



TÜRK KLİNİK BİYOKİMYA DERNEĞİ
İSTANBUL ŞUBESİ

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Biyokimya AD

28. yıl

Sunu Planı

- Vaka örnekleri
- Kalp yetmezliği tanımı, önemi
- Tıbbi biyokimya testleri
- Natriüretik peptidler
- Gelecekte beklenenler
- Öneriler – sözün özü

Vaka 1

- 37 yaşında, erkek hasta
- Sağlık çalışanı
- Risk faktörleri (+), Soy geçmiş (+)
- Sabah ani başlayan göğüs ağrısı (15-20 dakika, 2 defa)
- Acile başvuru
- Fizik muayenede özellik yok
- EKG: Taşikardi
- Laboratuvar testleri

Vaka 1

- CBC:
Lökosit 7.9 k/ μ L, Hemoglobin 15,6 g/dL, Trombosit 247 k/ μ L
- D-dimer 20 ng/mL (0-400)
- CRP 1,8 mg/L (0-5)
- AST 20 U/L, ALT 33 U/L, BUN 16 mg/dL, Kreatinin 0,97 mg/dL
- Lipaz 152 U/L (73-392), GGT 70 U/L (15-85), LDH 160 U/L
- Na⁺ 140 mmol/L, K⁺ 4 mmol/L, Cl⁻ mmol/L
- INR 0,98, aPTT 29 sn
- CK-MB 1.9 ng/mL (0-6.6)

Vaka 1

- İlk ağrı başlangıcından 2 saat sonra alınan numunede
hs-cTnI :124 pg/mL(0-34)
- Akut koroner sendrom - NonST- MI

Vaka 1

- Radial Perkütan Koroner Anjiyoplasti uygulaması:
LAD Proksimal Segment Stent
- İlk ağrı başlangıcından 24 saat sonra alınan numunede:
hs-cTnI :1679 pg/mL(0-34)
- Salah ile taburcu

Vaka 2

- 41 yař, erkek
- Doktor
- Kardiyak arrest



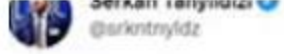
Vaka 2

- CPR'a başlanıyor
- CPR devam ederken koroner anjiyografi:
LAD stent – Tip 1 MI
- hs-cTt x5 URL ↑ ve CK-MB mass x10 URL ↑

Vaka 2

- Hemodinamik instabilitesi devam ediyor
- AKG derin metabolik asidoz
- Nüks kardiyak arrest
- CPR eşliğinde ECMO
- Sinüs ritmi sağlanınca acil CBAG kararı
- EF % 10'lerde

Vaka 2



@serkintnyldz

Doktor G ng r Sitar(41)  alıřtıęı hastaneye "Kalp krizi ge iriyorum" diye gelip kapıda yıęıldı.

İstanbul Sancaktepe Eęitim ve Arařtırma Hastanesinde  ok #acil A Rh (+) #kan ihtiya ı vardır.

Kızılay Kan Merkezlerinden hasta bilgileri ile baęıř yapılabilir.

İletişim 0555 837 9144

Arkadařımız
Dr. G ng r Sitar i in
A rh (+) tam kan ihtiya ı vardır.
Verebilecek olanlar
Sancaktepe İlhan Varank EAH
kan merkezine bařvurabilirler.

Ahbap Acil @ahbapacil · 25 Mar

#İstanbul Sancaktepe Eęitim ve Arařtırma Hastanesinde tedavi g rmekte olan G ng r Sitar i in  ok #acil A Rh (+) #kan ihtiya ı vardır.

"Kızılay Kan Merkezlerinden hasta bilgileri ile baęıř yapılabilir.

İletişim: 0555 837 9144



29 31

Hekimden Haber @hekimdenhaber · 25 Mar

  Acil Kan Aranıyor!
Sancaktepe EAH Dahiliye Uzmanımız i in:
"Hastanemiz dahiliye doktoru G ng r Sitar i in A+ kan ihtiya ı bulunmakta. Kan grubu uyan m sait olan var ise  ekmek y Madenler

Doktor Acil Destek



Vaka 2

- WBC 14 k/ μ L, CRP 198 mg/L, prokalsitonin 1.08 μ g/L (<0.05 μ g/L)

- Pnömonik infiltrasyonlara sekonder

ARDS

- hs-cTt artışı olmaksızın kreatin kinaz artışı başlıyor – x1000 URL

Kompartman Sendromu

- Hemoraji devam ediyor - hemoglobin 5 g/dL

Vaka 3

- 64 yaşında erkek hasta
- 4 aydır ilerleyici nefes darlığı
- Gece 3 yastık kullanıyor, sık sık uykudan uyanıyor
- Hipertansiyon, dislipidemi, diabetes mellitus ve 4 yıl önce geçirilmiş üçlü CABG öyküsü
- Aspirin, atorvastatin, amlodipin ve metformin kullanıyor

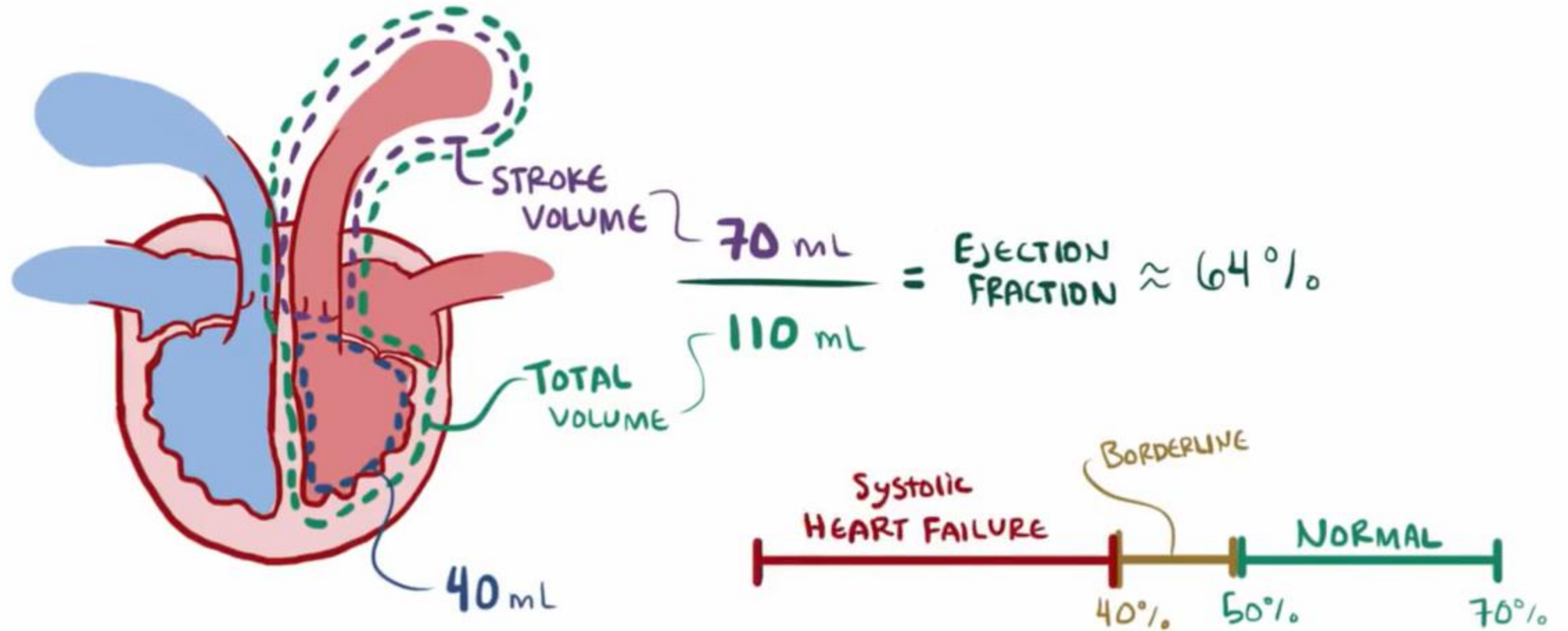
Vaka 3

- Aile hikayesinde özellik yok
- Hayati bulguları stabil
- Fizik muayenede akciğerlerde bilateral yaygın ral
- 2+ alt ekstremitelerde ödem
- EKG'de sol ventrikül hipertrofisi
- hsTroponin T < 14 ng/L

Kalp Yetmezliği

- Karmaşık bir klinik sendrom: sağ, sol
- Ventrikül dolumu veya kan atımı yapısal/işlevsel bozukluğu

Circulation. 2022;145:e895–e1032. 2022 AHA/ACC/HFSA Heart Failure Guideline



Osmosis.org

Kalp Yetmezliği Sınıflandırması

- Sol Ventriküler Ejeksiyon Fraksiyonu (LVEF)

LVEF $\leq 40\%$: HF with reduced ejection fraction «**HFrEF**»

LVEF $\geq 50\%$: HF with preserved EF «**HFpEF**» DİYASTOLİK KY

LVEF 41%–49%: HF with midrange EF or HF with mildly reduced EF «**HFmrEF**»

Önce LVEF $\leq 40\%$, ardından LVEF $> 40\%$: HF with improved EF «**HFimpEF**»

Yancy CW, et al. Circulation. 2013;128:e240–e327

Dunlay SM, et al. Nat Rev Cardiol. 2017;14:591–602

Wilcox JE, et al. J Am Coll Cardiol. 2020;76:719–734

Ejeksiyon Fraksiyonu

- Sistolik kalp yetmezliği √
- Diyastolik kalp yetmezliği ?
 - Frank Starling mekanizması
 - Preload↓

Kalp Yetmezliği Neden Önemli?

- Prevelans
- Hospitalizasyon
- Bütçeye yük
- Mortalite

Kalp Yetmezliği Nedenleri

- ABD’de

115 milyon hipertansiyon, 100 milyon obezite, 92 milyon prediyabet, 26 milyon diyabet

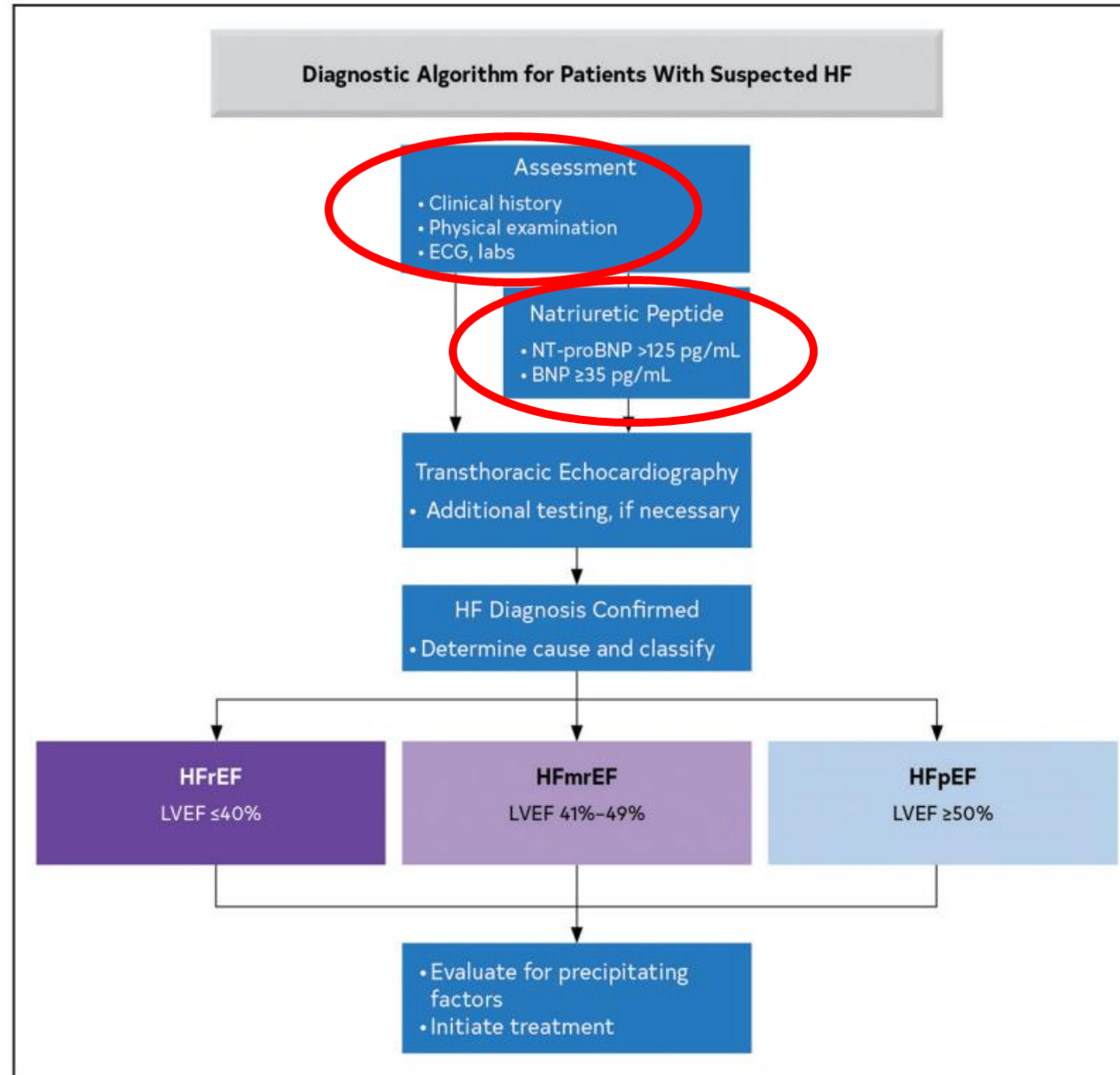
- Diğer nedenler:

kardiyomiyopatiler; amiloidoz; kemoterapi, alkol, kokain, metamfetamin; miyokardit; sarkoidoz; hemokromatozis; tiroid hastalıkları etc

Virani SS, et al. Circulation. 2021;143:e254–e743.

Belirteçlere İhtiyaç Var mı?

- New York Kalp Derneği (NYHA) fonksiyonel sınıflandırmaları I – IV
Objektif?
- Dispnenin nedenleri...
- Ventriküler disfonksiyonun sessiz ilerleyişi



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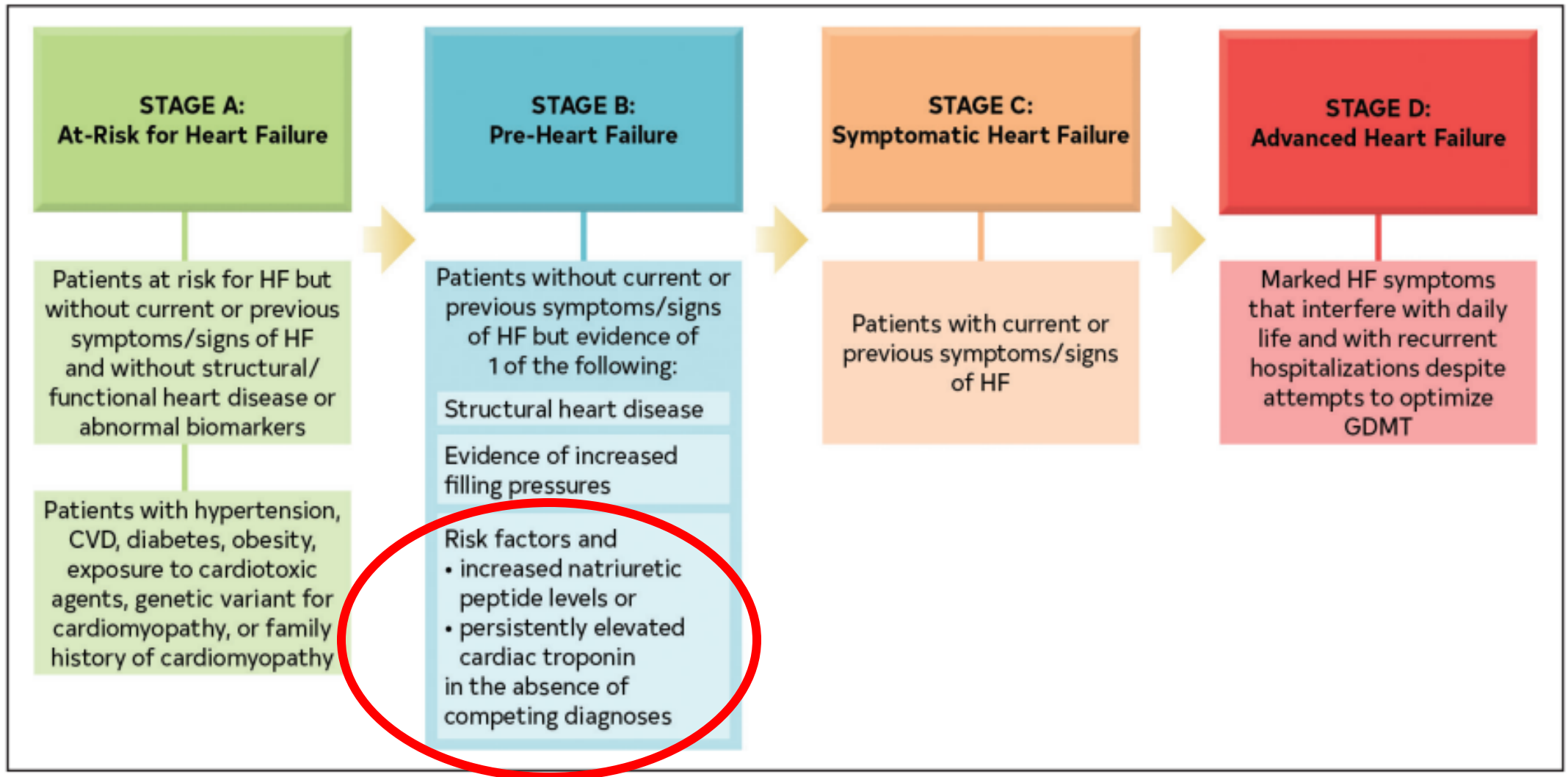


Figure 1. ACC/AHA Stages of HF.

The ACC/AHA stages of HF are shown. ACC indicates American College of Cardiology; AHA, American Heart Association; CVD, cardiovascular disease; GDMT, guideline-directed medical therapy; and HF, heart failure.

Öncelikli Testler

- American College of Cardiology Foundation/American Heart Association
- European Society of Cardiology (ESC)

McDonagh TA, et al. ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021 Sep 21;42(36):3599-3726.

Circulation. 2022;145:e895–e1032. 2022 AHA/ACC/HFSA Heart Failure Guideline

Öncelikli Testler

- Kalp yetmezliğinin potansiyel nedenleri olarak anemi veya enfeksiyonu gösterebilen **tam kan sayımı** (CBC)
- Kardiyovasküler hastalıklarla ilişkili olan **proteinüri**
- Sıvı retansiyonu veya böbrek fonksiyon bozukluğu - **serum elektrolit seviyeleri**

McDonagh TA, et al. ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021 Sep 21;42(36):3599-3726.

Circulation. 2022;145:e895–e1032. 2022 AHA/ACC/HFSA Heart Failure Guideline

Öncelikli Testler

- Kan üre azotu (**BUN**) ve serum **kreatinin**,
- Açlık kan şekeri,
- Yüksek karaciğer enzim seviyeleri gösterebilen ve kalp yetmezliğine bağlı karaciğer fonksiyon bozukluğunu gösteren **karaciğer fonksiyon** testleri,
- **Demir** profili – transferrin saturasyonu, ferritin

McDonagh TA, et al. ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021 Sep 21;42(36):3599-3726.

Circulation. 2022;145:e895–e1032. 2022 AHA/ACC/HFSA Heart Failure Guideline

Öncelikli Testler

- **Lipid profili**
- Tiroid uyarıcı hormon (**TSH**) seviyesi
- **Troponin I veya T** seviyeleri

McDonagh TA, et al. ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021 Sep 21;42(36):3599-3726.

Circulation. 2022;145:e895–e1032. 2022 AHA/ACC/HFSA Heart Failure Guideline

Natriüretik Peptidler

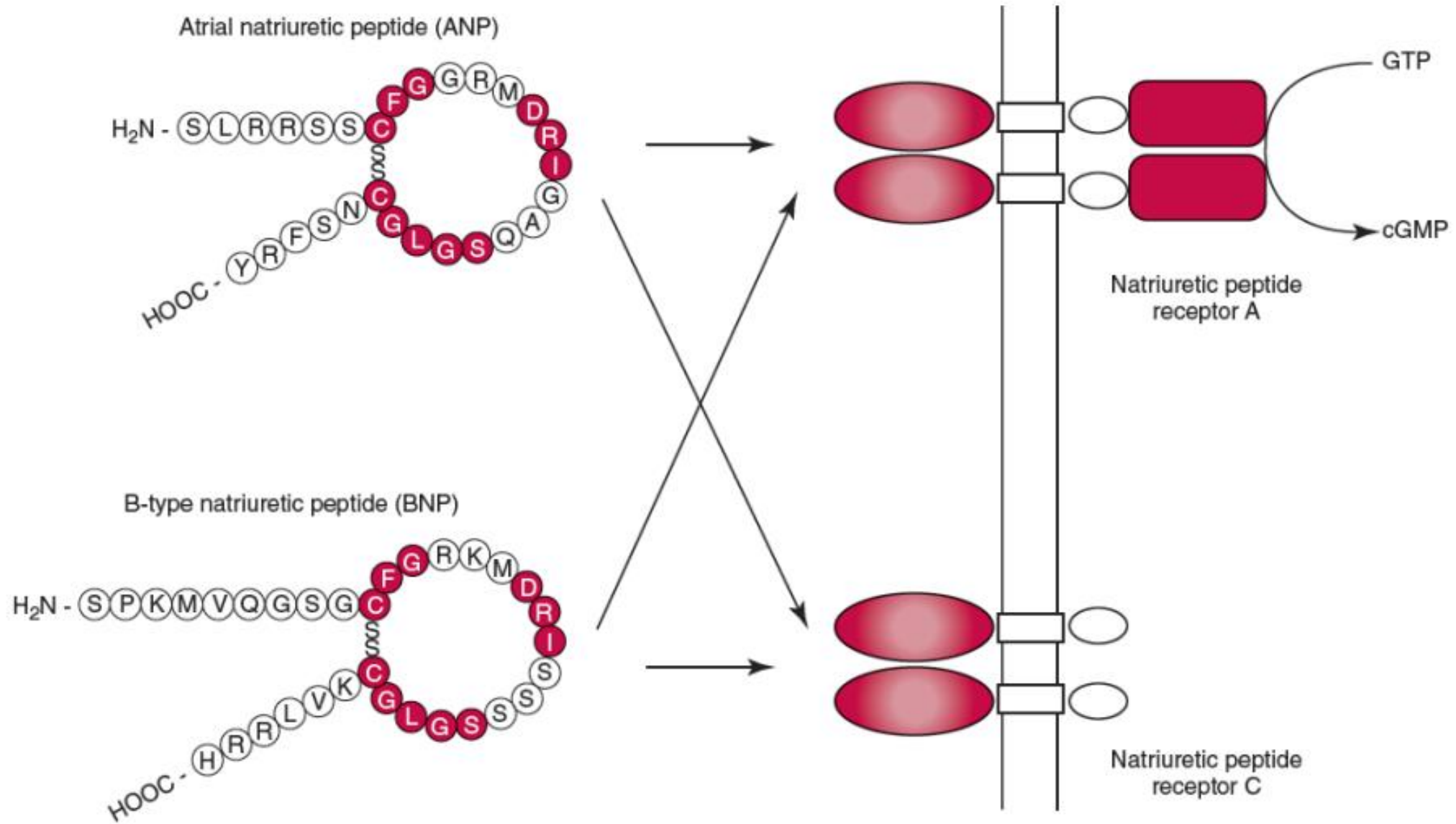
Kardiyak kökenli hormonlar:

- Atrial natriuretic peptide (ANP) – atriumlardan
- Brain (B-type) natriuretic peptide (BNP) – ventriküllerden
- C-type natriuretic peptide (CNP) – merkezi sinir sistemi

Goetze JP, et al. Clin Chim Acta. 2015

McPherson, et al. *Henry's clinical diagnosis and management by laboratory methods* .2021

Rifai, Nader. *Tietz Textbook of Laboratory Medicine-E-Book*. 2022



Appendix 3. Appendix for Tables 3 and 4: Suggested Thresholds for Structural Heart Disease and Evidence of Increased Filling Pressures

Morphology	• LAVI ≥ 29 mL/m² • LVMI $> 116/95$ g/m² • RWT > 0.42 • LV wall thickness ≥ 12 mm
Ventricular systolic function	• LVEF $< 50\%$ • GLS $< 16\%$
Ventricular diastolic function	• Average E/e' ≥ 15 for increased filling pressures • Septal e' < 7 cm/s • Lateral e' < 10 cm/s • TR velocity > 2.8 m/s • Estimated PA systolic pressure > 35 mm Hg
Biomarker	• BNP ≥ 35 pg/mL* • NT-proBNP ≥ 125 pg/mL*

AF indicates atrial fibrillation; BNP, brain natriuretic peptide; CKD, chronic kidney disease; GLS, global longitudinal strain; HF, heart failure; LAVI, left atrial volume index; LV, left ventricular; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; NT-proBNP, natriuretic peptide tests; PA, pulmonary artery; RWT, relative wall thickness; and TR, tricuspid regurgitation.

*Cutoffs provided for natriuretic peptide levels may have lower specificity, especially in older patients or in patients with AF or CKD. Usually, higher cutoff values are recommended for the diagnosis of HF in these patients. Natriuretic peptide cutoffs selected for population screening for pre-HF (stage B HF) may be $< 99\%$ reference limits and need to be defined according to the population at risk.

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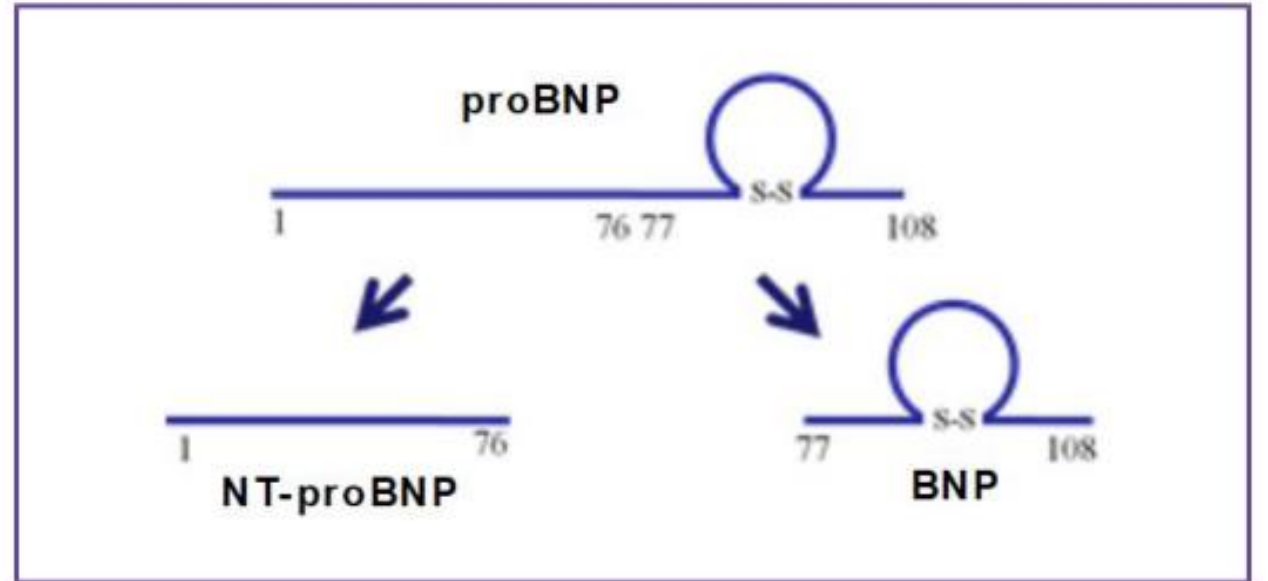
“NT-proBNP 1-76” “BNP-32”

- İki ana bölge:

73-76 proteoliz bölgesi (Arg-Ala-Pro-Arg)

Birinci bölge «proBNP» 1'den 76'ya kadar olan N-terminal fragmanı, inaktif

İkinci bölge, aktif C-terminali «BNP-32» (77 ila 108)



McPherson, et al. Henry's clinical diagnosis and management by laboratory methods .2021

Minamisawa, et al. *Journal of Cardiac Failure*. 2025

TABLE 48.4 Analytical Characteristics of Commercially Available Natriuretic Peptide Assays per the Manufacturer

TABLE 48.4 Analytical Characteristics of Commercially Available Natriuretic Peptide Assays per the Manufacturer		TABLE 48.4 Analytical Characteristics of Commercially Available Natriuretic Peptide Assays per the Manufacturer cont'd				
Assay	NT-proBNP	Assay	Capture Antibody	Detection Antibody	Standard Material	Claim
BNP						
Abbott Architect iSTAT	Alere Triage NT-proBNP	Response Biomedical RAMP	Murine MAb, aa 27–31	Central molecule, polyclonal sheep AB, aa 39–50	Synthetic NT-proBNP 1–76	Diagnosis HF; assess severity HF
Alere ^a Triage BNP	bioMérieux NT-proBNP1 V	Roche NT-proBNP I Elecsys, E170	NH2 terminus polyclonal sheep AB, aa 1–21	Central molecule, polyclonal sheep AB, aa 39–50	Synthetic NT-proBNP 1–76	Diagnosis HF; assess severity HF; risk ACS; risk HF
	NT-proBNP2 V	NT-proBNP II Elecsys, E170	MAb, aa 27–31	Sheep MAb, aa 42–46	Synthetic NT-proBNP 1–76	Treatment monitoring in LVD
Beckman Coulter Access, Access Dxl	Mitsubishi Chemical PATHFAST	Siemens (Dade Behring) Dimension RxL, Stratus CS, Dimension VISTA, Dimension EXL with LM	NH2 terminus monoclonal sheep AB, aa 22–28	Central molecule, Sheep MAb, aa 42–46	Synthetic NT-proBNP 1–76	Aid in the diagnosis of CHF and assessment of severity; risk stratification of patients with ACS and HF
Siemens (Bayer) 180, Advia Centaur	Nanogen LifeSign DXpress Reader	Siemens (DPC) Immulite 1000, 2000 2500	NH2 terminus polyclonal sheep AB, aa 1–21	Central molecule, polyclonal sheep AB, aa 39–50	Synthetic NT-proBNP 1–76	Not FDA cleared
Siemens (Dade Behring) Dimension VISTA, Dimension ExL	Ortho Clinical Diagnostics Vitec ECi					
Shionogi						
Tosoh ST AIA-PAC BNP	Radiometer AQL FLEX NT-proBNP	Thermo Fisher Scientific KRYPTOR	Polyclonal sheep AB, aa 50–72 of NT-proANP	Monoclonal rat AB, aa 73–90 of NT-proANP	Synthetic NTproANP 50–90	Not FDA cleared

Natriüretik Peptidler

- Erken teşhis
 - Triyajı kolaylaştırma
 - Tedavi takibi
 - Kısa ve uzun vadeli sonuçların değerlendirilmesi
-
- Yarı ömür BNP 20 dakika
 - Yarı ömür NT-proBNP 120 dakika

McPherson, et al. *Henry's clinical diagnosis and management by laboratory methods*.2021

Rifai, Nader. *Tietz Textbook of Laboratory Medicine-E-Book*. 2022

Circulation. 2022;145:e895–e1032. 2022 AHA/ACC/HFSA Heart Failure Guideline

Natriüretik Peptidler

- NT-pro BNP düzeyi < 125 pg/mL veya BNP < 35 pg/mL:
diğer tanılar göz önünde bulundurulmalıdır

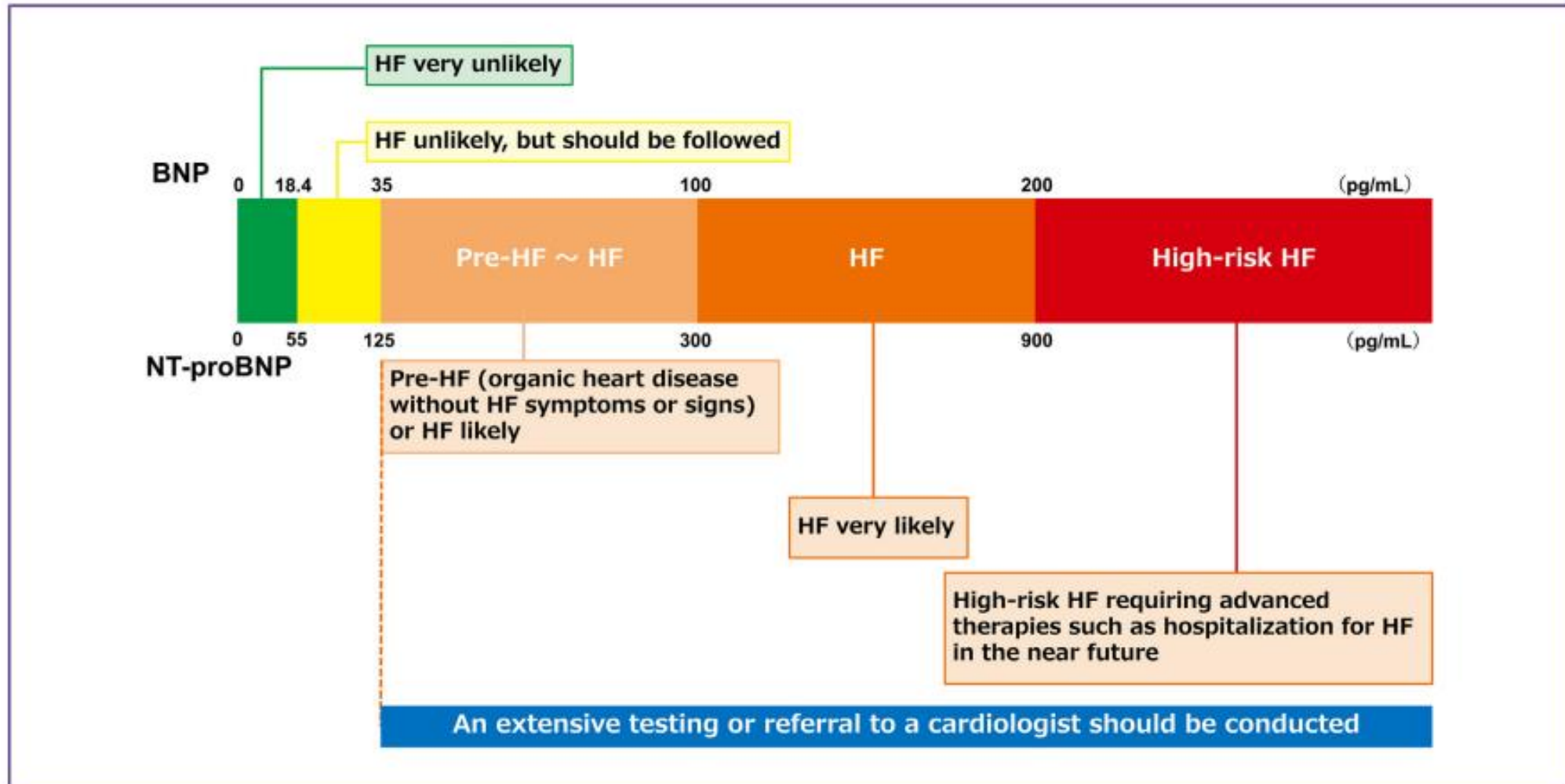
- NT-pro BNP ≥ 125 pg/mL* veya BNP ≥ 35 pg/mL:

*75 yaş üstü için >450 pg/mL

EKO ile KY tanısı

Chow SL, et al. Circulation. 2017

Pan, Shiyang, and Jinhai Tang, eds. *Clinical molecular diagnostics*. Springer Nature, 2021.



Minamisawa, et al. *Journal of Cardiac Failure*. 2025

Natriüretik Peptidler

KY için Yüksek Pozitif Prediktif Değer:

- NT-proBNP:

<50 yaş için >450 pg/mL,

50-75 yaş için >900 pg/mL

>75 yaş için >1800 pg/mL

- BNP >400 pg/mL

Chow SL, et al. Circulation. 2017

Natriüretik Peptidler

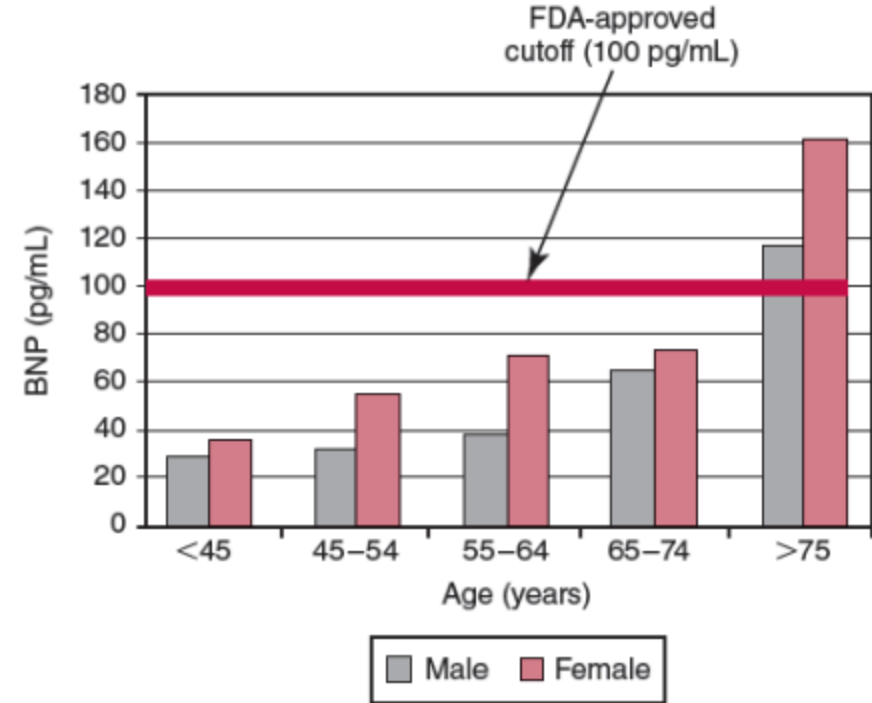
Analiz sorunları:

- HIL*
- Heterofil antikor
- Yüksek biyotin (> 5 mg/gün) ile tedavi
- Romatoid faktör interferansı
- Obezlerde BMI ile NP'ler ters ilişkide
- KRY'de klinik korelasyon zayıf

Farnsworth CW, et al. Clin Biochem 2018;59:50–5

Lewis LK, et al. Clin Chem 2019;65:1115–24

Rifai, Nader. *Tietz Textbook of Laboratory Medicine-E-Book*. 2022



Natriüretik Peptidler

BOX 48.5 Causes of Increased Natriuretic Peptides

1. Acute or chronic systolic or diastolic heart failure
2. Left ventricular hypertrophy
3. Inflammatory cardiac disease
4. Systemic arterial hypertension with left ventricular hypertrophy
5. Pulmonary hypertension
6. Acute or chronic renal failure
7. Ascitic liver cirrhosis
8. Endocrine disorders (e.g., hyperaldosteronism, Cushing syndrome)
9. Sepsis

Rifai, Nader. *Tietz Textbook of Laboratory Medicine-E-Book*. 2022

van Kimmenade et al. *Clin Chem* 2012;58:127–38

Table 6. Selected Potential Causes of Elevated Natriuretic Peptide Levels^{50–53}

Cardiac
HF, including RV HF syndromes
ACS
Heart muscle disease, including LVH
VHD
Pericardial disease
AF
Myocarditis
Cardiac surgery
Cardioversion
Toxic-metabolic myocardial insults, including cancer chemotherapy
Noncardiac
Advancing age
Anemia
Renal failure
Pulmonary: Obstructive sleep apnea, severe pneumonia
Pulmonary embolism, pulmonary arterial hypertension
Critical illness
Bacterial sepsis
Severe burns

ACS indicates acute coronary syndromes; AF, atrial fibrillation; HF, heart failure; LVH, left ventricular hypertrophy; RV, right ventricular; and VHD, valvular heart disease.

- Circulation.
2022;145:e895–e1032.
2022 AHA/ACC/HFSA
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Natriüretik Peptidler

	Kaynak	Total Allowable Error Table
BNP	CLIA	$\pm 30\%$
BNP	The Royal College of Pathologists of Australasia	± 20 ng/L or 20% if > 100 ng/L
Pro B-natriuretic Peptide (proBNP)	CLIA	$\pm 30\%$
B-natriuretic Peptide, Pro (proBNP)	The Royal College of Pathologists of Australasia	± 25 ng/L or 20% if > 125 ng/L

Natriüretik Peptidler

- Reference change value - %

	Within-day	Day-to-day	Week-to-week
BNP	±32	±74	±113
NT-proBNP	±25	±55	±98

Serge Masson, et al. *European Cardiovascular Disease* 2007;3(1):35–8

Bruins S, et al. *Clin Chem* 2004;50:2052–8.

Natriüretik Peptidler

Akut dekompanse KY'de NT-proBNP'de %30 düşüş



daha iyi bir prognoz

BNP %40 veya NT-proBNP %30 artış



KY 'de kötüleşme

Stienen S, et al. Eur J Heart Fail 2015;17:936–4

Meijers WC, et al. Eur J Heart Fail 2017;19:357–65

Gelecekte Beklentiler

- POCT – tam kan ile çalışma
- Yaşlanma
- 2035 yılında ABD nüfusunun %45,1'inin KVH (+)
- 2035 yılında ABD'de KVH maliyeti 1,1 trilyon dolar

Rifai, Nader. *Tietz Textbook of Laboratory Medicine-E-Book*. 2022

Gelecekte Beklentiler

- ST2 (suppression of tumorigenicity 2)

Yaş, böbrek fonksiyonu veya vücut kütlesinden etkilenmez
ST2 düzeylerinin <35 pg/mL olması düşük riski gösterir

- Galektin-3

Fibrotik süreçte etkin

Prognozda etkin

Felker GM, et al. Circ Heart Fail 2012;5:72–8

Aleksova A, et al. J Clin Med 8:270, 2019.

Pan, Shiyang, and Jinhai Tang, eds. *Clinical molecular diagnostics*. Springer Nature, 2021.

Vaka 1

- ProBNP 1.gün 25 pg/mL (<125)
- ProBNP 10. gün <10 pg/mL (<125)
- 5.yıl EF: % 60 – “Evre A” Kalp Yetmezliği Riski Altında

Vaka 2

- Post-op 2.gün apeks ve lateral duvar akinetik, 7 mm perikardiyal sıvı, EF % 10
- 6 ay sonra EF: % 47
- Tanı "HFimpEF"



Vaka 3

- NT pro-BNP: 874 pg/mL
- EF: 33%
- Tanı “HFrEF”

Sözün Özü

- Dispne ayırıcı tanısında hem akut hem kronik durumlarda NP'ler kullanılabilir
- Yüksek NP tanıyı destekler, ancak normal değer tanıyı dışlamaz
- NP seviyesi prognoz ile ilişkilendirilebilir

Referanslar

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- Dunlay SM, Roger VL, Redfield MM. Epidemiology of heart failure with preserved ejection fraction. *Nat Rev Cardiol*. 2017;14:591–602.
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- Virani SS, Alonso A, Aparicio HJ, et al. Heart disease and stroke statistics—2021 update: a report from the American Heart Association. *Circulation*. 2021;143:e254–e743.
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- Chow SL, Maisel AS, Anand I, et al. Role of biomarkers for the prevention, assessment, and management of heart failure: a scientific statement from the American heart association. *Circulation*. 2017;135:e1054–91
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- Peter A. Kavsak, Carolyn S.P. Lam, Amy K. Saenger, Allan S. Jaffe, Paul Collinson, Kari Pulkki, Tobjørn Omland, Guillaume Lefevre, Richard Body, Jordi Ordonez-Llanos and Fred S. Apple*. *Educational Recommendations on Selected Analytical and Clinical Aspects of Natriuretic Peptides with a Focus on Heart Failure: A Report from the IFCC C-CB. Clinical Chemistry* 65:10 1221–1227 (2019).
- Aleksova A, Paldino A, Beltrami AP, et al.: Cardiac biomarkers in the emergency department: the role of soluble ST2 (sST2) in acute heart failure and acute coronary syndrome- there is meat on the bone, *J Clin Med* 8: 270, 2019.
- Stienen S, Salah K, Eurlings LW, et al. Challenging the two concepts in determining the appropriate pre-discharge N-terminal pro-brain natriuretic peptide treatment target in acute decompensated heart failure patients: absolute or relative discharge levels? *Eur J Heart Fail* 2015;17:936–4
- Bayes-Genis A, Richards AM, Maisel AS, et al. Multimarker testing with ST2 in chronic heart failure. *Am J Cardiol* 2015;115:76B–80B
- Lewis LK, Raudsepp SD, Prickett TCR, et al. ProBNP that is not glycosylated at threonine 71 is decreased with obesity in patients with heart failure. *Clin Chem* 2019;65:1115–24
- Farnsworth CW, Bailey AL, Jaffe AS, Scott MG. Diagnostic concordance between NT-proBNP and BNP for suspected heart failure. *Clin Biochem* 2018;59:50–5
- van Kimmenade RR, Januzzi JL, Jr. Emerging biomarkers in heart failure. *Clin Chem* 2012;58:127–38
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“Hasta raporlarındaki rakamlar,
hastaların hayatlarına atılmış imzalardır”

Uzm. Dr. Tarkan YAZICI

Dinlediğiniz ve sabrınız için teşekkürler...