Combining Natriuretic Peptides and Necrosis Markers in the Assessment of Acute Coronary Syndromes

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Management of patients with acute coronary syndromes (ACS) is becoming more complex as the array of treatment options available to patients and physicians continues to expand. Cardiac biomarkers play an important role in risk stratification in ACS, and results of cardiac biomarker tests can be used to help guide choices between alternative therapies. In addition to biomarkers of myocyte necrosis, markers of neurohormonal activation, such as B-type natriuretic peptide (BNP), provide important prognostic information in ACS. In the future, multimarker strategies that incorporate panels of cardiac biomarkers are likely to be used for risk stratification and for pathophysiology-guided treatment in patients with ACS.
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Key words: Acute coronary syndromes • B-type natriuretic peptide • Cardiac troponins • C-reactive protein • Creatine kinase • Myoglobin

The acute coronary syndromes (ACS) are heterogeneous with respect to pathophysiology, clinical presentation, and response to therapy. Although plaque rupture, platelet deposition, and thrombus formation are key components of the underlying pathophysiology, it is increasingly recognized that many episodes of ACS do not follow this standard sequence of events.[1] For example, some patients appear to have ACS without evidence of plaque rup-

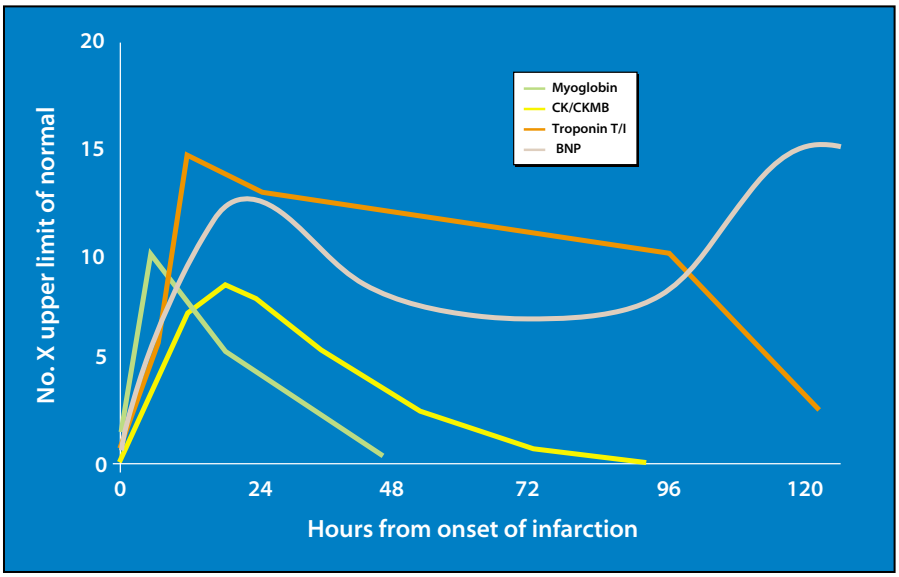

Figure 1. *Time course of elevation of cardiac biomarkers following myocardial infarction. BNP, B-type natriuretic peptide; CK, creatine kinase; CKMB, creatine kinase isoenzyme MB.*

ture, either because of erosion of the fibrous cap covering the plaque or progression of (stable) underlying atherosclerosis.[1] At the other extreme are those patients with ACS who appear by angiography to have multiple "culprit" lesions in the coronary circulation.[2] Similarly, clinical presentation varies tremendously: women, the elderly, and patients with diabetes commonly present with atypical symptoms despite objective evidence for ACS. Such patients commonly present with symptoms of dyspnea rather than chest discomfort.

The number of treatment options available for patients with ACS continues to evolve at a rapid pace. Physicians must now choose from a wide array of antiplatelet and antithrombotic therapies, and also determine which patients would benefit from an invasive management approach. These decisions have become more difficult with the introduction of newer drugs and drug classes, such as low molecular weight heparins, direct-acting antithrombins, thienopyridines, and glycoprotein IIb/IIIa inhibitors.

Simple tools, which often can be applied at the patient's bedside, can help physicians risk stratify their patients, choose the intensity of antiplatelet and antithrombotic therapy, and decide whether to use invasive coronary procedures. Cardiac biomarkers have proven to be particularly effective for these purposes. Biomarkers that are currently available in clinical practice include markers of myocardial necrosis (creatine kinase [CK] and CK isoenzyme MB [CKMB], myoglobin, and cardiac troponins T [cTnT] and I [cTnI]); markers of inflammation (C-reactive protein [CRP]); and markers of neurohormonal activation (B-type natriuretic peptide [BNP] and the N-terminal fragment of its prohormone [N-proBNP]).

Biomarkers of Cardiac Necrosis

CKMB

Serum levels of CK and CKMB become elevated 3–6 hours after the onset of symptoms of myocardial infarction (MI), peak at approximately 18 hours, and return to normal in approximately 3 days (Figure 1). Following successful fibrinolysis, CK and CKMB usually peak in <12 hours. Newer mass assays (ng/mL) for CKMB are more sensitive and specific than older activity assays and permit the detection of small elevations in CKMB without elevation in overall CK. These minor CKMB elevations have been associated with higher long-term risk of adverse cardiac events, particularly following percutaneous coronary intervention (PCI).[3] Despite recent recommendations to use a troponin standard for MI diagnosis, CKMB remains useful for diagnosis of early reinfarction and for noninvasive estimation of infarct size,[4] and may help to determine the etiology of nonspecific troponin elevation that occurs frequently with nonischemic etiologies of myocyte injury.[5]

Troponins T and I

Like CK and CKMB, the cardiac troponins are detectable in serum or plasma 3–6 hours after the onset of chest pain and peak at 14–20 hours (Figure 1). In contrast to other biomarkers, troponins remain elevated for up to 2 weeks after MI. This prolonged detection window makes troponins ideal for the late diagnosis of infarction but poorly suited for detecting reinfarction in a patient with a recent MI. Because cTnT and cTnI are not found in adult skeletal muscle, they are highly specific for myocardial injury. The high cardiac specificity allows the normal reference range for the troponins to be set at a very low level, which markedly improves clinical sensitivity for diagnosing MI. In most patients, cTnT and cTnI appear to provide similar information.

In addition to their diagnostic utility, cTnT and cTnI have been shown to provide important prognostic information in patients with

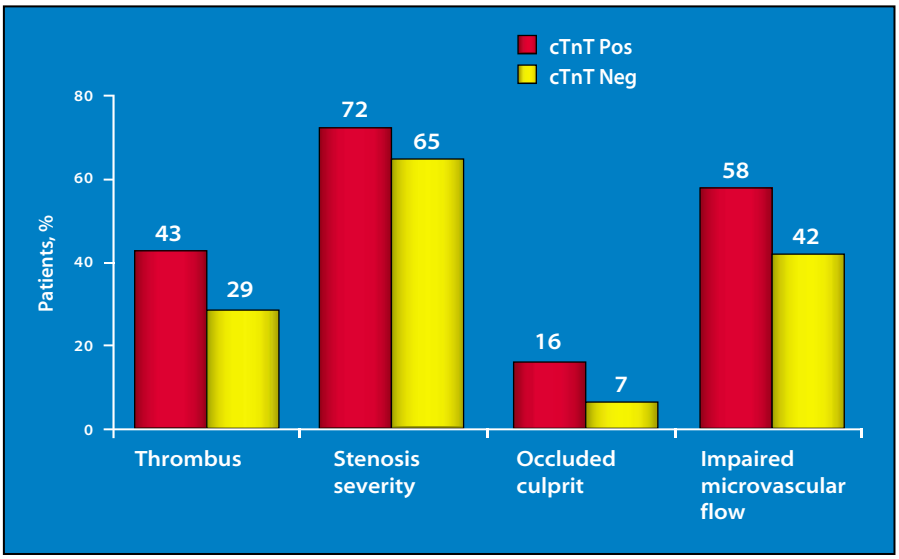

Figure 2. *Association between troponin elevation and angiographic findings in the TACTICS-TIMI (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy–Thrombolysis in Myocardial Infarction) 18 study. cTnT Neg, cardiac troponin T negative; cTnT Pos, cardiac troponin T positive. Data from Wong et al.*[7]

ACS. Of particular interest, in patients previously diagnosed with unstable angina (no infarction by CKMB or electrocardiographic [ECG] criteria), even minor elevations in cTnT and cTnI have been associated with an increased risk for death and recurrent ischemic events.[6] When compared to patients with normal troponin levels, those with minor troponin elevation are more likely to have severe underlying coronary disease, impaired epicardial blood flow in the culprit artery, a thrombus-filled lesion, and impairment in microvascular perfusion (Figure 2).[7] Thus, minor troponin elevation is associated with high-risk lesion morphology and a high probability of distal embolization. This likely explains the ability of troponin elevation to identify patients who derive greatest benefit from aggressive antiplatelet and antithrombotic therapies.

A series of studies has confirmed the powerful role of troponin testing in identifying patients with non-ST elevation ACS who are likely to benefit from treatment with GP IIb/IIIa inhibitors,[8] low molecular weight heparins,[9] and an early invasive management strategy.[10] Among troponin-positive patients, each of these therapies reduces composite cardiovascular events by >50% (Figure 3). In contrast, no benefit has been observed for these therapies among patients who are troponin negative.[8–10]

In 2000, a joint panel of the American College of Cardiology and the European Society of Cardiology recommended replacing the traditional World Health Organization diagnostic criteria for MI (which were based on CKMB) with a troponin standard.[11] Specifically, under this definition, any elevation of cardiac troponin T or I above the 99th percentile of a healthy reference population is diagnostic of MI in a patient with a clinical syndrome consistent with cardiac ischemia, provided the assay has acceptable precision within that range.[11] This change has important and far-reaching implications, and will likely have impact in areas as diverse as cardiovascular epidemiology, the design and construct of clinical trials, hospital reimbursement, and patient

Figure 3. *Benefit of aggressive therapies for acute coronary syndromes among patients with troponin elevation. CAPTURE, c7E3 Fab Antiplatelet Therapy in Unstable Refractory Angina study; GP IIb/IIIa, glycoprotein IIb/IIIa; LMWH, low molecular weight heparin; MI, myocardial infarction; TACTICS, Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy study; TIMI, Thrombolysis in Myocardial Infarction study. Data from Hamm et al,*[8] *and Morrow et al.*[9,10]

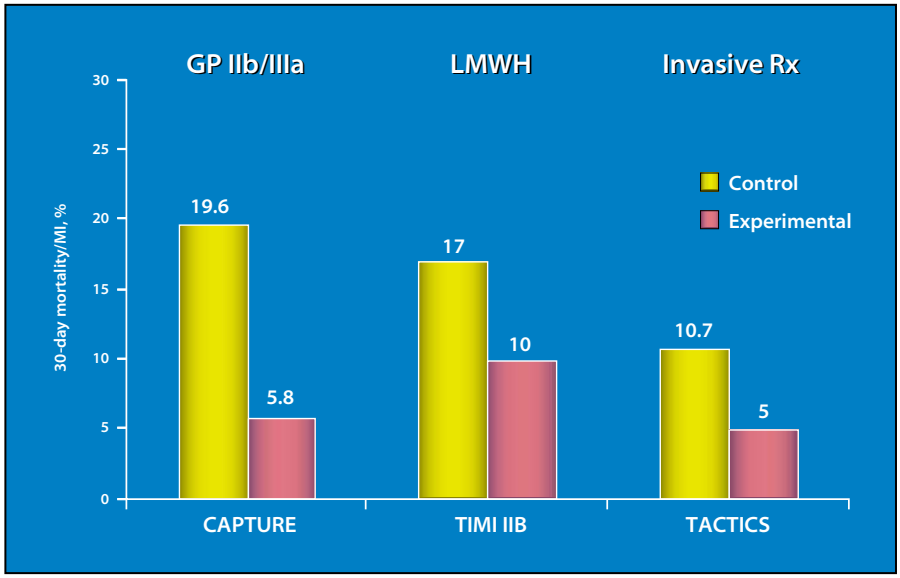

Table 1
Non–Acute Coronary Syndrome Causes of Troponin Elevation

- Myocarditis
- Cardiac contusion
- Cardioversion; radiofrequency ablation
- Congestive heart failure
- Chemotherapy (doxorubicin, 5-fluorouracil)
- Septic shock
- Extreme endurance athletics
- Pulmonary embolus

insurability. Finally, it is important to recognize that troponin elevation is not specific for ischemic necrosis of cardiac myocytes. Many other conditions associated with myocyte injury can cause nonspecific elevation in cardiac troponins (Table 1).

Myoglobin

Myoglobin is a cytosolic protein that is the smallest (17.8 kD) of the necrosis markers and is the first to rise following the onset of myocardial necrosis: Elevated levels of myoglobin can be detected as early as 2 hours following injury (see Figure 1). Myoglobin peaks at approximately 6 hours after MI and returns to normal levels within 18–24 hours. Although not specific for cardiac muscle, myoglobin is the most sensitive biomarker for diagnosing MI within the first 6 hours after symptom onset, and is the preferred marker for very early MI diagnosis.[12,13] Recently, very rapid "rule out MI" protocols have been evaluated that utilize serial myoglobin measurements over a short time period. In a study of 817 patients in an urban emergency department, McCord and colleagues[14] found that a normal myoglobin and cTnI value at 0 and 90 minutes after presentation had a 96.9% sensitivity and a 99.6% negative predictive value for diagnosing MI (ie, only 0.4% of patients with normal marker levels were eventually determined to have MI). Similarly, Ng and colleagues[15] have demonstrated in a higher-risk Veterans Affairs hospital that an accelerated pathway utilizing cTnI, CKMB, and myoglobin can accurately diagnose MI within 90 minutes of presentation.

In addition to its value as a diagnostic tool, myoglobin provides prognostic information that is independent of other clinical variables and also of other necrosis markers. In patients with ST-elevation MI, for example, patients with myoglobin elevation at the time of presentation are at threefold increased risk for mortality following the administration of fibrinolytic therapy, regardless of the ultimate success of reperfusion.[16] Myoglobin outperformed simple measures of time-to-reperfusion and infarct size, suggesting that it could provide an objective measurement of the amount of necrosis that had occurred prior to initiation of reperfusion therapy. For this purpose, myoglobin compares favorably to other necrosis markers: Because it rises earlier after the onset of symptoms, more patients present with myoglobin elevation than elevation in CKMB or troponin.

Recently, the prognostic value of myoglobin in patients with non–ST-elevation ACS has been investigated.[17,18] In substudies of the Thrombolysis in Myocardial Infarction (TIMI) 11B and Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy (TACTICS)-TIMI 18 studies, myoglobin elevation was associated with an increased risk for mortality, independent of traditional clinical risk factors, ECG changes, and levels of CKMB and cTnI. In contrast, myoglobin elevation was not predictive of recurrent ischemic events, whereas troponin elevation (particularly low-level troponin elevation) was highly associated with recurrent ischemia (Figure 4).[18]

The observation that myoglobin elevation is associated with increased mortality even after adjusting for troponin levels is particularly intriguing and indicates that important pathobiologic and kinetic differences exist between markers within the necrosis class. Myoglobin is smaller than CKMB and troponin and remains unbound in the cytoplasm of the cell. Release of myoglobin appears to follow a single-compartment model following myocardial infarction: The rise in serum levels of myoglobin is directly proportional to the depletion in myocardial levels. Troponin release is likely considerably more complex, with a number of factors other than infarct size contributing to the magnitude of troponin elevation.[18]

An accelerated pathway utilizing cTnI, CKMB, and myoglobin can accurately diagnose MI within 90 minutes of presentation.

Natriuretic Peptides as Prognostic Markers in ACS

BNP and N-proBNP are released from cardiac myocytes in response to increases in wall stress. As discussed in previous articles in this supplement, assays for these neurohormones are commercially available and in wide clinical use for the

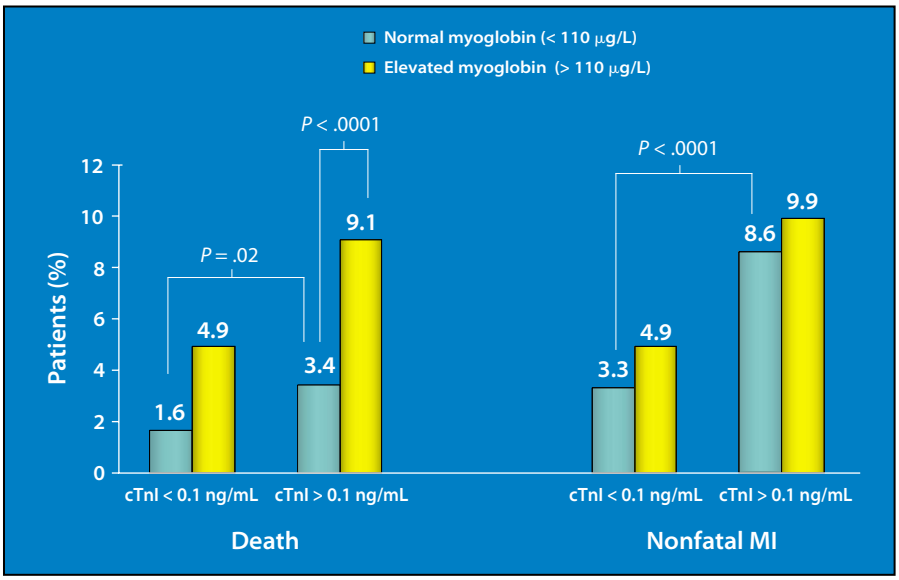

Figure 4. *Combined assessment of myoglobin and troponin I in the TIMI (Thrombolysis in Myocardial Infarction) 11B and TACTICS (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy)-TIMI 18 studies. cTnI, cardiac troponin I; MI, myocardial infarction. Adapted from de Lemos et al.*[18]

assessment of patients with suspected heart failure. Recently, BNP and N-proBNP have also been shown to provide important prognostic information in patients with ACS. Here, they appear to provide information that is distinct from and complementary to the necrosis markers described above.

The concept that ischemia may be an important stimulus for BNP release is supported by several observations. In experimental models of MI, BNP gene transcription is increased both in infarcted tissue and also in surrounding viable myocytes, which are often ischemic and under increased wall stress.[19] Hypoxia has also been shown to cause BNP release,[20] suggesting that myocardial ischemia (even without necrosis) stimulates the cardiac hormonal system. In patients referred for stress testing, it has been shown that BNP rises after exercise in patients with coronary disease, and the magnitude of BNP increase is proportional to the size of the ischemic territory as assessed with nuclear single-photon emission computed tomography imaging.[21] After uncomplicated percutaneous transluminal coronary angioplasty, BNP transiently increases, even when intracardiac filling pressures remain unchanged.[22]

These findings suggest that ischemia may be an important trigger for BNP release. This does not imply, however, that BNP will be useful for diagnosing ischemia, and BNP is unlikely to prove sensitive or specific enough for this purpose. The magnitude of BNP elevation seen in patients with ACS is lower than that associated with heart failure, and falls within the range seen in many other common conditions, such as left ventricular hypertrophy, asymptomatic left ventricular dysfunction, pulmonary embolism, and cor pulmonale.

Using BNP to Assess Prognosis in Patients with ACS

Initial studies of BNP and N-proBNP in ACS focused on patients with ST-elevation MI. In these cases, BNP levels rise rapidly and peak at approximately 24 hours, with the peak level proportional to the size of the MI.[23,24] In some patients, particularly those who eventually develop severe heart failure, a second peak may occur at approximately day 5, reflecting the development of adverse ventricular remodeling.[25] In patients with ST-elevation MI, higher BNP and N-proBNP levels have been shown to predict a greater likelihood of death or heart failure, independent of other prognostic variables, including left ventricular ejection fraction (LVEF).[26,27]

Recently, the prognostic value of BNP in ACS has been extended to patients with non–ST-elevation ACS, including those with no evidence of myocardial necrosis, using cardiac troponin. In a pilot study from the TIMI 11B trial, baseline levels of N-proBNP were higher among patients with unstable angina who subsequently died than among those who survived. In contrast, no difference in N-proBNP levels was observed between those with and without recurrent MI.[28] In a much larger substudy from the Orbofiban in Patients with Unstable Coronary Syndromes (OPUS)-TIMI 16 trial, BNP levels were measured a median of 40 hours after presentation in more than 2500 patients with ACS (ST-elevation MI, non–ST-elevation MI, or unstable angina).[29] Higher BNP levels were associated with older age, female gender, renal insufficiency, clinical evidence of heart failure, and more severe angiographic coronary artery disease. Patients with BNP elevation were also more likely to have ECG changes and elevated levels of CKMB, cTnI, and CRP.[29]

The rate of death at 10 months increased from <1% among patients with BNP levels in the lowest quartile to > 10% in those with BNP levels in the highest quartile ($P < .0001$).[29] The

very low mortality rate observed for patients with the lowest BNP levels (<43 pg/mL) has merited particular attention, leading some experts to suggest that less aggressive management strategies be employed in such patients.[30] The association between BNP and mortality persisted among patients without prior history or current evidence of heart failure, and among those with normal troponin levels, suggesting that stimuli other than heart failure and myocardial necrosis were responsible for BNP elevation. When multivariate techniques were used to adjust for other predictors of mortality, such as age, diabetes, renal failure, evidence for heart failure, ST segment changes on the ECG, and levels of cTnI and CRP, BNP remained strongly associated with mortality. In these multivariate analyses, elevated troponin I, CRP, and BNP were each independently predictive of higher 10-month mortality, demonstrating that each marker provides unique information about mortality following ACS (Figure 5).[28] Levels of BNP were also strongly associated with the development or progression of heart failure, but the association between BNP levels and the development of nonfatal recurrent MI was less impressive.[29]

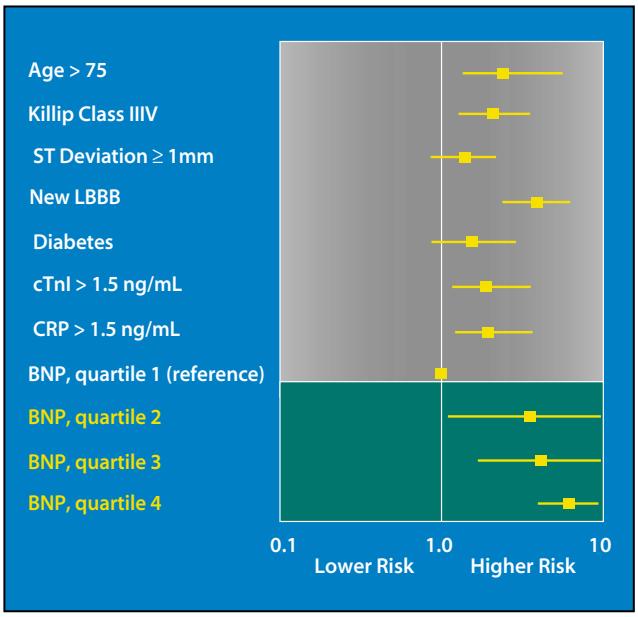

Figure 5. *Multivariate model showing variables independently associated with 10-month mortality in the OPUS-TIMI (Orbofiban in Patients with Unstable Coronary Syndromes–Thrombolysis in Myocardial Infarction) 16 study. Elevated levels of cardiac troponin I (cTnI), C-reactive protein (CRP), and B-type natriuretic peptide (BNP) were each independently associated with increased mortality. LBBB, left bundle branch block. Adapted from De Lemos et al.*[29]

A number of investigative groups have subsequently extended these findings, demonstrating that the predictive value of BNP and N-proBNP is also independent of LVEF. Omland[31] measured N-proBNP levels in a 609-patient cohort of patients with ACS who were followed for over 4 years. Patients with higher N-proBNP levels had more severe heart failure and worse left ventricular function as well as greater ST-segment deviation on the ECG and higher levels of cTnI. After adjusting for LVEF and clinical evidence of heart failure, higher N-proBNP levels remained associated with increased long-term mortality.[31]

The prognostic role of natriuretic peptide testing in the emergency department setting was evaluated by Jernberg and colleagues,[32] who measured N-proBNP on admission in patients with suspected ACS, rather than 2–3 days after symptom onset as in the previous studies. Patients were included only if they had chest pain and a nondiagnostic ECG and were excluded if they had ST elevation or Q waves. Thus, the patient population more closely reflected one seen in a typical emergency department. Compared with patients who had admission N-proBNP levels in the first quartile, the relative risk for mortality among patients in the second, third and fourth quartiles was 4.2, 10.7, and 26.6, respectively.[32] Whether patients had acute MI, unstable angina, or other cardiac causes of chest pain, N-proBNP accurately identified patients at risk for mortality. Once again, this association persisted after adjustment for age, diabetes, history of prior MI, heart failure, ECG changes, and cTnT levels.[32]

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The combined use of troponins and BNP was explored in more detail in a recent substudy from the TACTICS-TIMI 18 study.[33] Compared with patients with a BNP level ≤80 pg/mL, those with a BNP >80 pg/mL were at markedly increased risk for mortality, whether troponin was negative (odds ratio [OR] 6.9; 95% CI, 1.9-25.8) or positive (OR 4.1; 95% CI, 1.9-9.0) (Figure 6). In contrast, troponin elevation, but not BNP elevation, identified patients at risk for recurrent MI. In this study, the authors also compared different BNP decision limits and found that the prespecified cut point of 80 pg/mL provided the greatest discrimination for adverse outcomes. This study

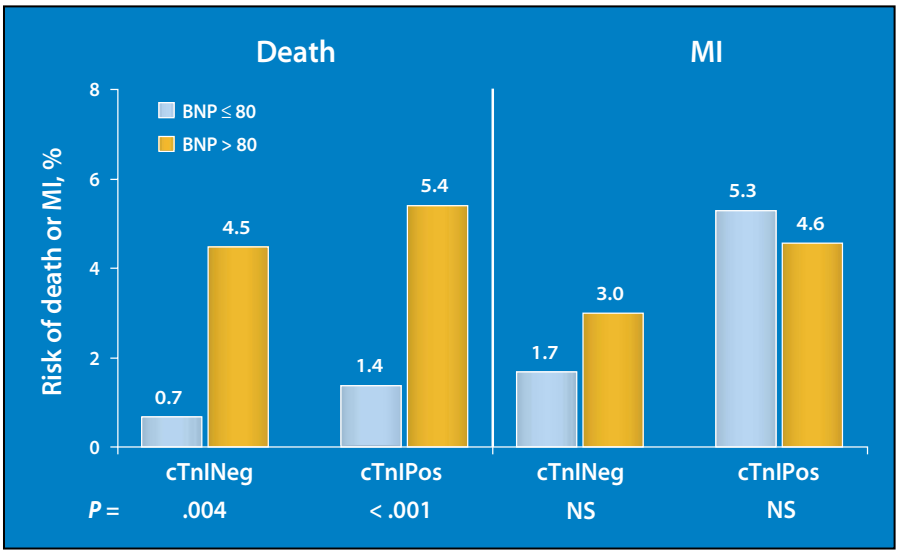

Figure 6. *Combined analysis of cardiac troponin I (cTnI) and B-type natriuretic peptide (BNP) in the TACTICS-TIMI (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy–Thrombolysis in Myocardial Infarction) 18 study. MI, myocardial infarction. Adapted from Morrow et al.*[33]

highlights differences in the predictive capacity of BNP and troponin for different clinical end points. Low-level troponin elevation is highly predictive of (nonfatal) recurrent ischemic events, whereas BNP appears to be a "pump failure" marker that is more closely associated with death and heart failure progression.[33] Using these two markers together improves the detection of patients at risk for adverse events.

Therapeutic Implications of BNP Elevation in ACS

In patients with suspected ACS, studies have consistently shown that BNP and N-proBNP add unique and important prognostic information. Although direct comparative data are limited, studies to date suggest the two biomarkers appear to provide similar prognostic information.[27] Patients with BNP or N-proBNP elevation following ACS are clearly at high risk for death and the development of heart failure, but given the novelty of these observations, the specific therapeutic implications of BNP elevation have not been defined. In particular, it is not known how clinicians should treat patients with BNP elevation but normal troponin levels and no clinical evidence of heart failure.

Few studies have been performed to test specific therapeutic approaches among patients with elevated BNP levels. In the TACTICS-TIMI 18 BNP substudy described above, an early invasive treatment strategy (routine catheterization with or without PCI/coronary artery bypass graft) was of no greater benefit among patients with BNP elevation (>80 pg/mL) than those without BNP elevation.[33] In contrast, patients with troponin elevation derived markedly greater benefit from the invasive approach than those without troponin elevation.[10] Because BNP is a marker of death and heart failure, whereas cardiac troponins are more predictive of nonfatal recurrent ischemic events, these findings are not surprising. Current antithrombotic and interventional therapies appear to selectively reduce nonfatal ischemic events rather than mortality. These findings support the emerging hypothesis that different biomarkers carry different implications for therapy.[34] Future studies will need to identify therapies that modify the risk associated with BNP elevation in ACS. A prospective study will be starting shortly that will evaluate the pulmonary capillary wedge pressure and other hemodynamic measurements in the setting of ACS with an elevated BNP. If elevation in BNP reflects early heart failure in ACS, then early triage to intervention and therapies that reduce left ventricular end-diastolic pressures and improve forward output may be beneficial.

Multimarker Strategies for Risk Stratification in ACS

Several factors have converged to heighten interest in the use of combinations of different biomarkers for risk prediction in ACS. First, the pathophysiology and clinical presentation of ACS are heterogeneous, and the "one size fits all" approach to ACS management is suboptimal. Second, as discussed above, different biomarkers clearly reflect different components of the pathophysiology of ACS, and when used together, these different biomarkers provide independent prognostic information.

Sabatine and colleagues[35] performed analyses in the OPUS-TIMI 16 and TACTICS-TIMI 18 studies using cTnI, CRP, and BNP in combination. In multivariate models, each

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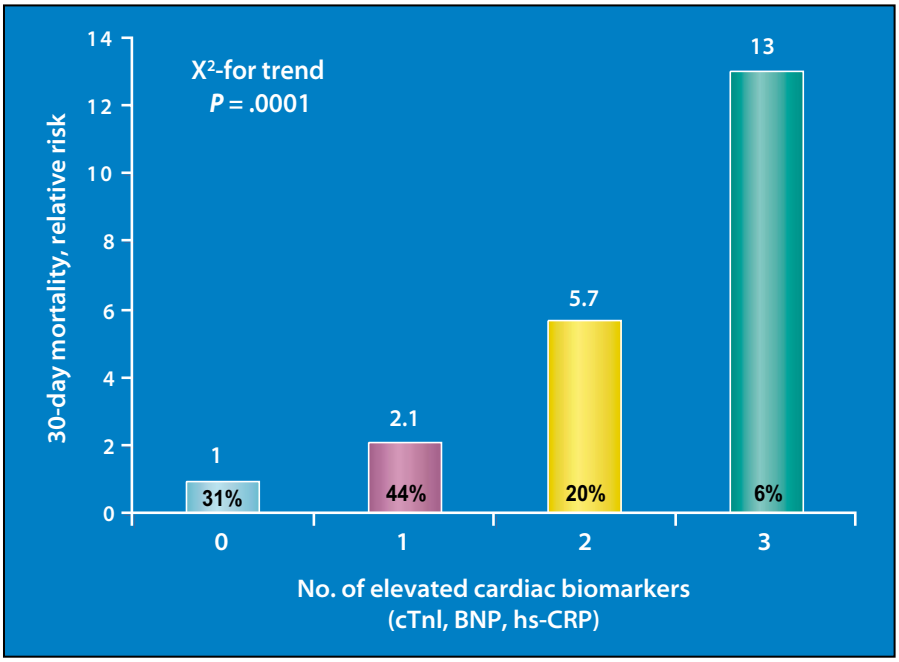

Figure 7. *Multimarker testing using cardiac troponin I (cTnI), high-sensitivity C-reactive protein (hs-CRP), and B-type natriuretic peptide (BNP) in the TACTICS-TIMI (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy–Thrombolysis in Myocardial Infarction) 18 study. The number of elevated biomarkers was significantly associated with 30-day mortality. Adapted from Sabatine et al.*[35]

of these biomarkers remained independently associated with adverse cardiac events, demonstrating the unique predictive information that each of these biomarkers provides. Using a readily accessible strategy, the investigators simply added up the number of biomarkers that were elevated (cTnI > 0.1 mg/L, CRP > 15 mg/L, BNP > 80 ng/dL) and correlated this integer marker score with the development of adverse cardiac events. Patients with normal levels of each of the three markers were at extremely low risk for death, heart failure, or recurrent MI. Risk increased sequentially among those with one, two, or all three biomarkers elevated (Figure 7). The number of elevated biomarkers was associated with multiple cardiac end points, including death, heart failure, and recurrent MI, and was predictive of both short- and long-term risk. Finally, the results were consistent between the two trial populations studied.

The Future: Targeting Therapy to Pathophysiology Using Cardiac Biomarkers

Future studies will undoubtedly expand on the multimarker concepts outlined above. Simply adding up the number of elevated biomarkers, although simple to implement in practice, does not take full advantage of the wealth of information provided by these biomarkers, and does not incorporate the differences between biomarkers with respect to predicting different adverse outcomes. Investigators and clinicians will need to balance the desire to provide maximal predictive value with the need to provide information in a simple, user-friendly format.

Tremendous efforts are under way to identify other cardiac biomarkers that reflect yet other components of the pathobiology of ACS. With a panel of biomarkers that covers the spectrum of pathology of ACS, it is hoped that this heterogeneous syndrome can be treated with a selective rather than a "shotgun" approach. In the future, clinicians may use a panel of cardiac biomarkers, each providing independent and unique information, to create a biomarker profile that can be used to select specific therapies targeted to underlying pathophysiology. ■

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Main Points

- Simple tools can help physicians risk stratify their patients, choose the intensity of antiplatelet and antithrombotic therapy, and decide whether to use invasive coronary procedures. Cardiac biomarkers have proven to be particularly effective for these purposes. Biomarkers that are currently available in clinical practice include markers of myocardial necrosis (creatine kinase [CK] and CK isoenzyme MB [CKMB], myoglobin, and cardiac troponins T and I); markers of inflammation (C-reactive protein [CRP]); and markers of neurohormonal activation (B-type natriuretic peptide [BNP] and N-proBNP).
- CKMB remains useful for diagnosis of early reinfarction and for noninvasive estimation of infarct size, and may help to determine the etiology of nonspecific troponin elevation that occurs frequently with nonischemic etiologies of myocyte injury.
- Minor troponin elevation is associated with high-risk lesion morphology and a high probability of distal embolization. This likely explains the ability of troponin elevation to identify patients who derive greatest benefit from aggressive antiplatelet and antithrombotic therapies.
- Although not specific for cardiac muscle, myoglobin is the most sensitive biomarker for diagnosing myocardial infarction (MI) within the first 6 hours after symptom onset, and is the preferred marker for very early MI diagnosis.
- In multivariate analyses, elevated troponin I, CRP, and BNP were each independently predictive of higher 10-month mortality, demonstrating that each marker provides unique information about mortality following acute coronary syndromes (ACS).
- Low-level troponin elevation is highly predictive of (nonfatal) recurrent ischemic events, whereas BNP appears to be a "pump failure" marker that is more closely associated with death and heart failure progression. Using these two markers together improves the detection of patients at risk for adverse events.
- In the TACTICS-TIMI 18 BNP substudy, an early invasive treatment strategy was of no greater benefit among patients with BNP elevation (>80 pg/mL) than those without BNP elevation. In contrast, patients with troponin elevation derived markedly greater benefit from the invasive approach than those without troponin elevation.
- The pathophysiology and clinical presentation of ACS are heterogeneous, and the "one size fits all" approach to ACS management is suboptimal. Also, different biomarkers clearly reflect different components of the pathophysiology of ACS, and when used together, these different biomarkers provide independent prognostic information.
- In the future, clinicians may use a panel of cardiac biomarkers, each providing independent and unique information, to create a biomarker "profile" that can be used to select specific therapies targeted to underlying pathophysiology.

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