COLLEGE of AMERICAN PATHOLOGISTS

Cardiac Marker Testing Practices

Version: 3.0
Date: Originally Published July 2017; reviewed April 2020, revised October 20, 2022

Author
Peter L. Perrotta, MD, FCAP, Department of Pathology, West Virginia University Hospital

Editors
Richard W. Brown, MD, FCAP*, Department of Pathology, Memorial Hermann Health System, Houston, TX, Barbara Blond, MBA, Thomas Long, MPH
* Senior Editor. All other editors are listed alphabetically

SYNOPSIS AND RELEVANCE

Guidelines have been published that recommend using cardiac troponin (cTn) as the preferred marker of acute myocardial injury (AMI). Adherence to these recommendations can:

1. Ensure that cTn is utilized properly and preferentially as a marker of AMI.
2. Reduce the utilization of other markers of AMI such as the creatine kinase MB (CK-MB) fraction. While this module focuses on cTn and CK-MB testing, a similar strategy could be used to evaluate other cardiac markers.
3. Impact patient care by establishing and following an effective approach for detecting AMI.

OBJECTIVES

1. Define which diagnostic tests are most useful to clinicians who are evaluating patients with suspected AMI.
2. Critically assess the clinical and technical issues that impact AMI testing.
3. Recognize ways to improve the selection of tests used to detect AMI.

BACKGROUND

For several decades the creatine kinase MB fraction had been used as a marker of acute myocardial injury (AMI). CK-MB is released into the blood following heart or skeletal muscle injury. The CK-MB "relative index", defined as the amount of CK-MB relative to total CK, is calculated to differentiate cardiac from skeletal muscle as the injury source. There is a delay in the appearance of measurable CK-MB following AMI due to the relatively large size of this molecule. The automated instruments in most laboratories are capable of running this test.

The development and widespread adoption of a more specific measure of myocardial injury, cardiac troponin (cTn), including troponin I(TnI) and troponin T(TnT), has called into question the need to routinely perform CK-MB testing. Following AMI, cTn is released before CK-MB and levels remain elevated longer than CK-MB due to myofibril degradation. Practice guidelines first published in 2007 state that the standard for diagnosing AMI is cTn because of its superior specificity and sensitivity. Opposition to removing CK-MB from test menus is usually based on concerns that reinfarction and injury post cardiac intervention may not be detected using only cTn due to its prolonged elevation following ischemia. In fact, it is now clear that reinfarction can be detected when there is re-elevation of cTn after it reaches a plateau stage or declines toward normal levels. cTn levels can also be used to estimate infarct size like CK-MB.

Optimizing the utilization of tests commonly used to detect AMI may increase the value of clinical cardiac services for providers and patients by:

- Improving the performance of the diagnostic strategy used at your institution to detect AMI.
- Streamlining the evaluation of patients with AMI for your health care professionals in a collaborative manner.
- Enhancing the training and education of providers who routinely order cardiac marker testing.

- Ensuring that your health information technology services support the decision making of health care providers who utilize cardiac marker testing by optimizing the electronic test ordering and laboratory test resulting systems.

INSIGHTS

1. cTn is the most widely available, sensitive and specific test used to detect AMI. There is only one FDA approved cTnT assay. There are more than a dozen cTnI assays that are FDA approved. While clinical concordance is typically excellent between cTnI assays or platforms if the assay's 99th percentile is used as the upper reference limit, there may not be good numerical agreement due to poor standardization among cTnI assays.
2. The CK-MB test provides little to no additional information to that provided by a cTn test when evaluating patients for AMI.

INTERVENTIONS

Investigate how providers order CK-MB levels: Providers may routinely order a CK-MB level whenever they order a cTn test. Evaluate your test ordering system (electronic and/or paper) to determine if it facilitates ordering both of these tests at the same time. Ensure that the cTn test is prominently displayed.

Limit the ability to order CK-MB in electronic and/or paper ordering systems: Most electronic ordering systems can facilitate the ordering of the most useful diagnostic tests. For example, screen "pop-ups" can be used to alert the provider that they are ordering a CK-MB level instead of a cTn level, or when they order both CK-MB and cTn at the same time. The "pop-up" screen can be designed so that the provider can easily cancel the CK-MB order. CK-MB levels should also be removed from electronic "order sets".

Provide information to providers and/or services regarding the utility of CK-MB levels: Targeted educational activities can be used to update providers when a test has become antiquated, or a more useful test is available that can replace an older test. In many cases providers are aware that a test has little clinical utility but have become accustomed to ordering that test.

Remove CK-MB from the laboratory test menu: The most effective way to reduce CK-MB levels is to remove the test from order sets. This will require interactions with hospital leadership, cardiologists, emergency physicians, etc. This project could be reviewed by a laboratory test utilization group, or other appropriate institutional committee. CK-MB levels can be eliminated from both electronic and paper ordering systems. The laboratory should notify providers when significant changes are made to the test ordering menu to avoid confusion and frustration.

INTERVENTION ANALYSIS

There are a number of ways that you can assess the effectiveness of cardiac monitoring practices depending on your goals for this project.

- You can begin with a "Self-Evaluation" by determining the total number of CK-MB and cTn levels performed over a period, for example, 3-12 months depending on test volume (see Appendix A).
- Calculate the ratio of the number of CK-MB to cTn levels performed over this period (ie, # cTn/# CK-MB). This ratio serves as a baseline indicator of test utilization and helps to standardize calculations based on test volume.
- Identify individual providers and groups of providers (ie, services) that order most of the CK-MB levels performed and ensure that they receive appropriate education.
- Implement interventions to reduce the number of CK-MB tests ordered; these interventions should be focused on providers and services that order the highest numbers of CK-MB tests.
- After interventions have been put in place, follow-up studies can be performed to assess the success of the interventions used to alter the number of CK-MB orders (see Appendix B).
    - Recalculate the ratio of cTn to CK-MB levels performed post-intervention. Select a period in months to make the calculations easier (eg, 1 month). Reduction in CK-MB use is suggested by a higher ratio of cTn to CK-MB tests performed.
    - Determine how CK-MB testing volume was altered following interventions by calculating how many CK-MB tests would not be performed over 12 months.

- You can show the value of this test utilization activity in various ways. For example, clinicians may experience fewer difficulties interpreting discordant cTn and CK-MB results. This could also be considered a patient safety issue. An analysis of these discrepancies at one's own institution may help to emphasize that both tests are not needed.

APPENDIX A: TESTING VOLUME

cTn & CK-MB Testing Volume		
# cTn (TnI and TnT) levels performed over 12 months	A1	
# CK-MB levels performed over 12 months	A2	
Calculate Ratio cTn to CK-MB levels = **A1/A2**	A3	
Providers who ordered highest # of CK-MB (top 5) Indicate the provider and # of tests ordered	Provider	#Tests
Provider #1 (#CK-MB):		
Provider #2 (#CK-MB):		
Provider #3 (#CK-MB):		
Provider #4 (#CK-MB):		
Provider #5 (#CK-MB):		
Services that ordered highest # of CK-MB (top 5) Indicate the service and # of tests ordered	Service	# Tests
Service #1 (#CK-MB):		
Service #2 (#CK-MB)		
Service #3 (#CK-MB)		
Service #4 (#CK-MB)		
Service #5 (#CK-MB)		

APPENDIX B: FOLLOW-UP: DETERMINE THE EFFECTIVENESS OF INTERVENTIONS USED TO REDUCE CK-MB TESTING

Post-Intervention Follow-up Data		
# cTn levels performed post-intervention	C1	
# CK-MB levels performed post-intervention	C2	
Post-intervention period (in months)	C3	
Ratio cTn to CK-MB levels = C1/C2	C4	
# CK-MB levels decreased per year = A2 – (C2*(12/C3))	C5	

QUESTIONS AND ANSWERS

QUESTION 1

OBJECTIVE

To understand which diagnostic tests are most useful to clinicians when evaluating patients with suspected AMI.

Which of the following is the most specific test used to detect acute myocardial injury?

A. Creatine kinase, MB fraction
B. Creatine kinase, total
C. Lactate dehydrogenase
D. Troponin I
E. Urine myoglobin

The correct answer is D. Cardiac troponins (TnI and TnT) are the most specific tests used to detect myocardial injury.

REFERENCE

Apple FS, Jesse RL, Newby LK, et al. National Academy of Clinical Biochemistry and IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory Medicine Practice Guidelines: Analytical issues for biochemical markers of acute coronary syndromes. *Clinical Chem*. 2007;53(4):547-551. doi: 10.1161/CIRCULATIONAHA.107.182881

QUESTION 2

OBJECTIVE

To determine the best alternative test to order when cardiac troponin testing is unavailable.

When cardiac troponin testing is not available, which of the following is the best alternative test?

A. Creatine kinase, MB fraction
B. Creatine kinase, total
C. Lactate dehydrogenase
D. Troponin I
E. Urine myoglobin

The correct answer is A. The next best alternative to cardiac troponin when this test is not available is CK-MB as measured by mass assay. Total CK is a sensitive marker of myocardial damage; however, it has poor specificity due to its high concentration in skeletal muscle. Lactate dehydrogenase is also non-specific. Myoglobin is not typically measured in urine.

REFERENCE

Apple FS, Jesse RL, Newby LK, et al. National Academy of Clinical Biochemistry and IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory Medicine Practice Guidelines: Analytical issues for biochemical markers of acute coronary syndromes. *Clin Chem*. 2007;53(4):547-551. doi: 10.1373/clinchem.2006.084715

QUESTION 3

OBJECTIVE

Understand interventions that can be used to decrease use of CK-MB testing for AMI.

Which of the following interventions is most likely to reduce the use of CK-MB testing in the diagnosis of acute myocardial injury?

A. Adding the CK-MB test to order sets used by emergency room physicians
B. Developing and performing a next generation method for CK-MB testing
C. Making the CK-MB test “not orderable” in the computer physician order entry system
D. Placing the CK-MB test on cardiology admission order sets

The correct answer is C. Limiting the ability to order the CK-MB test is most likely to reduce the utilization of this test. Electronic order sets used by providers to request tests should be examined so that the cardiac troponin test is emphasized.

REFERENCE

Baron JM, Dighe AS. The role of informatics and decision support in utilization management. *Clinica Chimica Acta*. 2014; 427:196-201**.** doi: 10.1016/j.cca.2013.09.027

MODULE REFERENCES

1. Alpert JS, Jaffe AS. Interpreting biomarkers during percutaneous coronary intervention: the need to reevaluate our approach. *Arch Intern Med*. 2012;172(6):508-509. doi:10.1001/archinternmed.2011.2284
2. Apple FS, Murakami MM. Cardiac troponin and creatine kinase MB monitoring during in-hospital myocardial reinfarction. *Clin Chem*. 2005;51(2):460-463. doi: 10.1373/clinchem.2004.042887
3. Apple FS, Jesse RL, Newby LK, et al. National Academy of Clinical Biochemistry and IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory Medicine Practice Guidelines: Analytical issues for biochemical markers of acute coronary syndromes. *Clin Chem*. 2007;53(4):547-551. doi: 10.1373/clinchem.2006.084715

4. Apple FS, Jesse RL, Newby LK, et al. National Academy of Clinical Biochemistry and IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory Medicine Practice Guidelines: Analytical issues for biochemical markers of acute coronary syndromes. *Circulation.* 2007;115(13):e352-355. doi: 10.1161/CIRCULATIONAHA.107.182881
5. Collinson PO, Gaze DC, Morris F, Morris B, Price A, Goodacre S. Comparison of biomarker strategies for rapid rule out of myocardial infarction in the emergency department using ACC/ESC diagnostic criteria. *Ann Clinc Biochem* 2006;43(Pt 4):273-280. doi: 10.1258/000456306777695555
6. Novack V, Pencina M, Cohen DJ, et al. Troponin criteria for myocardial infarction after percutaneous coronary intervention. *Arch Intern Med.* 2012;172(6):502-508. doi: 10.1001/archinternmed.2011.2275
7. Panteghini M, Cuccia C, Bonetti G, Giubbini R, Pagani F, Bonini E. Single-point cardiac troponin T at coronary care unit discharge after myocardial infarction correlates with infarct size and ejection fraction. *Clin Chem*. 2002;48(9):1432-1436.
8. Thygesen K, Alpert JS, White HD, et al. Universal definition of myocardial infarction. *Circulation.* 2007;116(22):2634-2653. doi: 10.1161/CIRCULATIONAHA.107.187397
9. Thygesen K, Alpert JS, Jaffe AS, Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction. *Circulation.* 2012;126(16):2020-2035. doi: 10.1161/CIR.0b013e31826e1058
10. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes. Executive summary. A report of the American College of Cardiology/American Heart Association task force on practice guidelines. *Circulation*. 2014; 130(25): 2354-2394. doi: 10.1161/CIR.0000000000000133