The use of HF biomarkers: 2017 guideline update[1,a]

Use	Recommendation	COR	LOE	New/ modified
Prevention	**NP biomarker-based screening followed by team-based care for patients at risk of developing HF**	**IIa**	**B-R**	**New**
Diagnosis	Measurement of NP biomarkers to support diagnosis or exclusion of HF	I	A	**Modified**
Prognosis	Measurement of NP biomarkers to establish prognosis or disease severity for patients with chronic HF	I	A	Same
	Measurement of NP biomarkers and/or cTn at hospital admission for acute decompensated HF	I	A	**Modified**
	Measurement of NP biomarkers during hospitalization to establish post-discharge prognosis	**IIa**	**B-NR**	**New**
Added risk stratification	Measurement of biomarkers of myocardial injury or fibrosis (cTn, gal-3, ST2, and other emerging biomarkers) in patients with chronic HF	IIb	**B-NR**	**Modified**

COR, Class of Recommendation; cTn, cardiac troponin; gal-3, galectin-3; LOE, Level of Evidence; NP, natriuretic peptide; NR, nonrandomized; R, randomized; ST2, suppresor of tumorigenicity-2.
[a]Bolded green text reflects 2017 guideline updates.

The 2017 guideline update made clear, specific recommendations for the use of biomarkers using evidence from recent clinical studies.[1]

References

1. Yancy CW, et al. *Circulation*. 2017;36(6):e137–61.
2. Richards AM, et al. *J Am Coll Cardiol*. 2001;37(7):1781–7.
3. Tang WH, et al. *Circulation*. 2003;108(24):2964–6.
4. Zaphiriou A, et al. *Eur J Heart Fail*. 2005;7:537–41.
5. Son CS, et al. *J Biomed Inform*. 2012;45(5):999–1008.
6. Kelder JC, et al. *Circulation*. 2011;124(25):2865–73.
7. Balion C, et al. [AHRQ website]. 13(14)-EHC118-EF ed. Rockville, MD: 2013.
8. Booth RA, et al. *Heart Fail Rev*. 2014;19:439–51.
9. Dao Q, et al. *J Am Coll Cardiol*. 2001;37(2):379–85.
10. Davis M, et al. *Lancet*. 1994;343(8895):440–4.
11. Maisel AS, et al. *N Engl J Med*. 2002;347(3):161–7.
12. Moe GW, et al. *Circulation*. 2007;115:3103–10.
13. Mueller C, et al. *N Engl J Med*. 2004;350(7):647–54.
14. van Kimmenade RR, et al. *Am J Cardiol*. 2006;98(3):386–90.
15. Januzzi JL Jr, et al. *Am J Cardiol*. 2008;101(3A):29–38.
16. Santaguida PL, et al. *Heart Fail Rev*. 2014;19(4):507–19.
17. Hill SA, et al. *Heart Fail Rev*. 2014;19(4):421–38.
18. Amsterdam EA, et al. *Circulation*. 2014;130(25):e433–4.
19. Ahmad T, et al. *JACC Heart Fail*. 2014;2(3):260–8.
20. Bayes-Genis A, et al. *J Am Coll Cardiol*. 2014;63(2):158–66.
21. Gaggin HK, et al. *JACC Heart Fail.* 2014;2(1):65–72.
22. Ky B, et al. *Circ Heart Fail*. 2012;5(2):183–90.
23. Sabatine MS, et al. *Circulation*. 2012;125(2):233–40.
24. Chow SL, et al. *Circulation*. 2017;135(22):e1054–91.
25. Ledwidge M, et al. *JAMA*. 2013;310:66–74.
26. Huelsmann M, et al. *J Am Coll Cardiol*. 2013;62:1365–72.

The clinical practice guidelines are categorized by Class of Recommendation (COR*) and Level of Evidence (LOE†).
*Reflects the strength of recommendation: I = strong; IIa = moderate; IIb = weak; III = no benefit or harm.
†Reflects the quality of evidence: A = high quality; B = moderate quality; C = limited data or expert opinion.

Biomarker assessments for patients with heart failure

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

The value of biomarker assessments for patients with heart failure (HF)

Biomarkers have been increasingly used to facilitate the diagnosis and help determine the prognosis of patients with HF[1]:

- Substantial evidence supports the use of natriuretic peptide (NP) biomarkers for the diagnosis or exclusion of HF in both the chronic ambulatory[2–8] and acute care settings[9–17]
- Cardiac troponin (cTn) I and T assessments provide prognostic value in patients with acute HF[18]
- Emerging biomarkers, including galectin-3 and suppressor of tumorigenicity 2 (ST2), provide incremental prognostic value over the use of NP biomarkers alone[19–21]
- To guide HF therapy, future clinical trials may show improved outcomes from strategies that combine multiple biomarkers[22,23]

HF biomarkers[1,24]

Marker	Biology	Condition
BNP and NT-proBNP	Increased concentrations of these NP biomarkers occur in response to myocardial stretch that results from increased volume or pressure. Because they track similarly, either may be employed so long as they are not used interchangeably.	HF
cTn	Concentrations of cTn are increased with myocardial necrosis; however, it is not specific to acute coronary syndrome and can be increased in any condition that results in myocardial damage.	MI, HF, CAD
Galectin-3	Increased expression occurs in activated macrophages, which stimulates myocardial remodeling through fibroblast proliferation and collagen deposition. Thus, it represents a link between inflammation and fibrosis.	HF
ST2	An IL-1–receptor family member that is expressed as a transmembrane (ST2L) and soluble isoform (sST2). Increased plasma sST2 concentrations lead to myocardial death and tissue fibrosis.	MI, HF

BNP, B-type natriuretic peptide; CAD, coronary artery disease; cTn, cardiac troponin; HF, heart failure; IL, interleukin; MI, myocardial infarction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; ST2, suppressor of tumorigenicity 2.

Biomarker-based screening is now recommended for the prevention of HF[1]

6.3.1 Biomarkers for Prevention: Recommendation

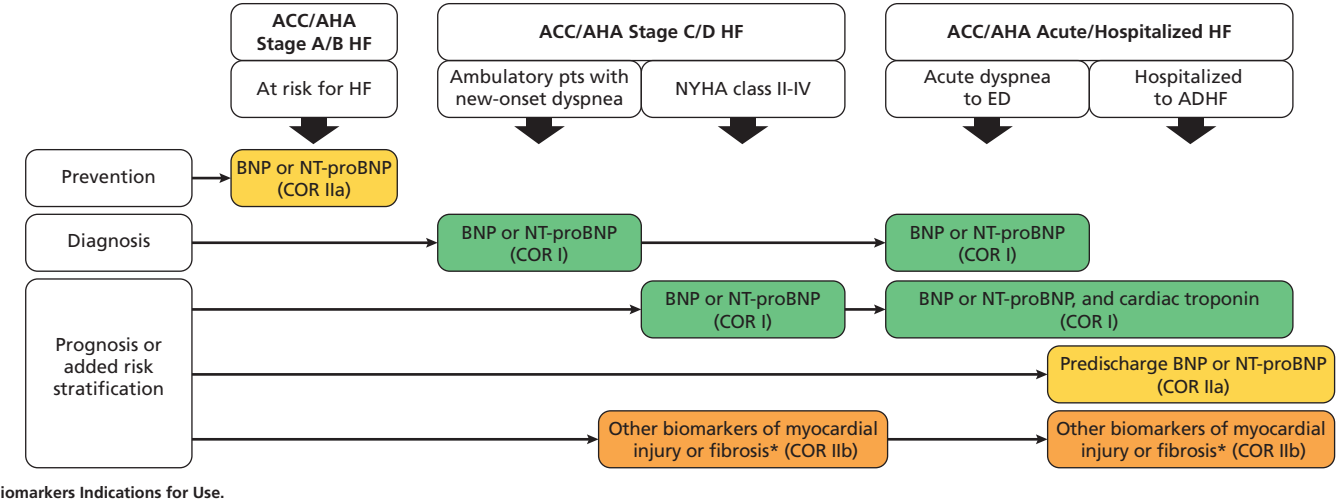
Biomarkers: Recommendation for Prevention of HF

COR*	LOE†	Recommendation	Comment/Rationale
IIa	B-R	**For patients at risk of developing HF, natriuretic peptide biomarker–based screening followed by team-based care, including a cardiovascular specialist optimizing GDMT, can be useful to prevent the development of left ventricular dysfunction (systolic or diastolic) or new-onset HF.[25,26]**	**NEW:** New data suggest that natriuretic peptide biomarker screening and early intervention may prevent HF.
See Online Data Supplements A and B.			

In a large-scale unblinded single-center study (STOP-HF [The St Vincent's Screening to Prevent Heart Failure]),[25] patients at risk of HF (identified by the presence of hypertension, diabetes mellitus, or known vascular disease [eg, stage A HF]), but without established left ventricular systolic dysfunction or symptomatic HF at baseline, were randomly assigned to receive screening with BNP testing or usual primary care. Intervention-group participants with BNP levels of ≥50 pg/mL underwent echocardiography and were referred to a cardiovascular specialist who decided on further investigation and management. All patients received further coaching by a specialist nurse who emphasized individual risk and the importance of adherence to medication and healthy lifestyle behaviors. BNP-based screening reduced the composite endpoint of asymptomatic left ventricular dysfunction (systolic or diastolic) with or without newly diagnosed HF.[25] Similarly, in another small, single-center RCT, accelerated up-titration of renin-angiotensin-aldosterone system antagonists and beta blockers reduced cardiac events in patients with diabetes mellitus and elevated NT-proBNP levels but without cardiac disease at baseline.[26] Developing a standardized strategy to screen and intervene in patients at risk of HF can be difficult because of different definitions of HF risk, heterogeneity of prevalence in different populations, variable duration until clinical HF or left ventricular dysfunction develops, and variable interventions for risk factor modification or treatment. Further studies are needed to determine cost-effectiveness and risk of such screening, as well as its impact on quality of life (QoL) and mortality rate.

COR, Class of Recommendation; GDMT, guideline-directed medical therapy; HF, heart failure; LOE, Level of Evidence; R, randomized; RCT, randomized controlled trial.

BNP and NT-proBNP biomarkers are widely accepted for HF diagnosis and management[1,24]



Biomarkers Indications for Use.
*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.