Summary guidelines for the utilization of Natriuretic Peptides in managing CHF

The 2014 Canadian Cardiovascular Society Heart Failure Management Guidelines Focus Update: Anemia, Biomarkers, and Recent Therapeutic Trial Implications[1]

Optimal Use of Biomarkers in HF

RECOMMENDATIONS

1. We recommend that B-type NP (BNP)/amino-terminal fragment of propeptide BNP (NT-proBNP) levels be measured to help confirm or rule out a diagnosis of HF in the acute or ambulatory care setting in patients in whom the clinical diagnosis is in doubt (Strong Recommendation; High-Quality Evidence).
2. We recommend that measurement of BNP/NT-proBNP levels be considered in patients with an established diagnosis of HF for prognostic stratification (Strong Recommendation; High-Quality Evidence).

Values and Preferences. These recommendations remain unchanged from previous CCS HF guidelines. The levels of NPs for ruling in and ruling out a diagnosis of HF are shown in Table 1.

Table 1. Natriuretic peptides cut points for the diagnosis of heart failure

	Age, Years	HF is unlikely	HF is possible but other diagnoses need to be considered	HF is very likely
BNP	All	< 100 pg/mL	100-500 pg/mL	> 500 pg/mL
NT-proBNP	< 50	< 300 pg/mL	300-450 pg/mL	> 450 pg/mL
	50-75	< 300 pg/mL	450-900 pg/mL	> 900 pg/mL
	> 75	< 300 pg/mL	900 - 1800 pg/mL	> 1800 pg/mL

BNP, B-type natriuretic peptide; HF, heart failure; NT-proBNP, amino-terminal fragment propeptide B-type natriuretic peptide.

NP-guided management

RECOMMENDATIONS

1. We suggest, in ambulatory patients with HF due to systolic dysfunction, measurement of BNP or NT-proBNP to guide management should be considered to decrease HF-related hospitalizations and potentially reduce mortality. The benefit is uncertain in individuals older than 75 years of age (Weak Recommendation; Moderate-Quality Evidence).

Values and Preferences. These recommendations are based on multiple small RCTs, most of which demonstrated benefit, and 3 meta-analyses, which universally demonstrated benefit. It is realized that there is still a large RCT ongoing that might modify the conclusions.

Hospital pre-discharge NP measurements
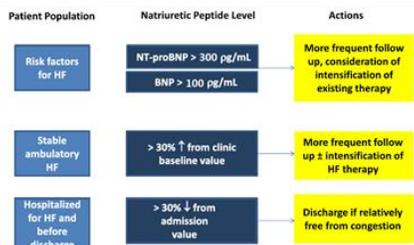
RECOMMENDATIONS

1. We suggest that measurement of BNP or NT-proBNP in patients hospitalized for HF should be considered before discharge, because of the prognostic value of these biomarkers in predicting rehospitalization and mortality (Strong Recommendation; Moderate-Quality Evidence).

Values and Preferences. This recommendation is based on multiple small RCTs, all of which demonstrated an association with clinical outcomes. Although the risk of readmission is decreased with lower NP levels, clinicians should also consider the limitations of delaying discharge from the hospital for this purpose.

Practical Tip: We suggest that individuals with risk factors for the development of HF, NP levels be used to implement strategies to prevent HF. An increased level of NP of BNP > 100 pg/mL and NT-proBNP > 300 pg/mL, higher values than those used in the 2 trials discussed below to avoid over screening, along with the presence of risk factors for HF, should at least trigger more intensive follow-up (see Prevention of HF).

A change of 30% in NP level likely exceeds the day-to-day variation and is in general considered relevant.[64] For ambulatory patients with HF who are evaluated in the clinic, a NP level that increases more than 30% should therefore call for more intensive follow-up and/or intensified medical treatments, even if they are not congested clinically. The latter can include diuretic therapy or intensification of ACE inhibitors, β-blockers, and mineralocorticoid receptor antagonists if their doses are not yet at the targets defined in clinical trials.

For patients who are about to be discharged from the hospital, physicians should ensure that the patients are relatively free from congestion clinically and with a NP level that is significantly lower than that on admission for HF. A suggested algorithm for management of different stages of HF using NP is shown in Figure 3.

Patient Population	Natriuretic Peptide Level	Actions
Risk factors for HF	NT-proBNP > 300 pg/mL / BNP > 100 pg/mL	More frequent follow up, consideration of intensification of existing therapy
Stable ambulatory HF	> 30% ↑ from clinic baseline value	More frequent follow up ± intensification of HF therapy
Hospitalized for HF and before discharge	> 30% ↓ from admission value	Discharge if relatively free from congestion

Figure 3. Algorithm of the use of natriuretic peptide in the prevention and management of ambulatory and hospitalized patients with heart failure. Clinical evaluation and the risks and benefits of the action suggested should be considered. BNP, B-type natriuretic peptide; HF, heart failure; NT-proBNP, amino-terminal fragment propeptide B-type natriuretic peptide.

Biomarkers: Recommendations

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A. Ambulatory/Outpatient

Class I

1. In ambulatory patients with dyspnea, measurement of BNP or N-terminal pro-B-type natriuretic peptide (NT-proBNP) is useful to support clinical decision making regarding the diagnosis of HF, especially in the setting of clinical uncertainty.[217-223] (*Level of Evidence: A*)
2. Measurement of BNP or NT-proBNP is useful for establishing prognosis or disease severity in chronic HF.[222,224-229] (*Level of Evidence: A*)

Class IIa

1. BNP- or NT-proBNP–guided HF therapy can be useful to achieve optimal dosing of GDMT in select clinically euvolemic patients followed in a well-structured HF disease management program.[230-237] (*Level of Evidence: B*)

Class IIb

1. The usefulness of serial measurement of BNP or NT-proBNP to reduce hospitalization or mortality in patients with HF is not well established.[230-237] (*Level of Evidence: B*)
2. Measurement of other clinically available tests such as biomarkers of myocardial injury or fibrosis may be considered for additive risk stratification in patients with chronic HF.[238-244] (*Level of Evidence: B*)

B. Hospitalized/Acute

Class I

1. Measurement of BNP or NT-proBNP is useful to support clinical judgment for the diagnosis of acutely decompensated HF, especially in the setting of uncertainty for the diagnosis.[212,245-250] (*Level of Evidence: A*)
2. Measurement of BNP or NT-proBNP and/or cardiac troponin is useful for establishing prognosis or disease severity in acutely decompensated HF.[248,251-258] (*Level of Evidence: A*)

Class IIb

1. The usefulness of BNP- or NT-proBNP–guided therapy for acutely decompensated HF is not well established.[259,260] (*Level of Evidence: C*)
2. Measurement of other clinically available tests such as biomarkers of myocardial injury or fibrosis may be considered for additive risk stratification in patients with acutely decompensated HF.[248,253,256,257,261-267] (*Level of Evidence: A*)

Table 23. ESC Definition of Advanced HF

1. Severe symptoms of HF with dyspnea and/or fatigue at rest or with minimal exertion (NYHA class III or IV)

2. Episodes of fluid retention (pulmonary and/or systemic congestion, peripheral edema) and/or reduced cardiac output at rest (peripheral hypoperfusion)

3. Objective evidence of severe cardiac dysfunction shown by at least 1 of the following:
   a. LVEF <30%
   b. Pseudonormal or restrictive mitral inflow pattern
   c. Mean PCWP >16 mm Hg and/or RAP >12 mm Hg by PA catheterization
   d. High BNP or NT-proBNP plasma levels in the absence of noncardiac causes

4. Severe impairment of functional capacity shown by 1 of the following:
   a. Inability to exercise
   b. 6-Minute walk distance ≤300 m
   c. Peak V_{O_2} <12 to 14 mL/kg/min

5. History of ≥1 HF hospitalization in past 6 mo

6. Presence of all the previous features despite "attempts to optimize" therapy, including diuretics and GDMT, unless these are poorly tolerated or contraindicated, and CRT when indicated

BNP indicates B-type natriuretic peptide; CRT, cardiac resynchronization therapy; ESC, European Society of Cardiology; GDMT, guideline-directed medical therapy; HF, heart failure; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; PA, pulmonary artery; PWCP, pulmonary capillary wedge pressure; and RAP, right atrial pressure.
Adapted from Metra et al.[32]

References

1. Moe, G. W. *et al.* The 2014 Canadian Cardiovascular Society Heart Failure Management Guidelines Focus Update: anemia, biomarkers, and recent therapeutic trial implications. *Can. J. Cardiol.* **31,** 3–16 (2015).
2. WRITING COMMITTEE MEMBERS *et al.* 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation* **128,** e240-327 (2013).