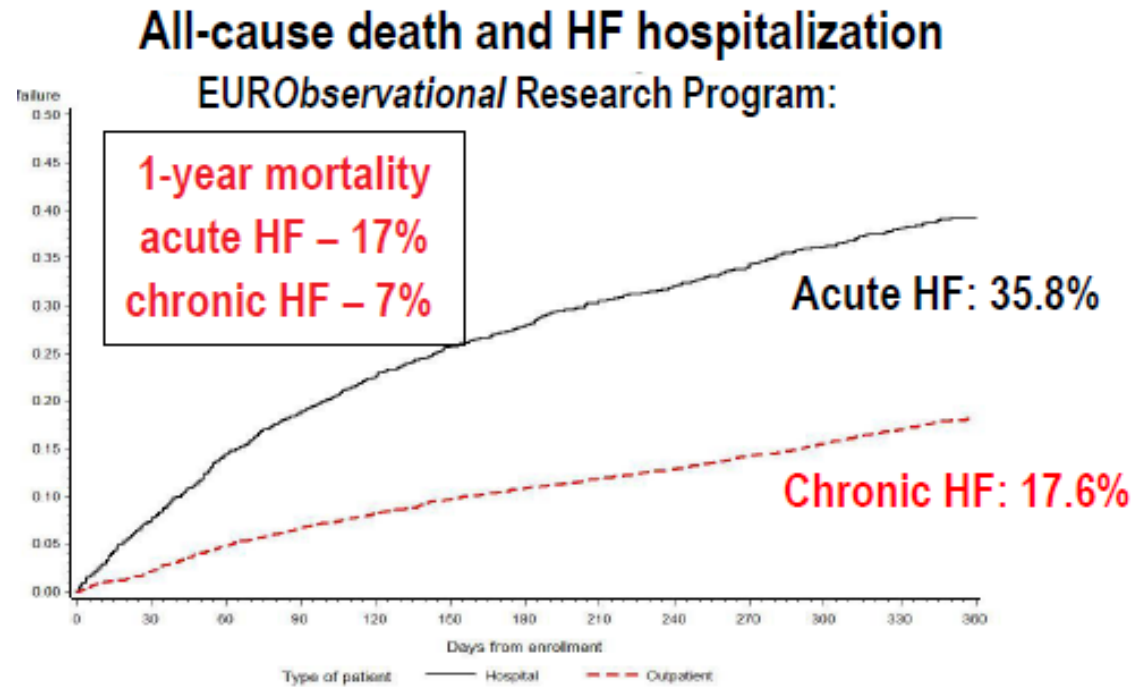
NT-proBNP	BNP
Passively by organs with high blood flow (kidneys, liver, muscles) ³	Actively by receptor mediated binding and by NEPs

BNP, B-type natriuretic peptide; NP, natriuretic peptide

1. Bayes-Genis A, Januzzi JL. NT-proBNP as a biomarker in CVD. 2008. Barcelona: Thomas Reuters; 2. Packer M, et al. Circulation 2014;131:54-61; 3. Thygesen K, et al. Euro Heart J 2012;33:2001-6; 4. Schou M, et al. J Appl Physiol 2005;99:1676-80; 5. DeFillippi C, et al. Clin Chem 2008;55:1271-3.

- **Kalp yetersizliđi (KY);** tipik semptomlar (nefes darlıđı, ayak bileđi řiřliđi ve halsizlik) ve beraberinde var olabilen bulgular (artmıř jugöler ven basıncı, pulmoner raller ve periferik ödem) ile karakterize, azalmıř kardiyak debi ve/veya istirahatte veya yüklenme anında artmıř intrakardiyak basınçlara yol açan yapısal ve/veya işlevsel bir kardiyak anormalliđin sebep olduđu bir klinik sendromdur.

Kalp Yetersizliğinde Mortalite ve Hospitalizasyon



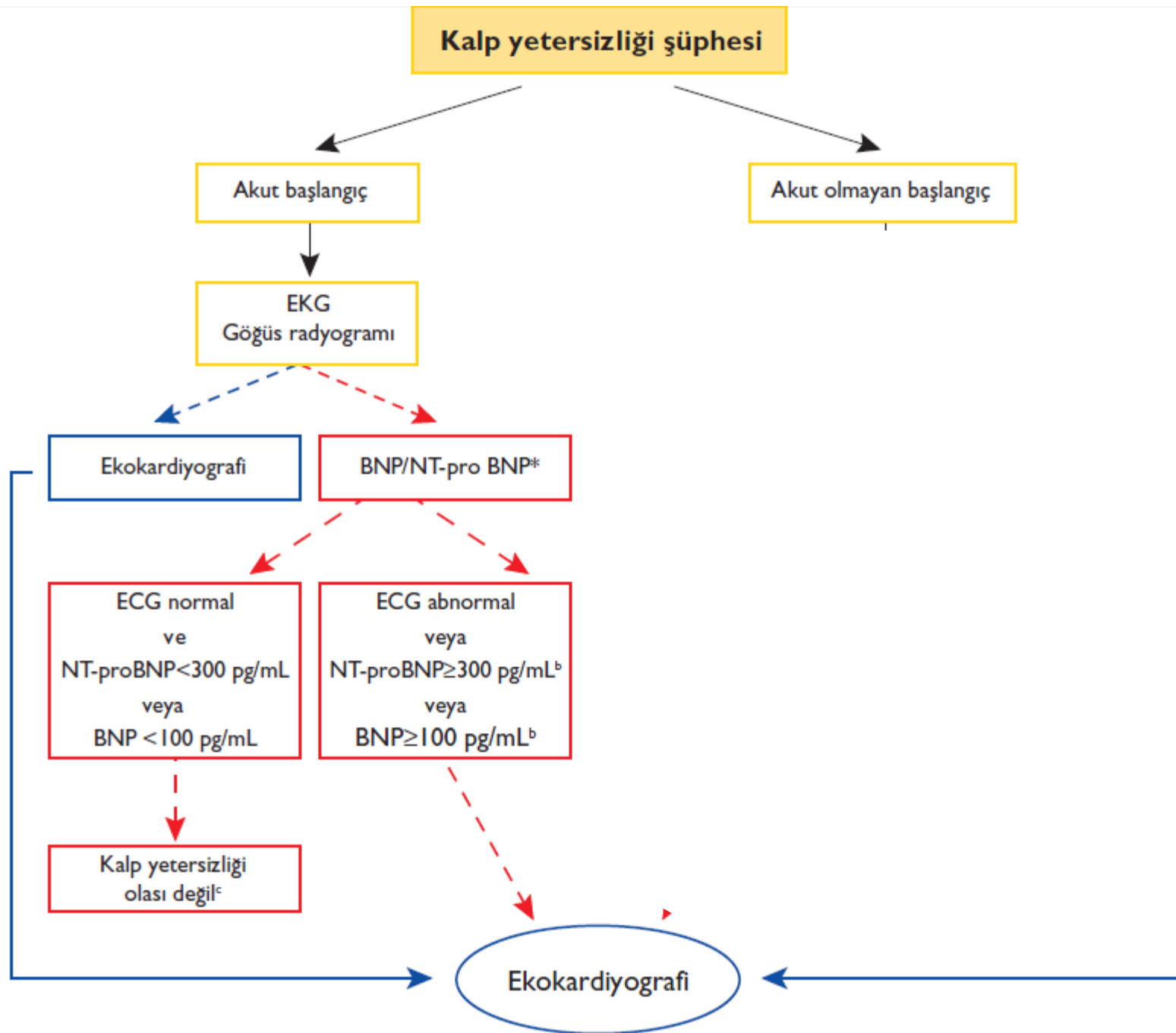
Maggioni et al. Eur J Heart Fail 2013;15:808-17

Fenotip		DEF-KY (Düşük ejeksiyon fraksiyonlu KY)	SEF-KY (sınırdan-orta aralıkta ejeksiyon fraksiyonlu KY)	KEF-KY (Korunmuş ejeksiyon fraksiyonlu KY)
Kriterler	1	Semptom±Bulgular	Semptom±Bulgular	Semptom±Bulgular
	2	SolV EF<%40	SolV EF %40-49	SolV EF≥%50
	3	-	1-Artmış natriüretik peptit düzeyleri 2-Aşağıdaki ilave kriterlerden en az 1 tanesi: a)İlişkili yapısal kalp hastalığı (SolV hipertrofisi ve/veya Sol atriyal genişleme b)Diyastolik işlev bozukluğu	1-Artmış natriüretik peptit düzeyleri 2-Aşağıdaki ilave kriterlerden en az 1 tanesi: a)İlişkili yapısal kalp hastalığı (SolV hipertrofisi ve/veya Sol atriyal genişleme b)Diyastolik işlev bozukluğu

KY'de bulgular erken evrelerde fark edilemeyebilir ya da tedavi ile fark edilemez düzeye kadar azalabilir
Natriüretik peptit için eşik değerler BNP>35 pg/ml, NTproBNP>125 pg/ml

Guideline	Recommendation	Level of Evidence/ Recommendation	Recommended Cut-off Value(s)
2017 AHA/ACCF/HFSA HF Update (34)	To diagnose HF or rule it out in patients who present with acute or chronic dyspnea	I/A	No certain cut-off value is specified.
2016 ESC HF Guideline (2)	To exclude HF diagnosis in non-acute conditions	1. For diagnosis– not specified 2. After diagnosis – IIa/C	For Exclusion BNP: 35 pg/ml NT-proBNP: 125 pg/ml
2010 NICE HF Guideline (55)	1. All patients without previous MI and with suspected HF. 2. Patients with normal EF on 2D echocardiography	Not specified	For Exclusion BNP <100 pg/ml NT-proBNP <400 pg/ml High Suspicion/Emergency Assessment BNP >400 pg/ml NT-proBNP >2000 pg/ml
2017 Canadian HF Guideline (57)	In acute or ambulatory patients, particularly if there is suspicion in diagnosis	Strong Recommendation /High-Quality Evidence	For Exclusion BNP: 50 pg/ml NT-proBNP: 125 pg/ml
2010 HFSA HF Guideline (58)	All patients for whom HF diagnosis is considered	Evidence level A	No certain value is specified.

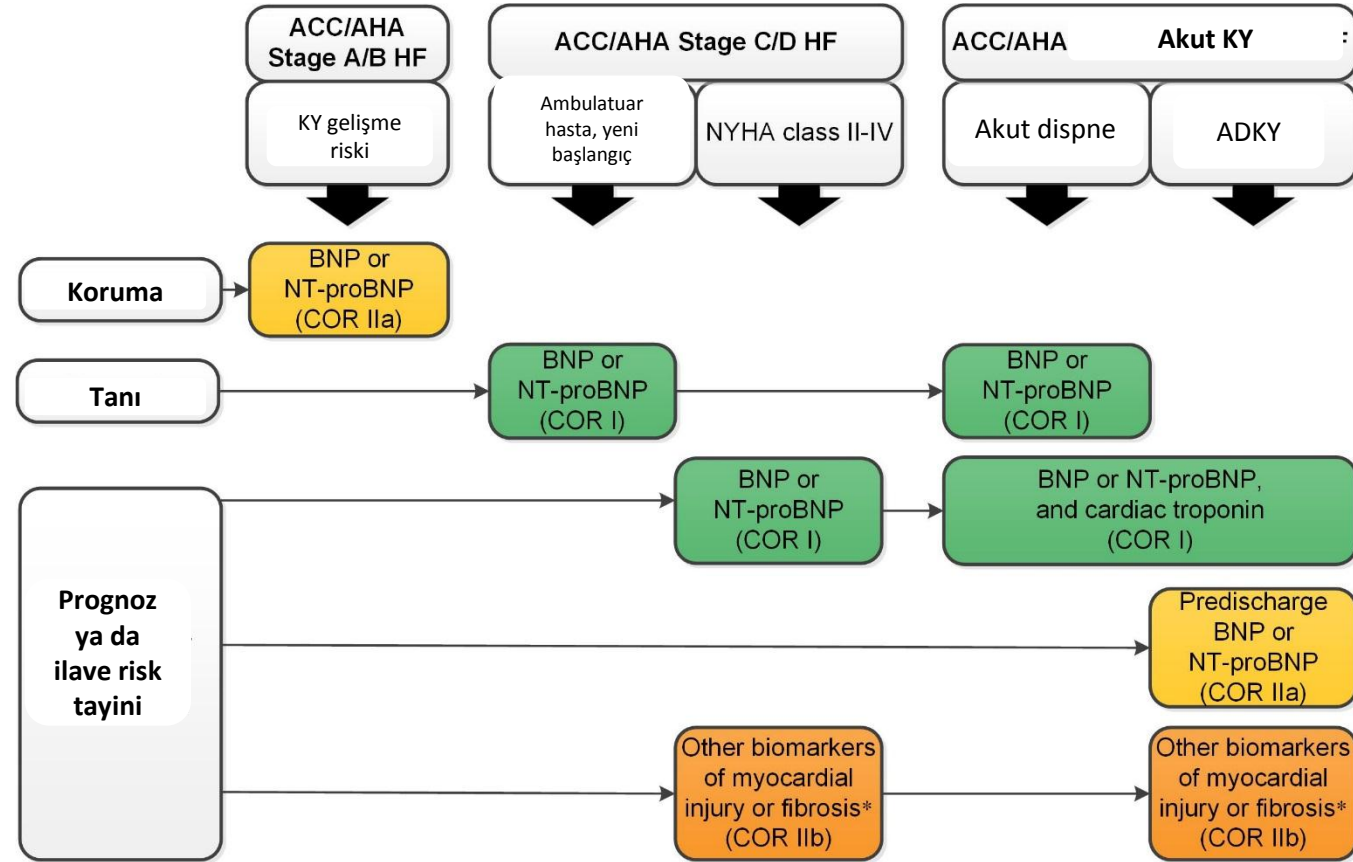
Guideline	Recommendation	Level of Evidence /Recommendation	Recommended Cut-off Value(s)
2017 AHA/ACCF/HFSA HF Update (34)	To diagnose HF or rule it out in patients who present with acute or chronic dyspnea	I/A	No certain cut-off value is specified.
2016 ESC HF Guideline (2)	To exclude HF diagnosis in patients who present with acute dyspnea	For diagnosis – not specified After diagnosis – IIa/C	To Exclude BNP: 100 pg/ml NT-proBNP: 300 pg/ml MR-proANP: 120 pmol/ml
2014 NICE HF Guideline (56)	All patients who present with acute dyspnea and have suspected HF	Not specified	BNP: 100 ng/L NT-proBNP: 300 ng/L
2017 Canadian HF Guideline (57)	In acute or ambulatory patients, particularly if there is suspicion in diagnosis	Strong Recommendation/ High-Quality Evidence	To Exclude BNP <100 pg/ml NT-proBNP <300 pg/ml High HF Suspicion BNP >400 pg/ml <50 years of age: NT-proBNP >450 pg/ml 50-75 years of age: NT-proBNP >900 pg/ml >75 years of age: NT-proBNP >1800 pg/ml No certain value is specified.
2010 HFSA HF Guideline (58)	All patients for whom HF diagnosis is considered	Evidence level A	



Artmış NP seviyeleri

Kardiyak	Nonkardiyak
• KY, RV sendromlar dahil • AKS • Kalp kası hastalığı (LVH dahil) • Kapak hastalığı • Perikard hastalığı • AF • Miyokardit • Kalp cerrahisi • Kardiyoversiyon	• İleri yaş • Anemi • Böbrek yetersizliği • Pulmoner sebepler: Obstrüktif uyku apnesi, ciddi pnömoni, PHT • Ciddi hastalık • Bakteriyel sepsis • Ciddi yanık • Toksik-metabolik müdahale (kanser kemoterapisi, zehirli hayvan ısırması)

KY'de Biyobelirteç Endikasyonları

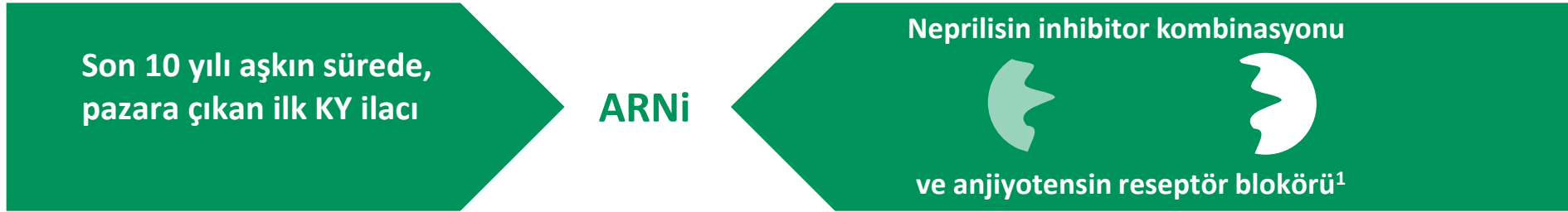


*Other biomarkers of injury or fibrosis include soluble ST2 receptor, galectin-3, and high-sensitivity troponin.

ACC indicates American College of Cardiology; AHA, American Heart Association; ADHF, acute decompensated heart failure; BNP, B-type natriuretic peptide; COR, Class of Recommendation; ED, emergency department; HF, heart failure; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; and pts, patients.

Sakubitril-Valsartan

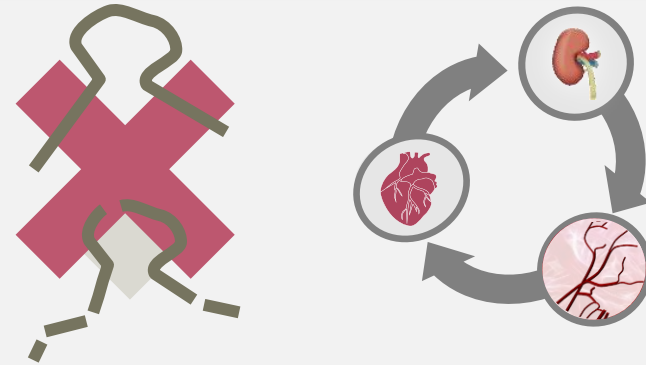
Son 10 yılda pazara çıkan ilk KY ilacı



Aksiyon Modeli

Konvensiyonel terapinin tersine, sakubitril-valsartan BNP degradasyonunu bloke ederek, protektif nörohomonal NP sistemini arttırmaktadır.

Konvansiyonel terapiye benzer olarak, sakubitril-valsartan RAAS sistemini baskılamaktadır.



ARB, angiotensin receptor blocker; ARNi, angiotensin receptor neprilysin inhibitor; HF, heart failure; NP, natriuretic peptide; RAAS, renin angiotensin aldosterone system

1. Voors, AA., et al. (2013). *Expert Opin Investig Drugs*, 22(8): 1041-1047.

Sakubitril-valsartan BNP seviyelerini etkilemektedir¹ *BNP seviyeleri yanlış yorumlamaya yol açabilir²*

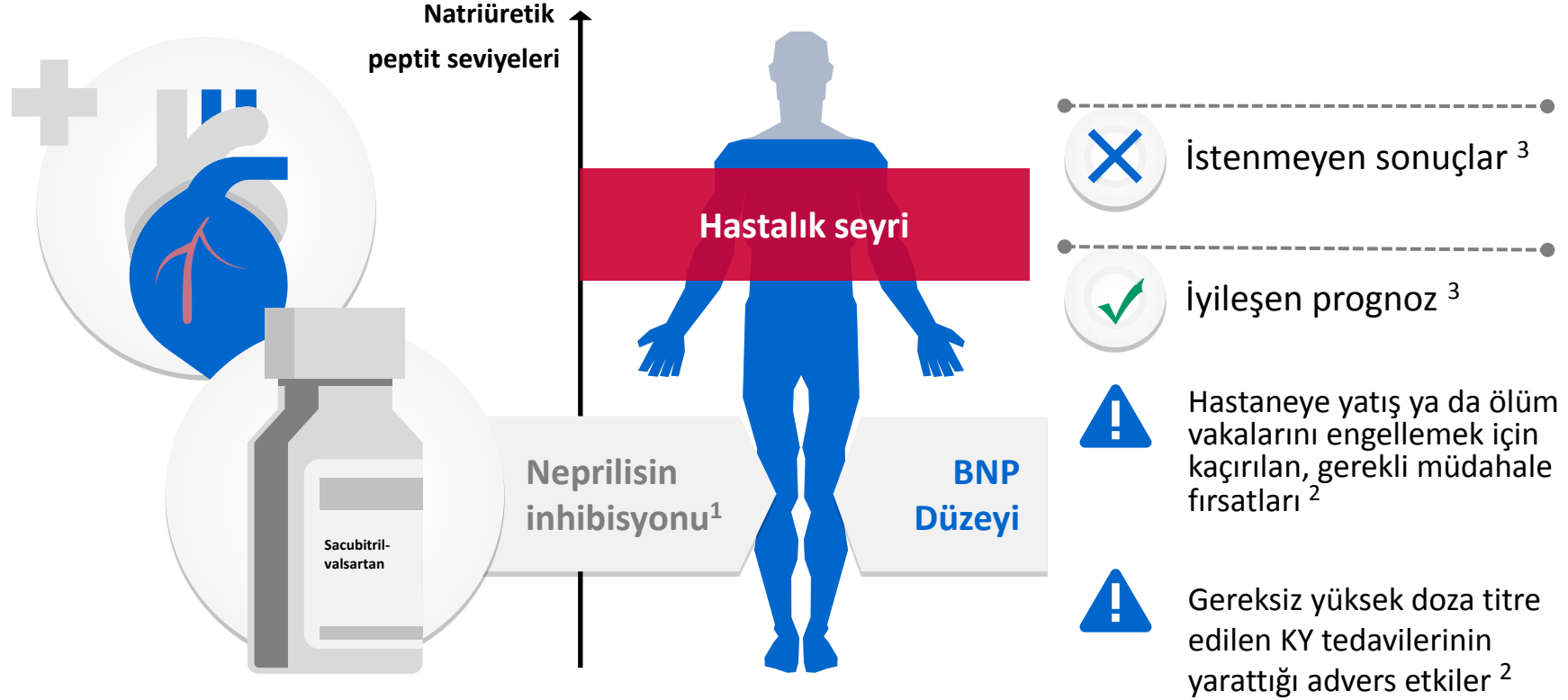


Table 7. Natriuretic peptides in prognosis assessment and therapy guidance in Acute and Chronic Heart Failure

Acute heart failure	On admission	In-hospital change prognosis	On discharge	In-hospital change therapy guidance
	+++	++	++	-?
Chronic heart failure	At baseline (dry)	Change in follow-up, prognosis		Change in follow-up, therapy guidance
	+++	++		+/-

Güncel Sorunlar

- Hafif Yükseklikleri nasıl yorumlamalıyım?
- Hiperakut dönemde değeri nedir?
- Her yüksek akut mu demektir?
- Kronik yüksek değerleri olan hastada ne yapalım? (%30 kuralı)