The growing impact of cardiac biomarkers in clinical chemistry

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Clinical chemistry measurements and calculations take into account an expansive set of analytes that reflect cardiac, liver, kidney, and other biological functions. Several of these discrete analytes are considered biomarkers, defined by Strimbu and Tavel as “a broad subcategory of medical signs [that are] objective indications of medical state observed from outside the patient which can be measured accurately and reproducibly.” In the case of cardiac biomarkers, the most common analytes are creatine kinase (CK), lactate dehydrogenase (LDH), and troponin (TNI). There are pros and cons to using these common chemistry tests as definitive cardiac biomarkers. However, other chemistry analytes and even some non-laboratory tests have been identified as potential cardiac biomarkers. Providing clinicians with accurate and thorough testing is important in contributing to diagnosis and ultimately to positive patient outcomes.

CK, LDH, and TNI

In a typical clinical chemistry test menu, analytes are “grouped” in terms of impact on organ systems, which leads to the typical cardiac, comprehensive, and liver panels. As noted above, the cardiac panel commonly contains CK, LDH, and TNI. These analytes measure the contraction of muscle and the conversion of lactate to pyruvic acid, a result of the muscle contraction. While these tests are excellent diagnostic tools, they can be impacted by different physiological states, resulting in changes to testing results. For example, if a patient is having heart problems, the doctor will order a cardiac panel. However, if that same person went to the gym recently and worked out hard, that could send the CK value skyrocketing—not because the person is having heart problems but because of the stress on the muscles overall.

Creatine kinase is a more general molecule measured as a cardiac biomarker. CK can be broken down to three isoforms that enable a more specific analyte to be measured. CK-MM is the isoenzyme typically measured overall, and it identifies damage to muscle cells in skeletal tissue in addition to heart muscle. CK-MB is found more specifically in the heart and rises significantly due to damaged heart muscle. CK-BB is the most specialized isoenzyme and is correlated to the brain. Analysis of CK-MB more closely links CK elevation to damaged heart muscle seen in myocardial infarction. Some labs can perform isoenzyme analysis, while others send this out to reference facilities.

That trip to the gym could also affect LDH results. LDH is a non-specific test that primarily demonstrates conversion of lactate to pyruvic acid. Lactate is found in typical blood samples, and damaged heart muscle can, for example, cause LDH to be elevated due to this conversion as a general indicator of tissue and cellular damage. While this can assist in identifying cardiac damage, LDH increase can also be a result of overworked muscle (the gym visit), anemia, and some cancers.

In recent years, the troponin (TNI) test has replaced both of these markers as an indicator of cardiac muscle damage. Troponin is currently the most commonly used indicator of cardiac damage, not only because of its quick reacting but because of its specificity to heart muscle damage. Troponin I raises quickly (within a few hours of damage to the heart) and can remain elevated for up to two weeks. *Alternative assays*

While those principle cardiac biomarkers are the most commonly used, there are several other tests that can be related to cardiac damage and thus can be used to evaluate a patient at risk of cardiac infarct.

Myeloperoxidase (MPO) is not generally used for cardiac assessment, but it can assist in predicting the risk of myocardial infarction. When the arterial walls are injured or inflamed, MPO is released by macrophages. MPO then oxidizes LDL, making it atherogenic, and also oxidizes HDL, rendering it non-functional. This results in inflammation linked to plaque formation. Formation of plaque can be a contributing factor, but it isn’t directly measured in standard clinical laboratory testing.

Brain natriuretic peptide (BNP) is measured for the diagnosis of heart failure in patients with acute dyspnea. Increased stress levels in the heart walls cause the synthesis of pre-proBNP, which cleaves and forms the terminal fragment NT-proBNP. NT-proBNP has a stability of one to two hours. It has been shown that NT-proBNP values are increased with age, and therefore the values are typically adjusted. BNP values are also increased due to renal disease, due to increase in functional pressures, and due to decreased filtration and excretion. NT-proBNP testing of patients presenting with dyspnea emphasizes that these assays are more sensitive than specific and more important in the diagnosing and monitoring of congestive heart failure.

D-dimer is a coagulation test, which identifies the protein fragment present in the blood after a blood clot is degraded by fibrinolysis. D-dimer, used in conjunction with scoring rule-out criteria such as Wells or Geneva, which is a tier grouping system, separates patients into a low, medium or high risk assessment. For example, normal D-dimer results in a low-risk patient would exclude acute but not chronic pulmonary embolism (PE). PE is a lung blood clot and is another cause of dyspnea and should be ruled out.

Inflammation markers such as CRP and interleukins (IL-6 and IL-18) can be used in the clinical setting to assist in the diagnosis of coronary heart disease. High levels of CRP are indicated in patients with unstable angina (chest pain) and are associated with worsening end results. Additionally, IL-6 and IL-18 also show increased levels in coronary heart problems. These markers, as well as CRP, are elevated in many other disease processes and should not be used solely in a clinical setting.

The measurement of the three common cardiac biomarkers is the hallmark of diagnosis for physicians. However, there are additional clinical laboratory tests sometimes used to reflect cardiac alterations in a patient. These additional tests are beneficial but are also reflective of changes in different

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biochemical and disease states such as kidney and liver function. This can make these additional tests somewhat suspicious for this level of diagnosis. Of course, the ordering of these additional tests is at the discretion of the treating provider, whose specialty and experience may impact his or her use of them to identify cardiac changes. As clinical laboratory scientists, our goal is to increase the capability of our laboratories and our ability to more accurately present data to the providers.

REFERENCES

4. AACC Lab Tests Online. Cardiac biomarkers. stsonline.org/understanding/analytes/cardiac biomarkers/.

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