Measuring Natriuretic Peptides in Acute Coronary Syndromes

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Participant Poll
In This Issue

- Integration of the Clinical Laboratory in Cardiovascular Medicine
  Peter A. McCullough, MD, MPH
- Capturing the Pathophysiology of Acute Coronary Syndromes With Circulating Biomarkers
  Peter A. McCullough, MD, MPH, W. Frank Peacock, MD, Brian O’Neill, MD, James A. de Lemos, MD
- Differential Diagnosis and Overlap of Acute Chest Discomfort and Dyspnea in the Emergency Department
  Norman E. Lepor, MD, Peter A. McCullough, MD, MPH
- Natriuretic Peptides in the Prognosis and Management of Acute Coronary Syndromes
  James A. de Lemos, MD, W. Frank Peacock, MD, Peter A. McCullough, MD, MPH
- Cardiac Computed Tomography in the Rapid Evaluation of Acute Cardiac Emergencies
  Brian O’Neill, MD, W. Frank Peacock, MD
- Time to Treatment and Acute Coronary Syndromes: Bridging the Gap in Rapid Decision Making
  W. Frank Peacock, MD
- An Evidence-Based Algorithm for the Use of B-Type Natriuretic Testing in Acute Coronary Syndromes
  Peter A. McCullough, MD, MPH, W. Frank Peacock, MD, Brian O’Neill, MD, James A. de Lemos, MD, Norman E. Leper, MD, Robert Berkowitz, MD
Unstable Plaque

VULNERABLE PLAQUE
- Fibrous cap
- Lipid-rich core

Cap disruption
- Vulnerability
- Triggers

UNSTABLE CORONARY ARTERY DISEASE

DETERMINANTS OF THROMBOSIS
- Local factors
- Systemic factors

Myocardial Infarction

Annual Admissions for Acute Coronary Syndrome (ACS)

~ 2.0 MM Patients Admitted to CCU or Telemetry Annually

600,000 ST-Segment Elevation MI

1.4 Million Non-ST-Segment Elevation ACS

Acute Evaluation of ACS

Presentation

ECG

Blood Marker Panel

Diagnosis

Chest Pain or Short of Breath

Normal

ST-Segment Depression

ST-Segment Elevation

Rule-Out

Unstable Angina

Acute MI

Adapted from Braunwald E, et al. Available at: http://www.americanheart.org/downloadable/heart/1022188973899unstable_may8.pdf.

NACB Guidelines

• Class IIA recommendation for use of biomarkers in risk stratification for ACS
  • Measurement of BNP or NT pro BNP may be useful in addition to a cardiac troponin for risk assessment in patients with a clinical syndrome consistent with ACS.

• Class IIB recommendation for use of biomarkers in risk stratification for ACS
  • A multimarker strategy that includes measurement of 2 or more pathobiologically diverse biomarkers in addition to a cardiac troponin may aid in enhancing risk stratification in patients with a clinical syndrome consistent with ACS.
Cardiac biomarkers should be measured in all patients who present with chest discomfort consistent with ACS.

A cardiac-specific troponin is the preferred marker, and if available, it should be measured in all patients who present with chest discomfort consistent with ACS.
Troponin
Changes in Focus on Heart Failure

Troponin and Mortality in NSTE ACS

Risk Ratio: 1.0

Antman

McCullough, Cardiac Biomarkers, 2008
Ultrasensitive Troponins

Figure 3. Area under the receiver operating characteristic curve for various more sensitive troponin assays compared with a standard assay in patients presenting with chest discomfort of < 3 hours in duration. The reference standard for myocardial infarction was a review of the history, physical examination, electrocardiogram, and all clinical tests by 2 independent cardiologists at 60 days after the event. Reprinted with permission from Reichlin T et al.19
Acute Coronary Syndrome Guidelines

Biomarker data be available to the physician within 30–60 minutes following the patient’s arrival in the ED

The Value of Bedside Cardiac Multibiomarker Assay in Rapid and Accurate Diagnosis of Acute Coronary Syndromes

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Abstract: For emergency department physicians, timely triage and risk stratification of chest pain patients remains a challenge. Faced with an aging population and the growing prevalence of heart disease, clinicians are seeking more effective ways to diagnose acute coronary syndromes rapidly and accurately. Emergency department physicians must make critical and time-sensitive decisions based on patient history, physical examination, and 12-lead electrocardiogram as justification for diagnosis of acute coronary syndromes. But because most of these tools are not reliable independently, these incomplete strategies can result in costly and inappropriate treatment decisions.

Key Words: point of care, acute coronary syndrome, bedside testing, cardiac markers, multimarker, chest pain center, troponin, BNP, natriuretic peptide, myoglobin, NEW ERA

(Crit Pathways in Cardiol 2007;6: 76–84)
St. Francis Hospital, Evanston, IL

**BNP Secretion Induced by Ischemia**

Figure 5. Median changes in B-type natriuretic peptide (BNP) levels in response to exercise stress testing in patients with no ischemia (white bar), with no ischemia on scintigraphy but subsequently shown to have critical coronary disease (light gray bar), with mild-to-moderate ischemia (dark gray bar), and with severe ischemia (black bar). Numbers within each bar represent the number of patients in that group. The p values by each bar are for the median change. The p value at the far right is for the trend across ischemic categories. cath = cardiac catheterization; ECG = electrocardiographic; Immed = immediately; IQR = interquartile range; sx = symptoms.
Results of BNP Testing in ACS

Frequency of Baseline BNP > 80 pg/ml

Morrow DA JACC 2003; 41:1264-72
Probability of Death Through 30 Days Stratified by B-Type Natriuretic Peptide (BNP)


- **BNP >80 pg/ml**
  - 7 Days: 15.2% vs. 1.3%, *P* < 0.0001
  - 48 Hours: 8.7% vs. 1.3%, *P* = 0.001
  - 30 Days: 100% vs. 1.3%, *P* < 0.0001

- **BNP ≤80 pg/ml**
  - 48 Hours: 1.3% vs. 1.3%, *P* = 0.001
  - 7 Days: 1.3% vs. 1.3%
  - 30 Days: 1.3% vs. 1.3%
BNP In the Prediction of In-hospital Mortality

Figure 3. The interaction among troponin, BNP, and in-hospital mortality. BNP, B-type natriuretic peptide.
Cumulative Incidence of Subsequent Death or New or Worsening CHF

B-Type Natriuretic Peptide Levels
Baseline-Month 4

No. at Risk
High-High 137 128 121 91 59 35
Low-High 77 77 70 65 43 17
High-Low 330 322 292 225 161 97
Low-Low 2929 2877 2777 2539 2232 1649

Figure 2  (A) Kaplan-Meier survival curves for cardiovascular events. High BNP defined as >80 pg/ml and high GRACE score defined as >119 points. High GRACE-high BNP (RR 6.00 (95% CI 2.40 to 14.83)), low GRACE-high BNP (RR 5.27 (95% CI 1.88 to 14.77)) and high GRACE-low BNP (RR 2.40 (95% CI 0.76 to 7.56)). Log-rank test p<0.001. (B) Kaplan-Meier survival curves for mortality. High BNP defined as >80 pg/ml and high GRACE score defined as >119 points. High GRACE-high BNP (RR 12.81 (95% CI 1.74 to 94.31)), low GRACE-high BNP (RR 4.12 (95% CI 0.37 to 45.39)) and high GRACE-low BNP (RR 3.45 (95% CI 0.31 to 38.07)). Log-rank test p = 0.002. BNP, B-type natriuretic peptide; GRACE, Global Registry of Acute Coronary Events; TIMI, thrombolysis in myocardial infarction.

| No. at risk |  |  |  |  |  |  |  |
|-------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Low G-low B | 97            | 96             | 94             | 94             | 92             | 92             | 92             |
| High G-Low B| 58            | 56             | 55             | 54             | 54             | 53             | 51             |
| Low G-high B| 53            | 49             | 48             | 45             | 42             | 42             | 40             |
| High G-high B| 235           | 214            | 207            | 197            | 188            | 181            | 171            |

Elevated BNP in ACS

- Large zones of ischemia
  - Left main lesions
  - Severe 3-vessel disease
- Large infarctions
- Pre-existing LV impairment
  - Systolic
  - Diastolic
- Renal dysfunction

Markedly Elevated BNP in ACS and Multivessel Disease

BNP and the number of vessels with significant stenoses (at least one lesion >75%), p=0.0006.

*Median (25th, 75th)*

Markedly Elevated BNP in ACS and Multivessel Disease

BNP at Markedly Elevated Levels and In-Hospital Mortality

Why Draw BNP in the ED? Powerful Tool.

**Relationship Between BNP Value and In-Hospital Death**

- **In-Hospital Mortality Rate**
- **95% Confidence Limits**

**Figure 1.** Continuous distribution of BNP levels with unadjusted in-hospital mortality. BNP, B-type natriuretic peptide.
Class IIb: Measurement of B-type natriuretic peptide (BNP) or NT-pro-BNP may be considered to supplement assessment of global risk in patients with suspected ACS. (Level of Evidence: B)
Teachable Algorithm: BNP and NT-proBNP

- Elevated
- Clinical Grey Zone
- Age Grey Zone
- Normal

Grey Zone:
- eGFR < 60 ml/min
- Cardiac Ischemia
- RV Source (PE/Cor Pulmonale)
- Sepsis

McCullough, Cardiac Biomarkers, 2008
McCullough PA, AACC 2006
Chest Pain or Short of Breath: ACS Considered

BNP Risk Stratification Algorithm

**ECG**

- Normal
  - No ischemic changes
  - Troponin, CK-MB (neg)
  - BNP <100 pg/ml
    - No ACS
      - CTA/GXT-MPI/2DE
      - Outpatient risk
      - Factor modification
  - BNP 6-12 weeks, 6-12 mos.

- ST-segment depression
  - ischemic T-wave changes
  - Troponin, CK-MB (pos)
  - Confirm AMI
  - BNP 100-500 pg/ml
    - High Risk
      - Higher TIMI/GRACE score
      - Prox LAD
      - Plaque Rupture
      - Older
      - Pre-existing LV Dysfxn
      - CKD
      - √BNP 6-12 weeks, 6-12 mos.
      - Late HF or death

- ST-segment elevation
  - Troponin, CK-MB (pos)
  - Confirm AMI
  - BNP >500 pg/ml
    - Very High Risk
      - LM or 3VD
      - Large ischemic zone
      - Complicated PCI expected
      - No reflow
      - Shock
      - Heart Failure
      - In hospital Death
      - √BNP 6-8 weeks, 6-12 mos.
      - Late HF or death

Triage BNP Indications

- Aid in the diagnosis of heart failure
- Assess the severity of heart failure
- **Risk stratification of patients with acute coronary syndromes**
- Prognostic aid in patients with heart failure

*Figure 1. Four major domains of activity in the use of the clinical laboratory.*