The Cardiac Profile and Proposed Practice Guideline for Acute Ischemic Heart Disease

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Presented with an ever-increasing array of potential tests of myocardial injury, the clinical pathologist in conjunction with physicians in primary care, cardiology, and other clinical disciplines must evolve a practical approach for each individual institution. This involves identifying the tests available for immediate (stat) or timed performance, the appropriate patients for whom testing is desired, the schedule of frequency and duration of testing, and the manner in which the test results are to be interpreted. A guideline is presented to address these issues with the purpose of stimulating local adoption of an appropriately modified version to accommodate the current state of the art. Selective choice of an early marker, creatine kinase MB by mass immunoassay, in conjunction with cardiac troponin I (cTnI), is proposed as the appropriate combination of laboratory tests that emphasizes the cardiac specificity of cTnI for the variety of applications in which the "cardiac profile" formerly has been used, including the spectrum of clinical settings in which suspected myocardial infarction must be considered. A rationale is provided with emphasis on the relative merit of the various biochemical markers in contrast with other modalities for evaluating suspected myocardial injury. (Key words: Creatine kinase; CK-MB; Troponin I; Practice guideline; Cardiac profile; Ischemia) Am J Clin Pathol 1997;107:398-409.

Applied clinical medicine demands answers to questions that are always incompletely addressed by the clinical literature. Invariably, published studies exclude patients commonly encountered in real practice or raise other questions that have not been adequately addressed by controlled prospective studies. Herein lies the art of medicine built on a limited science. The purpose of this article is to offer a practice guideline as a complement to my previous review of the diverse elements involved in the clinical application of the biochemical markers of myocardial injury. As such, it represents a synthesis of the scientific literature on the subject to facilitate discussion and collaboration among relevant parties, particularly emergency physicians, primary care physicians, cardiologists, and pathologists. The universe of available test selection is enriched by a wide array of improved analytical procedures for quantitating previously established analytes and by the introduction of innovative markers. Each institution must develop a finite and realistically achievable approach to the common problem of assessing suspected myocardial injury in complex and diverse states. As such, any proposed "guideline" will be incomplete and limited. This document is offered in that light. It will be of value if it provides nothing more than proximal cause to stimulate collaboration among the medical community in improving and, hopefully, optimizing the care of these patients. It is in this sense that I offer the following considerations.

All tests are not needed. All are not additive in value. Some cannot replace others. Consequently, I offer a practical guideline for a selective protocol integrating clinical considerations with laboratory test selection. Specific protocols that have been chosen for emphasis are those from Gibler et al,2 Lee et al,3 and Mair et al.4 These have been integrated with continuously evolving new information, particularly with regard to cardiac troponin I (cTnI). In the absence of a defined protocol, there is diagnostic chaos, inefficiency, inaccuracy, risk exposure, and support of imprecise diagnosis and treatment along with wasteful expense. While any practice guideline should be regularly updated, sufficient evidence exists for development of such an applied
approach now. In fact, there is an outspoken demand for specific test selection intervals, frequency and length of testing, observational duration, and ranges of expected values. A practice guideline is desired and appropriate.

The biochemical markers of myocardial injury do not replace clinical history and the effective use of the electrocardiogram. They supplement it. One must understand that patients with classic history and electrocardiographic findings consistent with myocardial injury are to be urgently examined for consideration of reperfusion therapy, thrombolytic therapy, or angioplasty. It is beyond the scope of this discussion to extensively detail these subjects; however, this premise is a necessary precondition for further discussion of the appropriateness of biochemical monitoring. Continuous electrocardiographic monitoring is a presumed element in the evaluation and, when informative, provides immediate information before biochemical testing.

The use of the "cardiac profile guideline" is particularly appropriate for the patient at low to moderate risk who seeks care at the emergency room (ER) with an uncertain and transient clinical manifestation of symptoms and in whom ruling out a diagnosis of myocardial infarction is desirable. Having said this, it is also important to emphasize that no other practical cardiac study, including coronary arteriography, echocardiography, stress testing, scintigraphy, or alternative combined approaches can exclude the significance of serial rise and fall of cardiac-specific biochemical markers. All other modalities are proved to be less sensitive than the biochemical markers. This does not create a great dilemma. Rather, it simply requires that the laboratory provide highly reliable analytical data that then must be integrated in an appropriate fashion by wise informed physicians. The reader is referred to other publications for further discourse on this series of points.

**SPECTRUM OF MYOCARDIAL INJURY**

Our concept of the pathophysiologic changes of ischemic myocardial insult now recognizes a continuum from unstable angina through non-Q-wave to Q-wave acute myocardial infarction (AMI) with or without chest pain. In fact, although Braunwald's classification of unstable angina did not invoke biochemical criteria, Braunwald and the Thrombolysis in Myocardial Ischemia (TIMI) III group recently observed the following: "... patients with unstable angina pectoris or non-Q-wave myocardial infarction ... are two acute ischemic syndromes ... often considered together because they typically present in a similar way and can be distinguished only in retrospect based on the evolution of serum enzymes and electrocardiograms." Further, they specified this as serial

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rise of total creatine kinase (TCK) and creatine kinase-MB (CK-MB) isoenzyme beyond the reference ranges in the absence of a developing Q-wave. It is clear that an evolving consensus holds that the diagnosis of unstable angina is a diagnosis of biochemical exclusion. Thus, we can understand that microinfarction has confounded many older studies of the biochemical markers, leading to misleading statistics of sensitivity and specificity based on clinical criteria for distinguishing unstable angina from AMI. The real question is whether there is evidence of active plaque rupture and coronary thrombosis with attendant risk. While intracoronary angioscopy is the most direct method of seeking truth about active plaque rupture and coronary thrombosis, serial rise and fall of the biochemical markers are the most definitive readily available evidence of this.

**CURRENT STATE OF BIOCHEMICAL MARKERS OF INJURY**

At this time, the most valuable markers seem to be CK-MB and cTnl. Many current protocols recommend myoglobin as an early marker. This preference for myoglobin may reflect comparisons with older methods of assaying CK-MB, such as electrophoresis. The time until positive results are obtained (time to positive), variably reported, also depends on the time to presentation and the population included or excluded in the studies. In some studies, CK-MB approximates, and possibly equals, the early sensitivity and time to positive associated with myoglobin. Others challenge this finding, although assay differences and reference ranges may contribute to the conflict. When combined with TCK, CK-MB is more specific for cardiac injury than myoglobin and thus more appropriate for medical decision making. CK-MB should be measured only by mass immunoassay. In the future, with the commercial availability of a new analyte specific for skeletal muscle, carbonic anhydrase III (CA-III), simultaneous measurement of myoglobin, CA-III, and cTnl warrant consideration. The cTnl continues to hold up as the ultimate test of choice, primarily because of its cardiосpecificity and prolonged elevation, but it should be supplemented in the ER setting with an early test of positivity, such as CK-MB or myoglobin, if preferred, with cTnl serving to confirm the early marker.

**Total Creatine Kinase**

In previous conventional guidelines, the easily performed TCK served as a gatekeeper to assist in efficient selection of samples for subsequent testing for CK-MB. When CK-MB was subsequently determined to be present, the TCK served to assist in interpreting the cardiac significance of this analyte because a small and variable amount of CK-MB is routinely present in skeletal muscle and in sera with high levels of TCK. We can now discontinue this practice. Most important, it is now clearly established that individuals with a low TCK, below the level of the “gatekeeper guideline” commonly used by many institutions, may experience myocardial infarction. This is increasingly apparent with recognition of patients with non-Q-wave infarction as a subset of patients who were formerly classified within the unstable angina category. Because prognostic significance is associated with low levels of CK-MB and other myocardial markers, and because methods are available for automated assay of CK-MB on demand, routinely, and relatively inexpensively, the requirement for TCK on all samples is no longer defensible. In fact, sequential performance, first of TCK, inevitably delays determination of the more important CK-MB data.

The cardiac index, an expression of the CK-MB mass as a ratio to the TCK should be routinely calculated when the result exceeds the reference range, using the selected manufacturer’s calculation. At our institution, we recommend calculation of the index when the CK-MB exceeds 4 ng/mL when measured by the Stratus fluorescence immunoassay (Dade International, Miami, Fla). The index is useful when it is extremely high or low, but is of limited value and reduces the sensitivity of CK-MB data.

**Why Cardiac Troponin I Is the Test of Choice**

The diagnosis of myocardial infarction and related coronary artery ischemic syndromes of a lesser degree is extremely challenging. The prototypic myocardial infarction is not difficult to diagnose, and this is the event currently targeted for rapid intervention with thrombolytic therapy, angioplasty, or both. Biochemical markers are not yet considered appropriate indicators for this application, although this may be revised. The real challenge in the emergency clinic setting is recognition of the patient with atypical symptoms or equivocal evidence of myocardial infarction with indeterminate results of an electrocardiogram (ECG). Biochemical testing can provide clarification in making a diagnosis for these patients, who constitute the majority of patients seen typically in an ER setting. When we also consider the perioperative patients with a suspected infarction and those with
extension of myocardial infarction, the diagnosis of AMI becomes even more difficult, suitably invoking the use of biochemical testing. When this need occurs, one seeks an organ-specific marker that is not confounded by other complex pathophysiologic events and specifically identifies myocardial injury. Cardiac-specific cTnl provides this tool even in the most complex settings.

Recently, Guest et al.\(^3\) published a report about 209 challenging and complex patients to determine the incidence and effect of unrecognized cardiac injury in critically ill patients. The patients were located in the medical and respiratory intensive care units of a tertiary care referral center. Many patients had numerous interventions, including manipulation associated with skeletal muscle injury. In addition, many had medical conditions, such as electrolyte disturbances, and were receiving drug therapy, including digoxin, symptom-suppressing analgesics, and psychotropic drugs, that complicated the clinical assessment, a typical and common reality encountered in acute medical care. The study disclosed that cTnl was frequently present in the absence of clinical recognition of myocardial ischemia, and myocardial ischemia was diagnosed in a significant number of patients in whom biochemical confirmation was not present. In fact, only one third of the patients experiencing AMI were given a correct diagnosis by the intensive care unit staff. In 4 of 16 patients in whom the diagnosis was made clinically, biochemical evidence contradicted this. In a subsequent letter to the editor, Beck expressed concern about this article because, “Diagnoses of acute infarction made by the ICU team were not confirmed by elevated levels of cardiac troponin I and were considered false-positive diagnoses.”\(^3\) He further stated, “This operational definition of myocardial injury implies two conclusions: that cardiac troponin I is 100% sensitive and 100% specific and/or that clinicians at the institution have difficulty diagnosing myocardial infarction using currently established tools. Clearly, neither of these conclusions is correct.”\(^3\) Guest et al.\(^3\) responded in effect by stating that they meant exactly what they said, that cTnl was the “gold standard” for the study based on a series of studies that they had referenced in their earlier publication. Their points were as follows:

1. Cardiac troponin I is only found in heart muscle during adult life and embryogenesis.
2. Cardiac troponin I is not expressed in response to skeletal muscle injury.
3. The antibodies used in the assay for cTnl do not cross-react with skeletal muscle troponin I.
4. Cardiac troponin I is not elevated in patients with acute or chronic muscle disease, after endurance exercise, or in patients with renal failure who have elevated levels of CK-MB fraction unless concomitant cardiac injury is present.
5. Elevations of cTnl correlate closely with evidence of myocardial injury demonstrated by echocardiography.
6. There is a 13-fold greater concentration of cTnl than CK-MB in the heart.
7. Elevations of cTnl are at least as sensitive for the clinical detection of cardiac injury as CK-MB.

In addition to the evidence cited by Guest et al.\(^3\),\(^3\) newer publications identify the absence of interference with cTnl in hypothyroidism, more elaborate exclusion of skeletal muscle expression, and favorable experience in uremia and skeletal muscle trauma.\(^3\) Thus, when cTnl is detectable in a peripheral venous sample, the physician can confidently know a cardiac insult is, in fact, present.

Other Cardiac Markers

Troponin T (TnT) is of limited value because it is available on a stat basis only with a qualitative result or with a quantitative immunoassay test system currently requiring at least 45 minutes to perform, which is not suitable for stat needs. In addition, interference occurs in cases involving severe muscle injury, or uremia.\(^3\) Cardiac isoform methods remain less satisfactory for routine use as contrasted with conventional quantitative automated immunoassay.\(^3\) Others advocate the use of these markers, and the reader is urged to consider the issues on the basis of their own circumstances and experience. Although a revised format of the assay for TnT has been announced, preliminary published data acknowledged persistent specificity deficiencies, although less than with the earlier version of the assay.\(^4\)

CHEST PAIN–CARDIAC PROFILE PRACTICE GUIDELINE

There is a need for objective evidence to differentiate patients with coronary heart disease from those who have other causes of chest pain. In a recent editorial, Pepine appropriately stated unequivocally that the clinical distinction between patients “with biologically stable coronary artery disease and those with unstable disease is often unreliable when based on symptoms alone.”\(^4\) Consequently, the use of systematic and disciplined biochemical monitoring in the context of clinical
evaluation has proved essential to the reliable distinction of these syndromes in practice. Gibler et al address this well with the following five points:2

1. "The 12-lead (ECG) is diagnostic in only 50% of patients presenting to the emergency department (ED) with acute myocardial infarction (AMI)."

2. "A single determination of serum marker for myocardial injury obtained on presentation to the ED, has a sensitivity of 35% for detecting AMI because of the kinetics of creatine kinase release."

3. "Approximately 2% to 5% of patients presenting to the ED with chest discomfort and AMI are inadvertently released home."

4. "Twenty percent of the malpractice dollars awarded from the practice of emergency medicine in the United States are associated with the treatment of myocardial ischemia and AMI."

5. "Costs for the admission and inpatient evaluation of patients with chest pain are substantial, with estimates ranging from $5 to $10 billion each year."

In view of these considerations, development of a standardized cardiac profile and chest pain evaluation guideline emphasizing serial testing of biochemical markers using appropriately timed samples is desirable for each institution. The introduction of such a guideline should be an opportunity for performance improvement as a quality assurance project in the sense advocated by the Joint Commission on Accreditation of Healthcare Organizations to compare existing practices with the parallel implementation and use of this guideline.

While a decision to admit or discharge a patient to or from the hospital is the immediate concern, risk stratification is the ultimate goal of assessment of patients with chest pain in the emergency setting. In a recent report, Braunwald’s group reported a 10% increase in risk of mortality for each increment of cTnl elevation after adjustment for other factors.42 Thus, risk stratification is the goal of testing clinically and biochemically and drives options regarding treatment.

Goal of the Practice Guideline

Elements and details of an institution’s practice guideline will be influenced by the answer(s) to the question: What is (are) the goal(s) for the practice guideline?

1. To rapidly “rule in” AMI for admission and disposition, implying the need for continuous frequent testing emphasizing early sensitivity
2. To rapidly institute thrombolytic therapy
3. To rapidly institute primary angioplasty
4. To avoid sending home a patient experiencing an evolving acute ischemic syndrome, implying the need for adequate time for observation and serial biochemical testing
5. To provide documentation that may avert litigation for alleged malpractice, implying the need for sensitive assays corroborating clinical judgment
6. To minimize unnecessary admissions and associated expenses

I. Acknowledgment of limitations

Biochemical monitoring alone only can exclude injury to the myocardium and is imperfect for recognition of impending injury. One must err on the side of conservative management by appropriate use of this guideline in the context of good clinical practice and selective use of other modalities. The questions to apply are these:

A. Has the patient experienced necrosis (infarction)?
B. Is the patient experiencing an ischemic syndrome in the absence of necrosis?

The latter restores the emphasis on clinical assessment.

II. Eligibility of patient for application of this guideline

A. Is the patient excluded because of high risk?
B. Is the patient included because of a threat of:
   1. Acute ischemic heart disease
   2. Other acute cardiac pathophysiological changes
   3. Acute noncardiac disease masquerading as possible cardiac disease

III. Patient selection for emergency clinic evaluation application

A. High risk: patients in hemodynamically unstable condition43 and victims of trauma are not candidates for this practice guideline, Table 2. Patients with an obvious chest pain symptom pattern consistent with infarction or new Q-wave or elevation of the ST segment are appropriately admitted for rapid definitive examination and immediate therapy.44,45 This group is outside the scope of the guideline under discussion, which is appropriately focused on the residual group identifiable as medium to low risk.
B. Medium to low risk: this group is the focus of the proposed practice guideline, which by definition excludes patients with high risk.
IV. Strength of biochemical monitors
While the biochemical markers do not define AMI, their application is similar to the use of assays for human chorionic gonadotropin (hCG) in the diagnosis of pregnancy. One is extremely unwise to diagnose pregnancy in the absence of elevated serum hCG. Conversely, hCG may be produced by proliferating trophoblastic tissue in the absence of pregnancy. So, too, the physician is unwise to diagnose myocardial infarction in the absence of cTnl, yet, this marker can be present with alternative pathophysiologic processes that injure myocardial tissue including trauma, or myocarditis.

A. There is an opportunity for 100% sensitivity and detection of hemodynamically significant acute myocardial infarction.\textsuperscript{1,12}
B. The absence of elevation of biochemical markers in serially timed samples is a practical definition of exclusion of AMI, even when small non-Q-wave infarctions are considered and is used as such in the established literature.\textsuperscript{16,46}
C. Cardiospecific markers define, even with relatively low levels, a group with an adverse long-term prognosis who are at risk.\textsuperscript{17,28}
D. Although they are frequently diagnostic earlier, beyond 9 to 12 hours, biochemical markers can confidently exclude infarction occurring at the time of symptom onset.\textsuperscript{2,4}

V. Monitor ECG throughout
A. A powerful tool; the evolving changes occur promptly following the development of new evolution of coronary occlusive processes.\textsuperscript{47,48}
B. Evolving criteria and computer-assisted interpretation continue to enhance this modality.\textsuperscript{46,48}

VI. Groups to be tested
In contrast with the former widespread application of a standard “cardiac profile” for all considerations of possible AMI, depending on the application, the composition of the test profile and frequency of application may appropriately vary according to:

A. The ER patient group
1. Rule in: consider time to presentation and goal for early triage. Evaluate results of biochemical markers from frequent sampling and the implication of nonconcordant markers. Will therapy be instituted?
2. Rule out: consider time of symptoms and at least 9 to 12 hours subsequent observation.
B. Cardiac surgery: inevitable myocardial insult occurs in a context of skeletal muscle trauma.
C. Perioperative noncardiac surgery: is reperfusion therapy a possibility? If not, frequent testing offers less value.
D. Cardiac trauma: Distinguish myocardial necrosis and predisposition to arrhythmogenesis.
E. Recent AMI, rule out extension: is reperfusion therapy a likely option?

**Emergency Room Group**

The Figure defines the guideline flow for patients with acute manifestations wherein the goal is early reperfusion therapy for some and exclusion of ischemic threat for others.

Triage as follows:

1. High risk: History of severe typical chest pain consistent with cardiac origin or electrocardiographically unequivocal findings. Obtain stat baseline laboratory samples for testing and perform ECG with immediate consideration for therapeutic reperfusion options before the availability of laboratory test results.\textsuperscript{44,45}

Groups with classic pain or ECG results will include baseline testing for CK-MB and cTnl. Repeat testing at 12 hours for retrospective confirmation. Therapy is not likely to be based on serial biochemical criteria, and, for this reason, only a repeated test at 12 hours is needed to confirm the diagnosis. If the diagnosis was in error, this will become apparent. In prospective studies, 10% of “diagnostic” ECG cases did not have an infarction.\textsuperscript{49}

**TABLE 2. CARDIOVASCULAR RISK FACTORS: ACUTE CHEST PAIN**

| 1. ST elevation or Q-wave |
| 2. Other electrocardiographic changes of ischemia |
| 3. Low systolic blood pressure |
| 4. Rales above bases of the lungs |
| 5. Exacerbation of known ischemic heart disease |

Adapted from Goldman et al.\textsuperscript{45}
Emergency room flow: the place of biochemical markers of myocardial injury. ECG = electrocardiogram; AMI = acute myocardial infarction; cTnl = cardiac troponin I; CK-MB = creatine kinase-MB; Neg = negative result; Pos = positive result; TCK = total creatine kinase; 2D = two-dimensional.
2. Low to moderate risk: history atypical, ECG negative or equivocal (low-to-medium risk group): Assay for cTnl to assess for earlier occult AMI and for CK-MB as a baseline. If CK-MB is more than 4.0 ng/mL (or equivalent by other mass assay), then perform TCK and CK indexes. Repeat the CK-MB at 4, 8, and 12 hours after arrival at the ER. Confirm the appearance or rise of CK-MB with concurrent and subsequent cTnl measurements. If the cTnl baseline is positive, then it is appropriate to monitor the patient with cTnl only.

Disposition when biochemical markers are positive.—If CK-MB is more than 4.0 ng/mL (Stratus, Dade International) or its equivalent in other assays, and the CK index is positive or cTnl is detected, consider admission to the intensive care unit or continue observation in the special coronary care environment of the ER. If serial testing confirms a rising slope of the CK-MB with evolution of positive results on the cTnl test, rule in as myocardial injury. Evaluate for evolving AMI, and consider alternative diagnoses that include previously unsuspected chest trauma, myocarditis, vasculitis, cardiomyopathy states, or other entities that may cause myocardial cell damage. As a practical consideration, there is no reliable clinical distinction between ischemia or necrosis. Biochemical evidence should be considered as evidence of necrosis as microinfarction or macroinfarction. The presence in serum of any cTnl, detectable with analytical confidence, should be treated as positive for ischemic threat or minimal myocardial damage and should at least provoke obtaining a later sample for repeat testing. Typically, the presence of a low level of cTnl reflects a declining trend, and, when available, an earlier serum sample may confirm this observation.

Disposition when biochemical markers are negative.—Persistently negative CK-MB testing at 12 hours after obtaining serial specimens from a patient with an atypical history and negative ECG findings should support consideration of discharge from the ER after clinical assessment of the need for alternative studies that could include two-dimensional echocardiography, perfusion scintigraphy, exercise stress testing, and cardiology consultation.2,7,12

Note: The decision to discharge assumes that the presenting symptoms were transient, that is, that the symptoms abated shortly after the presentation to the ER. Biochemical evidence accurately excludes an ischemic event that progresses to necrosis (infarction) within 9 hours or less before the sampling of the last specimen. Because most patients delay coming to the ER, commonly for 2 hours, a protocol that includes testing for 12 hours from appearance in the ER will usually cover a period of approximately 14 hours from symptom onset. Consequently, unless the patient has recurrent symptomatology, the 12-hour protocol should be conservatively sufficient and is supported by the published literature.2,3,12,25,50 No patient should be discharged solely on the basis of exclusion of necrosis because this does not address the question of ischemia and the risk of progression. A thoughtful review of the entire presentation clinically, electrocardiographically, and biochemically is the final challenge to the physician’s judgment.

Pathologist review and comment.—Particularly during a transition from the former practice of combined CK and lactate dehydrogenase (LD) isoenzyme–based cardiac profiling, it is optimal for the pathologist, with an understanding of the analytical system used for testing and of the pathologic and pathophysiologic changes predisposing to the multiple findings, which may be varied, to review and comment on the data. Consequently, the following are recommended:

1. Ideally, a graphic report should be presented providing serial demonstration of the data with a slope that will, when combining the early marker (CK-MB or myoglobin) and the marker of late infarction, cTnl, err in defining the time of the myocardial event. Commonly, the slope will decline, not rise, indicating a late evolving infarction.
2. Assess the pattern and congruity of the data in light of the variable interferences of skeletal muscle trauma on the nonspecific markers when nonconcordant data are present.
3. Suggest extension of the profile when appropriate, for example, when there is a rise of CK-MB from undetectable to detectable, but that is below the laboratory’s generally applicable reference range. In the absence of a disproportionate elevation of TCK as evidence of skeletal muscle injury, a definite change of CK-MB from undetectable to definitely detectable, even in the absence of cTnl, strongly suggests the need for obtaining a further follow-up sample for both in view of the reality of silent ischemia and the slightly earlier appearance of CK-MB in
infarction. Thus, the reviewing pathologist is in a position to alert the clinician to extend the profile.

Attributes of This Guideline

1. The use of cTnl in the baseline sample covers recent, occult, ischemic events that are commonly encountered because of "preinfarctional" states that actually represent a recent infarction.

2. The guideline avoids the delay of obtaining TCK testing before the CK-MB. TCK is only useful if the CK-MB is positive. It eliminates the routine TCK and associated unnecessary expense unless the presence of some CK-MB provokes the need to assess the likelihood of a skeletal muscle source. A concurrent positive cTnl makes this a moot point.

3. Performance of a batch analyzer mass immunoassay CK-MB as a first and less expensive test than cTnl is a current practical reality.

4. It recognizes the slightly earlier appearance of CK-MB in the ER group as generally reported and as corroborated by my experience.

5. Myoglobin is not included, although some centers may wish to include this selectively for patients believed to have no interfering muscle disease. The key issue is whether a physician wishes to act on the myoglobin data. If the assay data will not result in initiation of alternative treatment or admission, then it is of no value. It is the test advocated by some before discharge from the ER because its greatest strength is early sensitivity. Obligatory serial testing of other biochemical markers for 4, 8, 12 hours negates this advantage.

6. Total LD and LD isoenzymes have been omitted from the guideline because they contribute no additional information compared with cTnl data. Further, commonly used electrophoretic methods are labor intensive, subjective, and semiquantitative, and they cause delays and wasted expense.

Prognosis Issues

Short- and long-term prognoses must be distinguished. It is known that patients with a characteristic Q-wave and chest pain have greater short-term prognostic risks than do patients whose conditions are detected only with biochemical abnormalities. The association of ischemia and an adverse outcome, possibly paradoxically, "appears to be strongest in patients with acute ischemic syndromes such as unstable angina and post-infarction ischemia." As a consequence, no single group should be dismissed in the presence of biochemical evidence of myocardial injury. The recent data on risk stratification emphasize the importance of cTnl. Conclusive evidence of the rise and fall of myocardial biochemical markers, even in patients at low risk, implies ruptured plaque with coronary thrombosis and variable coronary occlusion, defining an unstable situation with potential impending catastrophic progression.

Protocols for General Diagnosis and Management of Chest Pain

More detailed protocols have been published by authoritative sources that incorporate more extensive clinical information. These include a formal clinical policy published by the American College of Emergency Physicians and the policy developed by the National Heart Attack Alert Program Coordinating Committee 60-Minutes-to-Treatment Working Group. Both are recommended for review by groups entertaining development of a local practice guideline. They focus on early identification of candidates for thrombolytic therapy or other interventional procedures. That is not the primary focus of this guideline.

Additional sources previously mentioned that provide more focused procedures associated with ruling out myocardial infarction and the disposition of patients, including clinical context in greater detail, are Lee et al and Gibler et al. Gibler et al published the results of more than 1,000 patients with symptoms that suggested an acute ischemic coronary syndrome. The study by Gibler et al presents hard data about the disposition and characterization of the patients. It incorporates a routine cardiology consultation before discharge that may not be feasible in all settings. In addition, two-dimensional echocardiography was included in the protocol, although Sayer and Gibler recently reported that this has not been found productive; their findings agree with the findings of Levitt et al.

Perioperative Group

Noncardiac surgical group.—Included in this group are patients at high risk because of known cardiac disease or older than 55 years who have undergone major surgical procedures, such as hip replacement, colectomy, and other stressful procedures, and those with a known history of coronary artery disease. Testing should include baseline cTnl if possible, to exclude...
occult preexisting infarction, and repeat testing at 6, 12, and 24 hours after operation.

Cardiac surgical group.—This group includes all patients who have undergone bypass grafting or valve replacement surgical procedures. Testing should include cTnl only, at baseline before the operation, and at time zero and 6 and 12 hours after removal of the cross clamps.

Interpretation in the noncardiac surgical group.—Because cTnl is not normally detected in the absence of myocardial injury, appearance of this marker indicates perioperative ischemia. The absence of significant elevation of cTnl excludes intraoperative infarction. Postoperative ischemia may occur at any time during the subsequent period with higher frequency. At the time of suspected late ischemia, institute a repeat protocol based on possible interventional strategies. If thrombolytic therapy is excluded, only retrospective diagnosis may be required, at which point obtaining a repeat sample in 12 hours may be sufficient. Patient testing should be customized to individual needs.

Interpretation in the cardiac surgical group.—My experience has shown that non-Q-wave AMI produces low levels of cTnl, while more obvious clinical events are associated with substantial elevations of cTnl. Readers are referred to the recent publications by Etievent et al and Mair et al for more extensive discussion of cTnl levels in cardiac surgery. Low levels of cTnl, typically below 10 ng/mL will be routinely encountered, reflecting cardioplegia and inevitable operative insult. Higher levels correlate with impaired ventricular ejection performance and clinically detectable intraoperative infarction. Monitoring the cTnl level can provide quality assurance data and an objective modality for assessing an institution’s overall perioperative rate of ischemic complications, and it may evolve to a national standard.

Cardiac Trauma

Published experience with blunt cardiac trauma is limited, but growing experience is encouraging. It seems desirable to substitute cTnl for CK and CK-MB in the obviously traumatized group in whom the results of the latter will be suspect. Consequently, I advocate cTnl testing at 4, 8, and 12 hours initially to evaluate for concurrent AMI or obvious myocardial contusion with or without rupture of the papillary muscle, traumatic coronary thrombosis, laceration of the myocardium, tear of an epicardial artery, or predisposing AMI. Subsequently, sampling at 12-hour intervals up to 48 hours seems reasonable when occult trauma is suspected. The appearance of cTnl at any time warrants close observation and further evaluation, typically with echocardiography.

Postinfarction or Extension Group

After AMI, approximately 20% of patients experience an extension of the infarct or have another infarct. Recently, a thoroughly documented study confirmed the significance of silent ischemia in this group. Thus, it may be appropriate to monitor the continuing decline of cTnl or CK-MB daily, for approximately 5 days. The levels of CK-MB may be more labile than those of cTnl in this group because of earlier clearance. Data available cannot definitively answer this question. Experience may lead to a single daily cTnl measurement in the group, if, as I suspect, cTnl rises proportionately with extension of AMI and if the CK-MB value is frequently suspect in these patients because of confounding concomitant alternative explanations.

SUMMARY AND CONCLUSION

Inevitably, application of the medical literature to applied clinical practice leaves voids. Yet, patient care decisions demand resolution in the individual case. This practice guideline is intended to offer practitioners a skeletal outline to be refined, amended, tested, modified, or challenged in the interest of the art and science of medicine. Undoubtedly, there is error here, but I do not know where. The guideline is certainly incomplete. Thus, it must be continuously revised and updated. So, too, the art and science of medicine will continue to evolve.

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REFERENCES


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