



## Complete Summary

---

### GUIDELINE TITLE

National Academy of Clinical Biochemistry laboratory medicine practice guidelines: Clinical utilization of cardiac biomarker testing in heart failure.

### BIBLIOGRAPHIC SOURCE(S)

Tang WH, Francis GS, Morrow DA, Newby LK, Cannon CP, Jesse RL, Storrow AB, Christenson RH, Apple FS, Ravkilde J, Wu AH, National Academy of Clinical Biochemistry Laboratory Medicine. National Academy of Clinical Biochemistry Laboratory Medicine practice guidelines: Clinical utilization of cardiac biomarker testing in heart failure. *Circulation* 2007 Jul 31;116(5):e99-109. [148 references] [PubMed](#)

Tang WH, Francis GS, Morrow DA, Newby LK, Cannon CP, Jesse RL, Storrow AB, Christenson RH, NACB Committee. National Academy of Clinical Biochemistry laboratory medicine practice guidelines: clinical utilization of cardiac biomarker testing in heart failure. *Clin Biochem* 2008 Mar;41(4-5):210-21. [PubMed](#)

### GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Wu AH, Apple FS, Gibler WB, Jesse RL, Warsaw MM, Valdes R Jr. National Academy of Clinical Biochemistry Standards of Laboratory Practice: recommendations for the use of cardiac markers in coronary artery diseases. *Clin Chem* 1999 Jul;45(7):1104-21. [119 references] [PubMed](#)

## \*\* REGULATORY ALERT \*\*

### FDA WARNING/REGULATORY ALERT

**Note from the National Guideline Clearinghouse:** This guideline references a drug(s)/intervention(s) for which important revised regulatory and/or warning information has been released.

- [June 8, 2007, Troponin-I Immunoassay](#): Class I Recall of all lots of the Architect Stat Troponin-I Immunoassay. The assay may report falsely elevated or falsely decreased results at and near a low level, which may impact patient treatment.

## COMPLETE SUMMARY CONTENT

\*\* REGULATORY ALERT \*\*

SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis  
RECOMMENDATIONS  
EVIDENCE SUPPORTING THE RECOMMENDATIONS  
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS  
QUALIFYING STATEMENTS  
IMPLEMENTATION OF THE GUIDELINE  
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT  
CATEGORIES  
IDENTIFYING INFORMATION AND AVAILABILITY  
DISCLAIMER

## SCOPE

### **DISEASE/CONDITION(S)**

Heart failure

### **GUIDELINE CATEGORY**

Diagnosis  
Management  
Risk Assessment  
Screening

### **CLINICAL SPECIALTY**

Cardiology  
Emergency Medicine  
Family Practice  
Internal Medicine  
Pathology

### **INTENDED USERS**

Advanced Practice Nurses  
Allied Health Personnel  
Clinical Laboratory Personnel  
Emergency Medical Technicians/Paramedics  
Health Care Providers  
Hospitals  
Nurses  
Physician Assistants  
Physicians

### **GUIDELINE OBJECTIVE(S)**

- To provide analytical and clinical guidance for the measurement and interpretation of cardiac biochemical markers of heart failure
- To present recommendations on the clinical use of B-type natriuretic peptide (BNP)/N-terminal pro-BNP (NT-proBNP) and cardiac troponin testing in the

context of heart failure diagnosis, risk stratification and management, including therapeutic guidance in adult patients

### **TARGET POPULATION**

Adult patients with suspected or known heart failure

### **INTERVENTIONS AND PRACTICES CONSIDERED**

Use of biochemical markers (B-type natriuretic peptide [BNP]/N-terminal pro-BNP [NT-proBNP] and cardiac troponin) in the evaluation of heart failure and screening for cardiac dysfunction

### **MAJOR OUTCOMES CONSIDERED**

Clinical effectiveness (sensitivity and specificity) and prognostic/therapeutic utility of clinical biomarker testing in heart failure

## **METHODOLOGY**

### **METHODS USED TO COLLECT/SELECT EVIDENCE**

Hand-searches of Published Literature (Primary Sources)  
Searches of Electronic Databases  
Searches of Unpublished Data

### **DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE**

These National Academy of Clinical Biochemistry (NACB) guidelines were developed rigorously; however it was possible to include only papers published in the English language. The specified method for developing the evidence base for recommendations listed involved use of PubMed, EMBASE, and other databases that were not necessarily published. Systematic methods were used whenever available; searches were first set to be sensitive to avoid missing papers of possible interest, and then narrowed to sort through the literature in order to enhance specificity. The writing group contacted recognized experts to assure that important evidence had not been missed. Literature up to June 2007 was included in this search.

### **NUMBER OF SOURCE DOCUMENTS**

Not stated

### **METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Weighting According to a Rating Scheme (Scheme Given)

### **RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

## **Weight of Evidence**

**A** - Data derived from multiple randomized or appropriately designed clinical trials that involved large numbers of patients

**B** - Data derived from a limited number of randomized or appropriately designed trials that involved small numbers of patients or from careful analyses of observational registries

**C** - Expert Consensus was the primary basis for the recommendation

## **METHODS USED TO ANALYZE THE EVIDENCE**

Systematic Review

## **DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

Not stated

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

The National Academy of Clinical Biochemistry's (NACB) Laboratory Medicine Practice Guidelines (LMPG) for use of cardiac markers in coronary artery diseases were published in July of 1999. Since production of this initial document, numerous published studies and presented data have added significantly to the knowledge base for cardiac biomarkers. This increased knowledge has substantially expanded the scope of recommendations for cardiac biomarker utilization since the 1999 document, and in particular has required the inclusion of recommendations regarding biomarkers that extend beyond myocardial necrosis. Toward addressing these advances and their impact on biomarker utilization in clinical practice, the NACB appointed a chair and members of a LMPG committee that was charged with the overall objective of revising and extending the earlier recommendations by establishing modern guidelines for Utilization of Biomarkers in Acute Coronary Syndrome and Heart Failure. This LMPG is aimed at providing analytical and clinical guidance for the measurement and interpretation of cardiac biochemical markers of acute coronary syndromes (ACS), heart failure and point-of-care measurement and logistics of providing ACS biomarker data for patient care; guidance for interpretation of biomarkers in etiologies other than ACS and Heart Failure is included as well.

These guidelines and their recommendations are structured into six chapters that include Chapter 1: Clinical Utilization of Biomarkers in Acute Coronary Syndromes (ACS); Chapter 2: Analytical Issues of ACS Biomarkers; Chapter 3: Clinical Utilization of Biomarkers of Heart Failure; Chapter 4: Analytical Issues of Heart Failure Biomarkers; Chapter 5: Point of Care Testing and Logistics; and Chapter 6: Cardiac Biomarkers and Other Etiologies. Each chapter was spearheaded by a

writing group, which was a subset of the overall committee. In addition, other ad hoc expertise contributed to the writing group of some subsections and chapters to optimize the content and quality of the guidelines. The "questions" for each chapter are in the form of issues addressed and specified in the organization of each individual chapter. The chapter design of the guidelines was used to facilitate finding guidance by users; this format was also used, in part, to provide an easy and focused procedure for updating the guidelines in the future. Also, the chapter design allowed publication of sections in appropriate laboratory medicine and clinical specialty journals.

Stakeholder involvement in development and refinement of these guidelines was substantial. The guideline team was comprised of laboratory medicine, ACS cardiology experts, and heart failure cardiology experts. As these guidelines target acutely ill patients, Emergency Medicine stakeholders were represented by a specialist; it is also noteworthy that all of the laboratory professionals and cardiology experts on the guideline committee have substantial interaction, knowledge, and publications in the area of laboratory and clinical medicine in the Emergency Medicine environment.

## **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

### **Modified American College of Cardiology/American Heart Association Classifications: Summary of Indications**

**Class I:** Conditions for which there is evidence and/or general agreement that a given laboratory procedure or treatment is useful and effective.

**Class II:** Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a laboratory procedure or 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:** Conditions for which there is evidence and/or general agreement that the laboratory procedure/treatment is not useful/effective and in some cases may be harmful.

## **COST ANALYSIS**

The guideline developers reviewed published cost analyses.

- Although somewhat controversial, there is evidence that use of natriuretic peptide testing in the context of heart failure decreases cost without increasing patient risk. Costs were considered by the committee in formulating recommendations; however, the costs were considered modest compared with the total care of heart failure patients, and this view is supported by evidence.
- In a recent randomized controlled trial comparing a diagnostic strategy involving blood B-type natriuretic peptide (BNP) testing versus clinical

- assessment alone, blood BNP testing in the emergency department improved the evaluation and treatment of patients with acute dyspnea, reducing the time to discharge and the total cost of treatment.
- Blood BNP or N-terminal pro-BNP (NT-proBNP) testing can be helpful to identify selected patients with left ventricular systolic dysfunction in the post-infarction setting or to identify patients at high risk of developing heart failure (e.g., history of myocardial infarction, diabetes mellitus). However, the diagnostic ranges and cost-effectiveness in different populations remain controversial.

## METHOD OF GUIDELINE VALIDATION

Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Stakeholder involvement in development and refinement of these guidelines was substantial. To further enhance stakeholder input, draft revisions of the Guidelines were prepared and placed for comment on the National Academy of Clinical Biochemistry (NACB) World Wide Web site (<http://www.aacc.org/AACC/members/nacb/LMPG/OnlineGuide/DraftGuidelines/BoHearFailure/>). The draft Laboratory Medicine Practice Guidelines (LMPG) and suggested revisions were also presented for public and stakeholder comment at the October 2004 Arnold O. Beckman Conference titled *Cardiac Markers: Establishing Guidelines and Improving Results*. Refer to Table 1 of the Preamble to the original guideline document for a list of the various stakeholder groups that agreed to examine the documents and were represented at the conference.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Definitions of the weight of evidence (A-C) and the summary of indications (Classes I, II, IIa, IIb, III) are presented at the end of the "Major Recommendations" field.

**Note from the National Academy of Clinical Biochemistry (NACB) and the National Guideline Clearinghouse (NGC):** The Laboratory Medicine Practice Guidelines (LMPG) for utilization of biochemical markers in acute coronary syndromes and heart failure have been divided into individual summaries. In addition to the current summary, the following are available:

- [Chapter 1: Clinical characteristics and utilization of biochemical markers in acute coronary syndromes](#)
- [Chapter 2: Analytical issues for biochemical markers of acute coronary syndromes](#)
- [Chapter 4: Analytical issues for biomarkers of heart failure](#)
- [Chapter 5: Point of care testing, oversight and administration of cardiac biomarkers for acute coronary syndromes](#)

- [Chapter 6: Use of cardiac troponin and B-type natriuretic peptide or N-terminal proB-type natriuretic peptide for etiologies other than acute coronary syndromes and heart failure](#)

## **Use of Biochemical Markers in the Initial Evaluation of Heart Failure**

### **Diagnosis of Heart Failure**

Recommendations for use of biochemical markers for diagnosis of Heart Failure

#### ***Class I***

1. B-type natriuretic peptide (BNP) or N-terminal pro-BNP (NT-proBNP) testing can be used in the acute setting to rule out or to confirm the diagnosis of heart failure among patients presenting with ambiguous signs and symptoms. **(Level of Evidence: A)**

#### ***Class IIa***

1. BNP and NT-proBNP testing can be helpful to exclude the diagnosis of heart failure among patients with signs and symptoms suspicious of heart failure in the non-acute setting. **(Level of Evidence: C)**

#### ***Class III***

1. In diagnosing patients with heart failure, routine blood BNP or NT-proBNP testing for patients with an obvious clinical diagnosis of heart failure is not recommended. **(Level of Evidence: C)**
2. In diagnosing patients with heart failure, blood BNP or NT-proBNP testing should not be used to replace conventional clinical evaluation or assessment of the degree of left ventricular structural or functional abnormalities (e.g., echocardiography, invasive hemodynamic assessment). **(Level of Evidence: C)**

### **Risk Stratification of Heart Failure**

Recommendations for use of biochemical markers for risk stratification of Heart Failure

#### ***Class IIa***

1. Blood BNP or NT-proBNP testing can provide a useful addition to clinical assessment in selected situations when additional risk stratification is required. **(Level of Evidence: A)**
2. Serial blood BNP or NT-proBNP concentrations may be used to track changes in risk profiles and clinical status among patients with heart failure in selected situations where additional risk stratification is required. **(Level of Evidence: B)**

#### ***Class IIb***

1. Cardiac troponin testing can identify patients with heart failure at increased risk beyond the setting of acute coronary syndromes. **(Level of Evidence: B)**

### ***Class III***

1. Routine blood biomarker testing for the *sole* purpose of risk stratification in patients with heart failure is not warranted. **(Level of Evidence: B)**

### **Use of Biochemical Markers in Screening for Cardiac Dysfunction**

Recommendations for use of BNP and NT-proBNP in screening of Heart Failure

### ***Class IIb***

1. Blood BNP or NT-proBNP testing can be helpful to identify selected patients with left ventricular systolic dysfunction in the post-infarction setting or to identify patients at high risk of developing heart failure (e.g., history of myocardial infarction, diabetes mellitus). However, the diagnostic ranges and cost-effectiveness in different populations remain controversial. **(Level of Evidence: B)**

### ***Class III***

1. Routine blood natriuretic peptide (BNP or NTproBNP) testing is not recommended for screening large asymptomatic patient populations for left ventricular dysfunction. **(Level of Evidence: B)**

### **Use of Biochemical Markers in Guiding Management of Heart Failure**

Recommendations for use of biochemical markers in guiding management of Heart Failure patients

### ***Class III***

1. Routine blood BNP or NT-proBNP testing is not warranted for making specific therapeutic decisions for patients with acute or chronic heart failure because of the still emerging but incomplete data as well as intra and inter-individual variations. **(Level of Evidence: B)**

### **Definitions:**

#### **Weight of Evidence**

**A** - Data derived from multiple randomized or appropriately designed clinical trials that involved large numbers of patients

**B** - Data derived from a limited number of randomized or appropriately designed trials that involved small numbers of patients or from careful analyses of observational registries

**C** - Expert Consensus was the primary basis for the recommendation

### **Summary of Indications**

**Class I:** Conditions for which there is evidence and/or general agreement that a given laboratory procedure or treatment is useful and effective.

**Class II:** Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a laboratory procedure or 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:** Conditions for which there is evidence and/or general agreement that the laboratory procedure/treatment is not useful/effective and in some cases may be harmful.

### **CLINICAL ALGORITHM(S)**

None provided

## **EVIDENCE SUPPORTING THE RECOMMENDATIONS**

### **TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS**

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

## **BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS**

### **POTENTIAL BENEFITS**

Appropriate utilization of cardiac biomarker testing in patients with heart failure

### **POTENTIAL HARMS**

Side effects and risks of having knowledge of blood natriuretic peptide (BNP) and N-terminal pro-BNP (NT-proBNP) levels

## **QUALIFYING STATEMENTS**

### **QUALIFYING STATEMENTS**

- The materials in this publication represent the opinions of the authors and committee members, and do not necessarily represent the official position of the National Academy of Clinical Biochemistry (NACB). The National Academy

of Clinical Biochemistry is the academy of the American Association for Clinical Chemistry.

- It is most important to emphasize that validity of test results must complement clinical findings to define a disease process. Thus, biochemical marker testing (such as blood natriuretic peptide [BNP] and N-terminal pro-BNP [NT-proBNP] measurement) is not a stand-alone test, and must be used and interpreted in a larger clinical context, with confounding factors taken into account. Used appropriately in this context, the health benefits of testing far outweigh the side effects and risks of having knowledge of BNP and NT-proBNP levels.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better  
Living with Illness

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Tang WH, Francis GS, Morrow DA, Newby LK, Cannon CP, Jesse RL, Storrow AB, Christenson RH, Apple FS, Ravkilde J, Wu AH, National Academy of Clinical Biochemistry Laboratory Medicine. National Academy of Clinical Biochemistry Laboratory Medicine practice guidelines: Clinical utilization of cardiac biomarker testing in heart failure. *Circulation* 2007 Jul 31;116(5):e99-109. [148 references] [PubMed](#)

Tang WH, Francis GS, Morrow DA, Newby LK, Cannon CP, Jesse RL, Storrow AB, Christenson RH, NACB Committee. National Academy of Clinical Biochemistry laboratory medicine practice guidelines: clinical utilization of cardiac biomarker testing in heart failure. *Clin Biochem* 2008 Mar;41(4-5):210-21. [PubMed](#)

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

**DATE RELEASED**

1999 Jul (revised 2007 Jul)

**GUIDELINE DEVELOPER(S)**

National Academy of Clinical Biochemistry - Professional Association

**SOURCE(S) OF FUNDING**

National Academy of Clinical Biochemistry

**GUIDELINE COMMITTEE**

The National Academy of Clinical Biochemistry

**COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

*National Academy of Clinical Biochemistry (NACB) Writing Group Members:* W. H. Wilson Tang, MD; Gary S. Francis, MD; David A. Morrow, MD; L. Kristin Newby, MD; Christopher P. Cannon, MD, MHS; Robert L. Jesse, MD, PhD; Alan B. Storrow, MD; Robert H. Christenson, PhD

*NACB Committee Members:* Robert H. Christenson, *Chair*, University of Maryland School of Medicine, Baltimore, Maryland, USA; Fred S. Apple, Hennepin County Medical Center and University of Minnesota, Minneapolis, Minnesota, USA; Christopher P. Cannon, Brigham and Women's Hospital, Boston, Massachusetts, USA; Gary S. Francis, Cleveland Clinic Foundation, Cleveland, Ohio, USA; Robert L. Jesse, Medical College of Virginia, Richmond, Virginia, USA; David A. Morrow, Brigham and Women's Hospital, Boston, Massachusetts, USA; L. Kristin Newby, Duke University Medical Center, Durham, North Carolina, USA; Jan Ravkilde, Aarhus University Hospital, Aarhus, Denmark; Alan B. Storrow, Vanderbilt University, Nashville, Tennessee, USA; W. H. Wilson Tang, Cleveland Clinic Foundation, Cleveland, Ohio, USA; Alan H. B. Wu, San Francisco General Hospital and University of California at San Francisco, San Francisco, California, USA

*Ad Hoc members of the committee for selected sections:* Allan S. Jaffe, Mayo Clinic, Rochester, Minnesota, USA; Alan S. Maisel, University of California at San Diego, San Diego, California, USA; Mauro Panteghini, University of Milan, Milan, Italy

**FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

Other than modest funding from the National Academy of Clinical Biochemistry/American Association for Clinical Chemistry (NACB/AACC), development of these guidelines was a volunteer activity. Thus the guidelines are editorially independent from any funding body.

All potential conflicts of interest for the NACB guidelines committee and ad hoc members of the writing committees are listed at the following:

<http://www.aacc.org/AACC/members/nacb/LMPG/OnlineGuide/PublishedGuidelines/ACSHeart/heartpdf.htm>.

## **GUIDELINE STATUS**

This is the current release of the guideline.

This guideline updates a previous version: Wu AH, Apple FS, Gibler WB, Jesse RL, Warshaw MM, Valdes R Jr. National Academy of Clinical Biochemistry Standards of Laboratory Practice: recommendations for the use of cardiac markers in coronary artery diseases. Clin Chem 1999 Jul;45(7):1104-21. [119 references] [PubMed](#)

## **GUIDELINE AVAILABILITY**

Electronic copies: Available from the [National Academy of Clinical Biochemistry \(NACB\) Web site](#).

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or [custserv@aacc.org](mailto:custserv@aacc.org).

## **AVAILABILITY OF COMPANION DOCUMENTS**

The following is available:

- Preamble. National Academy of Clinical Biochemistry laboratory medicine practice guidelines for utilization of biochemical markers in acute coronary syndromes and heart failure. Washington (DC): National Academy of Clinical Biochemistry (NACB); 2007. p. 1-3.

Electronic copies: Available from the [National Academy of Clinical Biochemistry \(NACB\) Web site](#).

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or [custserv@aacc.org](mailto:custserv@aacc.org).

## **PATIENT RESOURCES**

None available

## **NGC STATUS**

This NGC summary was completed by ECRI Institute on March 12, 2008. The information was verified by the guideline developer on April 2, 2008.

## **COPYRIGHT STATEMENT**

National Academy of Clinical Biochemistry's (NACB) terms for reproduction of guidelines are posted with each set of guidelines.

## DISCLAIMER

### NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at <http://www.guideline.gov/about/inclusion.aspx>.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2008 National Guideline Clearinghouse

Date Modified: 11/3/2008

