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Clinical Utilization of Biomarker in Heart Failure : Current Guidelines

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So many (bio)-markers for Dx, Tx and risk stratification for heart failure!!

- **Standard Laboratory Markers**
  - Na+
  - BUN
  - Cr
  - Hb
  - WBC count
  - Lymphocyte count
  - RBC distribution width
  - Serum albumin
  - Total bilirubin
  - Uric acid
- **Neurohormones**
  - Catecholamines (norepinephrine, epinephrine)
  - Renin, ACE activity, angiotensin II, aldosterone
  - Natriuretic peptides (ANP, BNP, C-type, NT proANP, NT proBNP, mid-regional proANP)
  - Endothelin-1
  - Vasopressin/copeptin
  - Cardiotrophin-1
  - Novel vosodilators (adrenomedullin, mid-regional pro-adrenomedullin, urotensin-II, urocortin)

So many (bio)-markers for Dx, Tx and risk stratification for heart failure!!

- **Inflammatory Markers**
  - hsCRP
  - Myeloperoxidase
  - Galectin-3
  - Fatty acid binding protein
  - Soluble ST2 receptor
  - TNFα and receptors
  - Interleukin-6
  - Growth differentiation factor 15
  - Osteopontin
- **Metabolic Markers**
  - Leptin
  - Adiponectin
  - Ghrelin
  - Apelin
  - IGF-1
- **Other Miscellaneous Markers**
  - G-protein coupled receptor kinase-2 (GRK-2)
  - Cardiac troponin I or T
  - Myotrophin
  - ……

Which to select and how to utilize at bed-side??

ACC/AHA Practice Guidelines

ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure)

Recommendations for the Initial Clinical Assessment of Patients Presenting With HF

Class IIa

Measurement of B-type natriuretic peptide (BNP) can be useful in the evaluation of patients presenting in the urgent care setting in whom the clinical diagnosis of HF is uncertain. (*Level of Evidence: A*)

Class III

Routine measurement of circulating levels of neurohormones (e.g., norepinephrine or endothelin) is not recommended for patients presenting with HF. (*Level of Evidence: C*)

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Recommendations for Serial Clinical Assessment of Patients Presenting With HF

Class IIb

The value of serial measurements of BNP to guide therapy for patients with HF is not well established. (*Level of Evidence: C*)

ESC Guidelines

Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005)

The Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology

Natriuretc peptides

……

In clinical practice today, the place of BNP and NT-proBNP is as ‘rule out’ tests to exclude significant cardiac disease. Particularly in primary care but also in certain aspects of secondary care (e.g. the emergency room and clinics.) The cost-effectiveness of the test suggest that a normal result (*in untreated patients*) should obviate the need for further cardiological tests such as in the first instance echocardiography as well as more expensive investigations.

ESC Guidelines

Executive summary of the guidelines on the diagnosis and treatment of acute heart failure

The Task Fo…the European So…

Table 3 Laboratory tests in patients hospitalized with AHF

Blood count	Always
Platelet count	Always
INR	If patient anticoagulated or in severe heart failure
CRP	Always
D-dimer	Always (may be falsely positive if CRP elevated or patient has been hospitalized for prolonged period)
Urea and Electrolytes (Na^+, K^+, Urea, Creatinine)	Always
Blood glucose	Always
CKMB, cardiac TnI/TnT	Always
Arterial blood gases	In severe heart failure, or in diabetic patients
Transaminases	To be considered

troponin I; TnT = troponin T.

…… If AHF is confirmed, increased levels of plasma BNP and NT-proBNP carry important prognostic information. The exact role of BNP remains to be fully clarified.

HFSA 2006 Comprehensive Heart Failure Practice Guideline

HFSA 2006 Comprehensive Heart Failure Practice Guideline

Evaluation of Patients at Risk

Determination of plasma BNP or NT-proBNP concentration is not recommended as a routine part of the evaluation for structural heart disease in patients at risk but without signs or symptoms of HF. (Strength of Evidence = B)

Evaluation of Patients Suspected of Having HF

It is recommended that BNP or NT-proBNP levels be assessed in all patients suspected of having HF when the diagnosis is not certain. (Strength of Evidence = B)

Evaluation and Management of Patients With Acute Decompensated HF (ADHF)

When the diagnosis (of ADHF) is uncertain, determination of BNP or NT-proBNP concentration should be considered in patients being evaluated for dyspnea who have signs and symptoms compatible of HF. (Strength of Evidence = A)

Status of Biomarkers in Heart Failure Guidelines

	Initial Evaluation		Treatment Guidance	Prognostification
	At Risk	Symptomatic		
ACC/AHA 2005		BNP* (Class IIa, *LOE A*) Other neurohormones (Class III, *LOE C*)	BNP (Class IIb, *LOE C*)	
ESC 2005		BNP*: be considered (CRP: always) CK-MB: always Cardiac TnI/T: always		BNP?
HFSA 2006	BNP (routine): not recommended, *SOE B*	BNP*: recommended, *SOE B* should be considered, *SOE A*†		

* Or NT-proBNP; When diagnosis is not certain

† When diagnosis of ADHF is not certain

LOE, level of evidence

SOE, strength of evidence

ACC/AHA, ESC

Classes of recommendations

Class I Evidence and/or general agreement that a given diagnostic procedure/treatment is beneficial, useful, and effective

Class II Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of treatment

Class IIa Weight of evidence/opinion is in favor of usefulness/ efficacy

Class IIb Usefulness/ efficacy is less well established by evidence/ opinion

Class III Evidence or general agreement that the treatment is not useful/ effective and in some cases may be harmful

Levels of evidences (LOE)

LOE A Data derived from multiple randomized clinical trials or meta-analyses

LOE B Data derived from a single randomized clinical trial or large non-randomized studies

LOE C Consensus opinion of the experts and/or small studies

HFSA

Strength of recommendations

"Is recommended"

"Should be considered"

"May be considered"

"Is not recommended"

Strength of evidences (SOE)

SOE A Randomized, controlled, clinical trials
May be assigned based on results of a single trial

SOE B Cohort and case-control studies
Post-hoc, subgroup analysis, and meta-analyses, prospective observational studies or registries

SOE C Expert opinion
Observational studies-epidemiologic finding, safety reporting from large-scale use in practice

National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: Clinical Utilization of Cardiac Biomarker Testing in Heart Failure

Important Goals of Clinical Biomarker Testing in the Setting of Heart Failure

- Identify possible underlying (and potentially reversible) causes of heart failure
- Confirm the presence or absence of the heart failure syndrome
- Estimate the severity of heart failure and risk of disease progression

Important Considerations in Clinical Biomarker Testing

- C
- Clinical evidence that biomarker testing is helpful or useful

BNP or NT-proBNP and cardiac troponin I/T as recommended biomarkers in clinical practice as of 2007

Clinical Utilization : Current Guidelines

- Initial evaluation of HF

  Dx of HF

  Risk stratification

- Screening for cardiac dysfunction

  Screening of HF (stage A, B)

- Guiding management of HF

Clinical Utilization : Current Guidelines

- Initial evaluation of HF

  Dx of HF

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Clinical Utilization : Current Guidelines

- Initial evaluation of HF

  Dx of HF

Class I	BNP or NT-proBNP in acute setting to *rule out* or *to confirm* Dx of HF among patients with ambiguous signs or symptoms. (*LOE: A*)
Class IIa	BNP or NT-proBNP in non-acute setting to *exclude* Dx of HF among patients with signs or symptoms suspicious of HF. (*LOE: C*)
Class III	BNP or NT-proBNP as routine testing for patients with obvious clinical Dx of HF. (*LOE: C*) BNP or NT-proBNP testing to *replace* conventional clinical evaluation or assessment of degree of LV structural or functional abnormalities. (*LOE: C*)

Clinical Utilization : Current Guidelines

- Initial evaluation of HF

  Risk stratification

Class IIa	BNP or NT-proBNP for additional risk stratification in selected situations (e.g. ACS, stable CAD, stable chronic HF, decomensated HF, pulmonary embolism). (LOE: A) Serial BNP or NT-proBNP testing for additional risk stratification in selected situations (e.g. chronic HF, ACS). (LOE: B)
Class IIb	Cardiac troponin to identify patients at increased risk beyond the setting of ACS. (LOE: B)
Class III	Routine biomarker testing for the *sole* purpose of risk stratification. (*LOE: B*)

Clinical Utilization : Current Guidelines

- Initial evaluation of HF

  Dx of HF

  Risk stratification

- Screening for cardiac dysfunction

  Screening of HF (stage A, B)

- Guiding management of HF

Clinical Utilization : Current Guidelines

- Screening for cardiac dysfunction

  Screening of HF (stage A, B)

  Class IIb BNP or NT-proBNP to identify selected patients with LV systolic dysfunction in post-MI setting or to identify patients at high risk of developing HF (e.g. Hx of MI, diabetes, long-term hypertension, CAD, elderly) (*LOE: B*)

  Class III *Routine* BNP or NT-proBNP testing for screening large asymptomatic patients population for LV dysfunction. (*LOE: B*)

Clinical Utilization : Current Guidelines

- Initial evaluation of HF

  Dx of HF

  Risk stratification

- Screening for cardiac dysfunction

  Screening of HF (stage A, B)

- Guiding management of HF

Clinical Utilization : Current Guidelines

- Guiding management of HF

Class III *Routine* BNP or NT-proBNP testing for making specific therapeutic decision for patients with acute or chronic HF. (*LOE: B*)

Summary and Conclusion

- Numerous biomarkers are available or under study in HF, but their clinical role remains to be determined and validated.
- Among them, BNP or NT-proBNP and cardiac troponins are most extensively investigated clinically.
- Thus, current practice guidelines address appropriate clinical use of BNP or NT-proBNP and cardiac troponins testing in Dx, risk stratification, and management of HF.
- However, guidelines are subject to change with further clinical studies.