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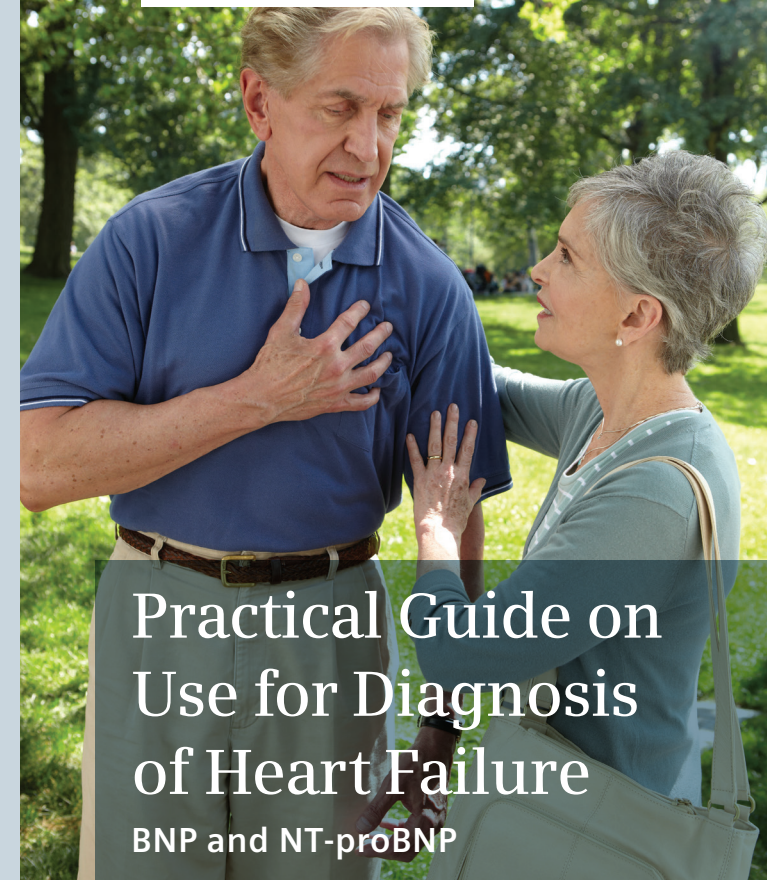
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Practical Guide on Use for Diagnosis of Heart Failure
BNP and NT-proBNP

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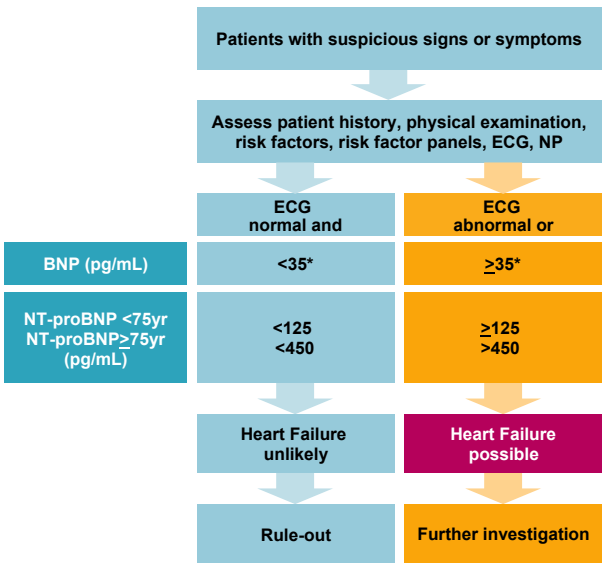# Natriuretic Peptides in the Approach to Dyspnea

In Non-acute Settings

Whom to Test[1-5]

Patients with: symptoms of dyspnea, known coronary artery disease, diabetes, hypertension, greater than 60 years

How to interpret[6-12]

Proposed Algorithm to Rule Out Heart Failure in Non-acute Settings[†]

Patients with suspicious signs or symptoms		
Assess patient history, physical examination, risk factors, risk factor panels, ECG, NP		
	ECG normal and	**ECG abnormal or**
BNP (pg/mL)	**<35***	**≥35***
NT-proBNP <75yr NT-proBNP≥75yr (pg/mL)	**<125 <450**	**≥125 >450**
	Heart Failure unlikely	**Heart Failure possible**
	Rule-out	**Further investigation**

The cut points are included in the Siemens NP assays' labeling.

*The cut point (35 pg/mL) is proposed by the European Society of Cardiology.[4,5]

- The information provided by NPs is incremental to that obtained from established risk factors.[13]
- The higher the value, the greater the risk for cardiovascular morbidity and mortality.[14]

Previously, for BNP, a rule-out value of < 50 pg/mL was proposed as it was reported to further increase the Negative Predictive Value over the recommended cut-off value (< 100 pg/mL) at that time in this setting.[15] NPs are not approved for monitoring.

Impact on Management[1-5]

- If an elevated NP is detected in at-risk individuals, a cardiovascular workup, with therapeutic intervention as appropriate for the cause of the NP elevation, is recommended.
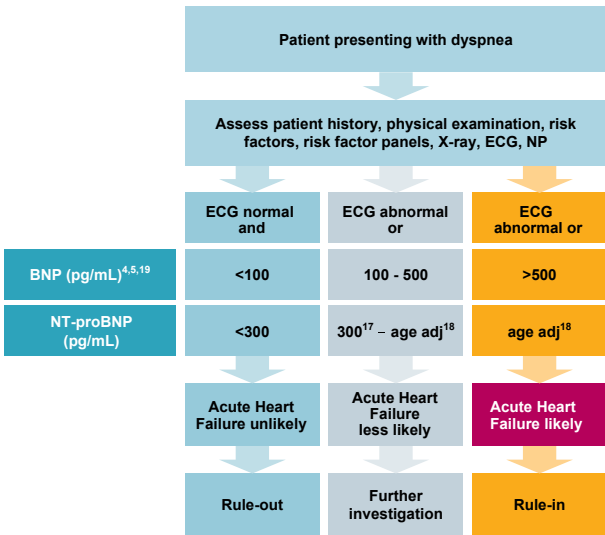
In Acute Settings

Whom to Test[4,5,16]

- Individuals suspected of having heart failure
- Patients arriving at the Emergency Department with dyspnea and/or chest pain

How to Interpret[4,5,16-19]

Proposed Algorithm to Rule Out/Rule In Acute Heart Failure in the Emergency Department[‡]

Patient presenting with dyspnea			
Assess patient history, physical examination, risk factors, risk factor panels, X-ray, ECG, NP			
	ECG normal and	**ECG abnormal or**	**ECG abnormal or**
BNP (pg/mL)[4,5,19]	**<100**	**100 - 500**	**>500**
NT-proBNP (pg/mL)	**<300**	**300[17] – age adj[18]**	**age adj[18]**
	Acute Heart Failure unlikely	**Acute Heart Failure less likely**	**Acute Heart Failure likely**
	Rule-out	**Further investigation**	**Rule-in**

‡The cut points shown are suggested by the BNP Consensus Panel 2004 and the ICON Study using non-Siemens assays and are currently not part of the Siemens NP assays' instructions for use. NPs are not approved for monitoring.

ICON NT-proBNP Age-adjusted Cut Points[18]

Age Strata	Cut Point pg/mL	PPV	NPV
≤50 (n=183)	450	76%	99%
50-75 (554)	900	82%	88%
≥75 (n=513)	1800	92%	55%
Overall Average		88%	66%

- The optimal application of NP testing is in conjunction with a good history, physical exam and knowledge of the differential diagnosis of an elevated NP value (see below).
- The higher the value, the higher the risk for cardiovascular morbidity and mortality. In particular, BNP > 800 pg/mL or NT-proBNP > 5000 pg/mL indicates a higher risk of short-term mortality. Patients with concomitant elevated troponin levels are at even higher risk.[20]

Impact on Management[21,22]

- When used in conjunction with other clinical information, measurement of NPs in an acute setting improves the care of acutely dyspneic patients and reduces time to discharge as well as total cost of treatment.

Prognostic Capabilities of NPs

- In addition to being an aid in the diagnosis and assessment of severity of heart failure, BNP and NT-proBNP are further indicated for the risk stratification of patients with ACS and heart failure.[6-8,11,12]
- In ACS patients, BNP > 80 pg/mL[11] or NT-proBNP > 250 pg/mL[23] is associated with an adverse prognosis which is proportional to the extent of the NP elevation.

Natriuretic peptide elevations can be observed in conditions other than heart failure and ACS, justifying the need for the mandatory incorporation of all clinical data into the interpretation of the NP value. Importantly, these elevated values should not be perceived as false positive due to their strong prognostic associations.[24,25] These conditions include heart muscle diseases, valvular heart disease, arrhythmia, anemia, critical illness, stroke, pulmonary diseases, congenital heart diseases, and chronic kidney disease.[26]

Acute Heart Failure Diagnosis and Prognosis in Patients with Chronic Kidney Disease

For patients with impaired renal function [estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73m^2] higher cut points are needed to ensure the diagnostic accuracy of NPs. For these patients, the following cut points have been proposed:

- 225 pg/mL in place of 100 pg/mL for BNP[27]
- 1200 pg/mL in place of 900 pg/mL for NT-proBNP (if using this single cut point),[28] but no adjustment is needed if using the age-adjusted cut point shown earlier.[29]

Prognostically, these patients are at very high risk of 12-month mortality when BNP > 800 pg/mL or NT-proBNP > 6000 pg/mL.[30]

Other Important Considerations:

Obesity[31,32]

Natriuretic peptide levels can be reduced in obese patients, leading to a false-negative rate of 10 to 20%.

Neonatal / Pediatrics[33]

Concentrations of NPs are markedly elevated during the first hours of life, typically decreasing to normal concentrations after the first week of life. Different BNP cut off values have been proposed for neonates and children.[34]

After the first week, it is reasonable to use the adult-recommended decision values.