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Using troponin T to diagnose acute coronary syndromes

ABSTRACT

Elevated troponin T is a useful marker for acute myocardial infarction: it is more specific than is elevated creatine kinase MB isoenzyme, and it remains elevated for many days after creatine kinase levels have returned to normal, providing a useful indicator for late presentations. Nevertheless, creatine kinase MB still has many important roles, including providing estimates of infarct size and diagnosing acute myocardial infarction in patients with renal failure. Often, measuring both markers provides additional information. This article provides a diagnostic algorithm for using both markers.

KEY POINTS

Troponin T becomes detectable in the circulation within 4 to 6 hours of a myocardial infarction and remains detectable for 5 to 14 days. Creatine kinase MB levels rise at about the same rate but usually return to normal within 48 hours.

The threshold level of troponin T considered positive for myocardial infarction is 0.1 ng/mL in patients with normal renal function or 0.5 ng/mL in patients with renal impairment.

Lack of a troponin T elevation does not rule out an acute coronary syndrome; serial measurements should be obtained.

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IN PATIENTS with suspected acute coronary syndromes (unstable angina, non–Q-wave infarction, and ST-elevation myocardial infarction), troponin T is more specific for cardiac damage than the current gold standard, the creatine kinase MB isoenzyme (CK-MB). However, CK-MB still has many important roles, such as estimating the size of an infarction and detecting repeat infarctions. Often, measuring both markers together provides more information than measuring either alone.

This article discusses the importance of these two markers and presents an algorithm for using them in the diagnosis of the acute coronary syndromes.

WHAT IS TROPONIN T?

The cardiac troponin complex is part of the contractile apparatus of striated muscle. Acute myocardial injury breaks down troponin into its component subunits, labeled C, I, and T.

As a diagnostic marker, troponin T is quite cardiac-specific. Troponin I is similarly cardiac-specific, but troponin C is not. Myoglobin has been identified as an early marker, but it is not cardiac-specific and thus must be measured in tandem with other markers.

Troponin T can be detected in the circulation within 4 to 6 hours of myocardial infarction and remains detectable for 5 to 14 days. The level of troponin T considered positive for myocardial infarction is 0.1 ng/mL (0.1 µg/L) or higher.

HOW DOES TROPONIN T COMPARE WITH CK-MB?

Although the CK-MB level has become the gold standard for diagnosing acute myocardial

TABLE 1

In acute coronary syndromes, only 60% of patients with elevated markers have elevations at presentation

TIME	PERCENT NEWLY POSITIVE*	
	CK-MB†	TROPONIN T‡
Presentation	59.5%	58.3%
4 hours	28.7%	30.6%
8 hours	8.8%	6.9%
16 hours	2.9%	4.2%

*Of patients who tested positive at any time
†Threshold value > 8.8 ng/mL; n = 119
‡Threshold value > 0.1 ng/mL; n = 123

DATA FROM MCERLEAN ES, DELUCA SA, VAN LENTE F, ET AL. COMPARISON OF TROPONIN T VERSUS CK-MB IN SUSPECTED ACUTE CORONARY SYNDROMES. AM J CARDIOL 2000; 85:421–426.

infarction, many researchers have sought an alternative marker with even better diagnostic and prognostic value, one that is easier to measure, or one that allows quicker identification of myocardial infarction.

The relative diagnostic and prognostic values of troponin T and CK-MB are in dispute. Measuring both markers together is frequently useful.

Troponin T can be measured at the bedside

Troponin T is more specific

In most circumstances, troponins are more cardiac-specific than CK-MB, which can be elevated in patients with skeletal muscle trauma, myopathies, or multiorgan dysfunction.[1]

Measuring troponin T can be faster

Troponin T can be measured by immunoassay either qualitatively at the bedside (which can be done within 20 minutes of sampling and is useful in emergencies in which the laboratory turnaround time would be too long) or quantitatively in the laboratory. In contrast, measuring CK-MB requires special equipment. The bedside (qualitative) test provides a yes-or-no answer as to whether the troponin T level is higher than a defined threshold (either 0.1 or 0.2 ng/mL) and may be affected by subjective factors.

CK-MB is cleared faster

Although troponin T and CK-MB concentrations rise at about the same rate after myocardial necrosis (both reach a peak in about 24 hours), CK-MB is cleared much faster. CK-MB almost always returns to normal 48 hours after an event, but troponin T remains elevated for at least several days and at most 2 weeks.

Therefore, CK-MB is better for detecting reinfarctions soon after the first event. On the other hand, an elevated troponin T with a low CK-MB level in a patient with a clinical presentation and electrocardiographic changes consistent with ischemia suggests a late presentation of myocardial infarction.

Both markers require serial measurements

Neither CK-MB nor troponin T consistently appear in the blood within 6 hours after an ischemic event. Therefore, patients presenting early after symptom onset may not have detectable troponin T, even if they have positive electrocardiographic findings. Measuring CK-MB or troponin T once upon presentation does not detect all cases of myocardial infarction; serial testing dramatically enhances the diagnostic accuracy of both markers.[2,3]

We conducted a 700-patient trial to compare the usefulness of troponin T and CK-MB in suspected acute coronary syndromes.[4] Of the patients who eventually tested positive for troponin T (ie, who had a level > 0.1 ng/mL) or for CK-MB (ie, who had a level > 8.8 ng/mL), only approximately 60% tested positive at presentation; most of the rest became positive in the ensuing 8 hours (TABLE 1). The mean time from symptom onset to hospital presentation was 4.7 hours. Therefore, multiple blood samples should be evaluated over a period of at least 8 hours to definitively rule out myocardial necrosis.

Troponin T clearance is prolonged in patients with renal impairment

Many patients with coronary artery disease also have renal impairment, and there have been reports of apparent false-positive troponin T results in patients receiving hemodialysis.[5] Because the clearance of troponin T is prolonged in patients with renal impairment, it is difficult to discern whether a positive troponin T value is due to a recent event or a remote one.

We found that troponin T levels were not as accurate in predicting adverse outcomes in

patients with renal impairment as they were in those with normal renal function (TABLE 2).[6] Thus, if a patient has renal impairment, one should not diagnose an acute cardiac event unless the troponin T level reaches 0.5 ng/mL and increases with time.

To avoid this difficulty, it may be prudent to depend on CK-MB as the primary diagnostic marker in patients with renal impairment, as clearance of CK-MB is not affected by renal function. A persistently low CK-MB value can rule out an acute event in patients with renal impairment and positive troponin T values.

Troponin T predicts risk better

Troponin T provides more information than CK-MB does about the risk for future cardiac-related adverse events in patients presenting with acute coronary syndromes.[4,6,7–9]

In patients with acute myocardial ischemia and ST-segment changes on presentation, the GUSTO IIa study[8] found that the higher the troponin T level on presentation, the higher was the mortality rate at 30 days. The initial troponin T level added predictive information to that supplied by the baseline electrocardiogram.

In patients with chest pain of suspected cardiac origin, two other studies[10,11] found even patients with troponin T values in the "high-normal" range of 0.05 to 0.1 ng/mL had a higher risk of adverse events than did those with lower values. Possibly, patients with slight increases in troponin T have myocardium that remains at risk for recurrent ischemia or infarction; thus a small troponin T increase may identify a group of patients who would benefit from expedited care.

Troponin T predicts benefit of treatment

Several studies found that patients with elevated troponin T levels not only had a higher risk but derived more benefit from antithrombotic and antiplatelet treatment than did patients with low values.

The FRISC trial[12] looked at troponin T levels in patients with unstable angina or non–Q-wave myocardial infarction, who subsequently received subcutaneous injections of either the low-molecular weight heparin dalteparin (Fragmin) or placebo. At 40 days, in patients with an initial troponin T level of 0.1 ng/mL or higher, 7.4% of those receiving dalteparin had died or had a myocardial infarction, compared with 14.2% of those receiving placebo ($P < .01$). However, dalteparin produced no statistically significant difference in outcomes in patients with troponin T levels lower than 0.1 ng/mL; the 40-day adverse event rate was 5.7% in the dalteparin group compared with 4.7% in the placebo group.

Similarly, the CAPTURE trial[13] looked at troponin T levels in patients with refractory unstable angina who subsequently received the glycoprotein IIb/IIIa inhibitor abciximab (ReoPro) or placebo starting before and continuing through percutaneous coronary angioplasty. At 6 months, in those with troponin T levels higher than 0.1 ng/mL, 9.5% of those who received abciximab had died or had a myocardial infarction, compared with 23.9% of those who received placebo ($P < .001$). In patients with low troponin T, abciximab made no significant difference.

If these findings are confirmed, troponin T values, when combined with other objective measures of ischemia, can be used for spe-

TABLE 2

Troponin T levels in two patients with non–Q-wave acute myocardial infarction with and without renal impairment*

TIME	TROPONIN T LEVEL (NG/ML)	
	PATIENT WITH NORMAL RENAL FUNCTION†	PATIENT WITH RENAL IMPAIRMENT‡
Presentation	0.07	0.36
4 hours	0.36	1.71
8 hours	1.33	1.82
12 hours	1.70	1.80

*At all times, a patient with renal disease can be expected to have higher troponin T levels than a patient with normal kidney function; however, an initial high reading in a patient with renal disease should not be dismissed as falsely positive, as shown by the progressive rise over time and the peak troponin T value higher than 0.5 ng/mL.
†Serum creatinine level 0.9 mg/dL
‡Serum creatinine level 2.6 mg/dL

DATA FROM VAN LENTE F, MCERLEAN ES, DELUCA SA, ET AL. ABILITY OF TROPONINS TO PREDICT ADVERSE OUTCOMES IN PATIENTS WITH RENAL INSUFFICIENCY AND SUSPECTED ACUTE CORONARY SYNDROMES: A CASE-MATCHED STUDY. J AM COLL CARDIOL 1999; 33:471–478.

Creatine kinase may be a better marker in patients with renal impairment

cific treatment decisions in patients with unstable angina.

A negative troponin T result does not rule out disease

Of importance: a negative troponin T finding does not imply the absence of risk for future cardiac events. In our study,[4] 55% of the patients who experienced an in-hospital event had negative troponin T results. In contrast, another recent study[7] found that among low-risk patients presenting to the emergency department with chest pain, those with negative troponin T findings could be discharged safely. However, on balance, these findings suggest that negative findings for cardiac markers indicate the absence of myocardial necrosis, but do not necessarily rule out an acute coronary syndrome, particularly unstable angina.

CK-MB estimates the size of an infarction

CK-MB is more reliable than troponin T for estimating the size of an infarction, since its faster clearance allows it to be used for infarct sizing within the first 48 hours of presentation. In contrast, troponin T may provide information about infarct size but after a longer time course. This renders it less useful for this purpose.

Cardiac markers must be tracked over time

More is known about CK-MB

Finally, more is known about CK-MB than about troponin T in many situations simply because of a wealth of previous research on CK-MB as the gold standard in diagnosing myocardial infarction. For example, the prognostic implications of elevated CK-MB after percutaneous intervention are better documented than the implications of elevated troponin T in this situation.[14] Therefore, CK-MB should be evaluated after a percutaneous intervention. Similarly, there are limited data about the effect of cardiopulmonary bypass surgery or defibrillation on the release of troponin T.

TESTING IS BASED ON THE INITIAL ELECTROCARDIOGRAM

All patients who present with chest pain of possible cardiac origin should have a 12-lead electrocardiogram to obtain objective information about ST-segment and T-wave changes (FIGURE 1). Subsequent testing is based on the initial electrocardiographic findings.

ST-segment elevation

Patients with clear-cut ST-segment elevations and a clinical picture consistent with acute myocardial infarction can be admitted and treated on the basis of these findings alone.

Nevertheless, at presentation, troponin T and CK-MB should be measured in the laboratory to confirm these findings. Further CK-MB testing may be performed to estimate infarct size. Another reason for measuring troponin T is to assess short-term and long-term risk for subsequent cardiac-related adverse events.

ST-segment depression or T-wave inversion

Patients with ST-segment depression or T-wave inversion consistent with ischemia can be given a tentative diagnosis of unstable angina, although non–Q-wave myocardial infarction must be ruled out. They should be admitted, and troponin T or CK-MB or both should be monitored initially and at 6 and 12 hours either qualitatively at the bedside or quantitatively in the laboratory.

If the troponin T level reaches 0.1 ng/mL, the diagnosis of non–Q-wave infarction is made, and further quantification of troponin T and CK-MB is appropriate for evaluating infarct size. Aggressive management with reperfusion or antiplatelet therapy should be considered for troponin T-positive patients, even if the troponin T concentration is less than 0.1 ng/mL.

Nonspecific changes or normal findings

Electrocardiography has been shown to be nondiagnostic at presentation in over 40% of patients who ultimately are diagnosed with acute myocardial infarction.[2] In addition, some preexisting conditions limit the interpretation of the electrocardiogram, such as left bundle-branch block and ventricular paced rhythm.

In these situations, cardiac markers serve to confirm or exclude myocardial damage, especially if the patient has an atypical clinical history and nonspecific electrocardio-

Using the electrocardiogram and cardiac markers to assess and manage acute coronary syndromes

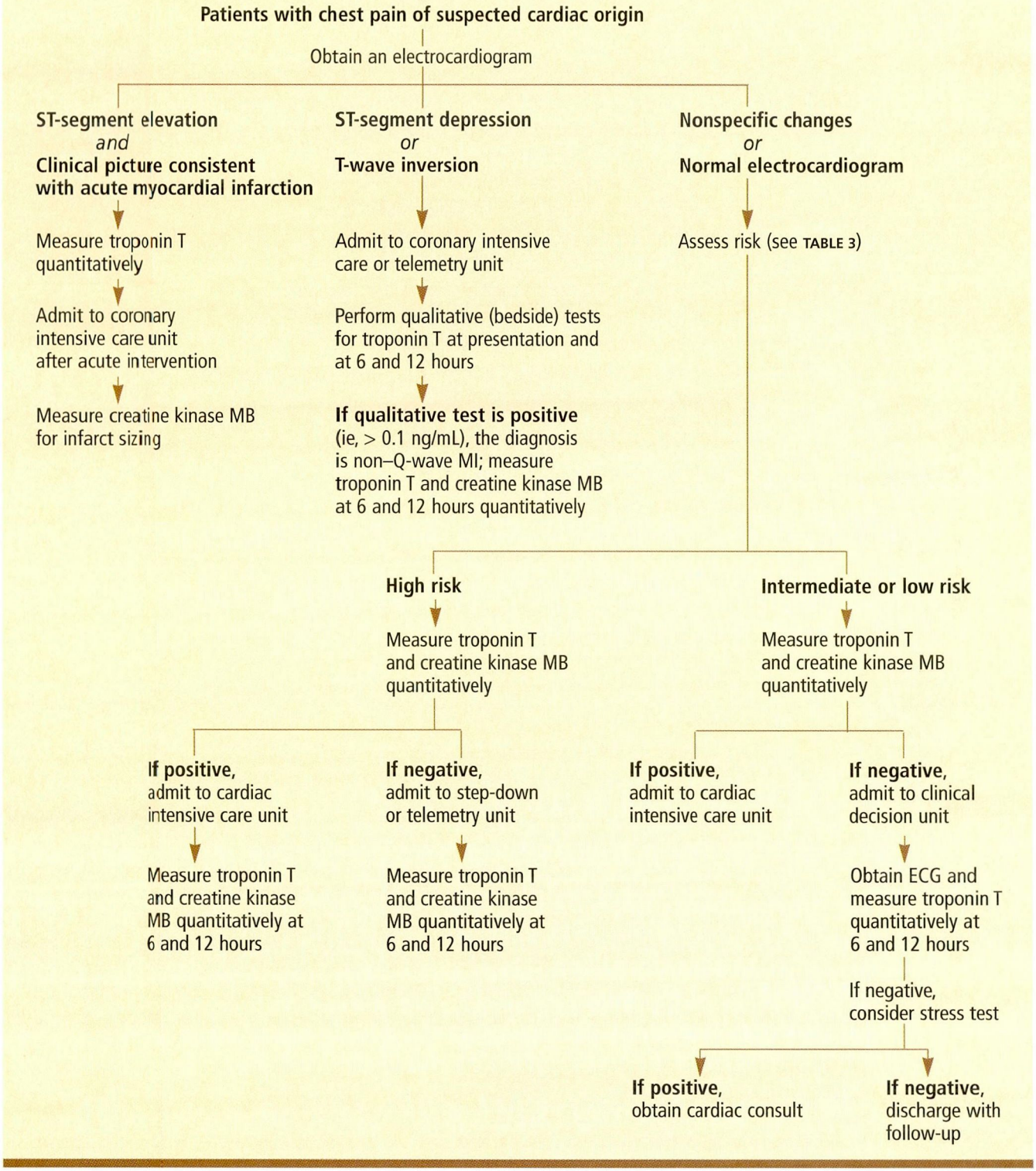

FIGURE 1

TABLE 3

Likelihood of significant coronary artery disease in patients with symptoms suggesting unstable angina*

High likelihood (85%–99%)
Any of the following features:
- History of prior myocardial infarction or sudden death or other known history of coronary artery disease
- Definite angina in a man ≥ 60 years of age or a woman ≥ 70 years of age
- Transient hemodynamic or electrocardiographic changes during pain
- Variant angina (pain with reversible ST-segment elevation)
- ST-segment elevation or depression ≥ 1 mm
- Marked symmetrical T-wave inversion in multiple precordial leads

Intermediate likelihood (15%–84%)
Absence of high-likelihood features and any of the following:
- Definite angina in a man < 60 years of age or a woman < 70 years of age
- Probable angina in a man ≥ 60 years of age or a woman ≥ 70 years of age
- Chest pain probably not angina in a patient with diabetes
- Chest pain probably not angina and two or three risk factors other than diabetes (ie, smoking, hypertension, and elevated cholesterol)
- Extracardiac vascular disease
- ST-segment depression 0.05–1 mm
- T-wave inversion ≥ 1 mm in leads with dominant R waves

Low likelihood (0.01%–14%)
Absence of high or intermediate likelihood features, but may have:
- Chest pain classified as probably not angina
- One risk factor other than diabetes
- T-wave flattening or inversion 1 mm in leads with dominant R waves
- Normal electrocardiogram

*Estimating the likelihood of significant coronary artery disease is a complex, multivariable process that cannot be fully specified in a table such as this; therefore, the table is meant to illustrate major relationships rather than offer rigid algorithms

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Predicting risk is more complex than a table can show

graphic changes or a number of risk factors for coronary artery disease.

It is important to assess the patient's clinical risk factors (TABLE 3). In patients with significant risk factors, either qualitative or quantitative troponin T testing should be performed initially and the result used to triage the patients appropriately.

If troponin T is elevated, consider admitting the patient to the cardiac intensive care unit regardless of his or her apparent clinical risk.

If troponin T is not elevated in a patient at low or intermediate risk, admit the patient to a clinical decision unit for observation.

If troponin T is not elevated in a patient at high risk, admit the patient to a telemetry hospital unit. Measure troponin T at 6 and 12 hours after presentation to rule in or rule out acute myocardial necrosis. Base subsequent management decisions on whether troponin T is elevated or not. A high troponin T level (> 0.1 ng/mL, measured quantitatively) indicates that the condition should be managed aggressively with antiplatelet and antithrombotic therapy.

In low-risk patients without troponin T elevation and negative ECG findings, consider a follow-up stress test.

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