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Title: “The Uses and Importance of Cardiac Biomarkers in the Diagnosis of Cardiovascular Diseases”

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Introduction

According to the World Health Organization (2023), cardiovascular diseases (CVDs) are considered to be the primary cause of death worldwide. With these deaths, about 85% were caused by heart attack and stroke (World Health Organization, 2023). Cardiovascular diseases are a group of diseases that affect the heart and the blood vessels. Some CVDs include coronary heart disease, cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease, and deep vein thrombosis. With cardiovascular diseases being considered as one of the leading causes of death, it is important to find ways to prevent and manage these cardiovascular diseases.

In the clinical laboratory, cardiovascular diseases can be detected and diagnosed with the use of cardiac biomarkers. Cardiac biomarkers are “endogenous substances that are released in the circulation when the heart is damaged or stressed” (Dasgupta & Wahed, 2021). They are typically released when there is “damage or death of the cardiac myocytes” (Dasgupta & Wahed, 2021). The typical cardiac biomarkers used in detecting and diagnosing cardiovascular diseases include cardiac troponin, creatinine kinase, CK-MB, and myoglobin. These particular biomarkers help determine if there is myocardial necrosis, which is the death of heart muscle due to a heart problem. There are also other cardiac biomarkers, such as lactate dehydrogenase, B-type natriuretic peptide, and C-reactive protein. These other biomarkers help to examine for myocardial ischemia, hemodynamic stress of the heart, or inflammation of the heart (Dasgupta & Wahed, 2021). While all of these cardiac biomarkers are useful in different ways for detecting and diagnosing CVDs, they do have advantages and disadvantages. It is vital to understand how
each of these cardiac biomarkers work and determine the best that could be used in the diagnosis and treatment of CVDs.

**The Advantages and Disadvantages of Cardiac Troponin**

Cardiac troponins (cTn) are currently known as one of the most powerful cardiac markers in diagnosing cardiovascular diseases, mainly diagnosis of myocardial infarction (Chaulin, 2022). Cardiac troponins (cTn) are very powerful cardiac biomarkers because of their high sensitivity in detecting damage of the myocytes. Cardiac troponins are considered a troponin complex that consists of three regulatory proteins (Omran et al., 2022). The three regulatory proteins of the troponin complex include troponin I (cTnI), troponin T (cTnT), and troponin C (cTnC).

In understanding the physiology of troponins, they are proteins that are bound to the protein, tropomyosin. Tropomyosin functions, along with actin, to form thin filaments that plays a role in the contraction of striated muscle cells, such as skeletal muscle and cardiac muscle. Troponin I is an inhibitory subunit that binds to actin when relaxed and prevents actomyosin’s ATPase activity. This, as a result, stops the contraction of muscle due to the loss of calcium ions (Chaulin, 2022). Troponin T is a regulatory subunit that secures the troponin complex to the thin filaments, allowing for muscle contraction to occur (Chaulin, 2022). Troponin C is a calcium-binding subunit that binds calcium ions and structurally changes the proteins within the troponin-tropomyosin complex (Chaulin, 2022). When a muscle receives a signal from the human body, the sarcoplasmic reticulum opens up its calcium ion channels. The sarcoplasmic reticulum sends out calcium ions into the sarcoplasm, which binds to troponin C. This ultimately allows for contraction of striated muscle to occur as the myosin heads interact with the actin molecules (Chaulin, 2022).
Cardiac troponin T and troponin I are primarily used in the clinical laboratory for diagnosing myocardial infarction. This is due to the fact that troponin T and troponin I are found exclusively in the heart, while troponin C can be found in the heart and skeletal muscles (Omran et al., 2022). Since troponin C is found in two different locations, it makes it more difficult for the diagnosis of cardiovascular diseases. By focusing on the use of only troponin I and troponin T, it helps to narrow down the patient’s diagnosis for a cardiovascular disease.

When examining these two main cardiac biomarkers, troponin T and troponin I, in the diagnosis of a myocardial injury, it is mainly used in the diagnosis of acute myocardial infarction (AMI). These two cardiac troponins typically elevate in number between 4 to 9 hours with the use of a conventional troponin assay and between 3 to 4 hours with the use of a high sensitivity troponin assay. After the elevation of these cardiac troponins, it eventually peaks around 12 to 24 hours. It will not return to its normal baseline until after 10 to 14 days later (Dasgupta & Wahed, 2021). While these two cardiac troponins are similar in when they increase in number, when they peak in number, and when they return back to its baseline, cardiac troponin I is typically the most specific biomarker for myocardial injury (Dasgupta & Wahed, 2021). On the other hand, cardiac troponin T is not as specific as cardiac troponin I, since it can also be elevated in a patient that has chronic renal failure (Dasgupta & Wahed, 2021).

Even with the high sensitivity of these cardiac troponins, it is important to understand that cardiac troponins can also elevate in other non-cardiovascular diseases. These other diseases include “sepsis, acute respiratory distress syndrome, chronic obstructive pulmonary disease, renal failure, diabetes, acute neurological event, chemotherapy, drugs, and toxins” (Omran et al., 2022). With cardiac troponins lacking specificity in determining the type of disease, it makes it more difficult to narrow down the cause of the disease. Furthermore, cardiac troponins also do
not fully narrow down the cause of a particular cardiovascular disease. Even if a patient’s disease is narrowed down to a cardiovascular disease, it does not necessarily determine the exact type of cardiovascular disease. It is important to increase the specificity of cardiac troponins to allow it to easily detect and determine the etiology of the patient’s disease. Along with the lack of specificity, it was found that cardiac troponins are elevated in more patients that do not have a cardiovascular disease. It is seen that there is a lot of inaccuracies and errors that can occur in the detection of cardiac troponins in cardiovascular diseases due to other secondary diseases that may be affecting the results (Omran et al, 2022).

Regardless of the limitations of cardiac troponins, it is still considered as one of the most powerful cardiac biomarkers for diagnosing cardiovascular diseases.

**The Advantages and Disadvantages of CK-MB**

Creatine kinase is an enzyme that helps form creatinine phosphate and ADP from the reaction of creatine and ATP. It is important in obtaining energy that is needed for the regeneration of ATP (Kurapati & Soos, 2022). Creatinine Kinase MB (CK-MB) is one of the isoenzymes of creatinine kinase that is specific for cardiac muscles. CK-MB was discovered in the year of 1966 along with two other isoenzymes. The two other isoenzymes of creatinine kinase include Creatinine Kinase BB (CK-BB) and Creatinine Kinase MM (CK-MM). CK-BB is typically found in brain tissue of the central nervous system. CK-MM is typically found in skeletal muscles (Kurapati & Soos, 2022). Because of the specificity of these creatinine kinase isoenzymes, it makes it easier to diagnose for a specific disease that can be found in either cardiac tissue, brain tissue, or skeletal muscles.

Among these creatinine kinase isoenzymes, CK-MB is considered the best isoenzyme for diagnosing cardiovascular diseases. Before cardiac troponins were used in the clinical laboratory,
CK-MB was mainly used as the primary cardiac biomarker in the 1980s (Omran et al., 2022). With the addition of cardiac troponins, CK-MB eventually became limited and not used as much as cardiac troponins in detecting cardiovascular diseases. When examining the use of the CK-MB as a cardiac biomarker, it is mainly used in diagnosing myocardial infarction (MI). In detecting myocardial infarction, CK-MB typically increases in number in 4 to 9 hours. CK-MB eventually peaks in about 24 hours. CK-MB would not return back to its baseline until 48 to 72 hours has passed (Dasgupta & Wahed, 2021). When measuring the levels of CK-MB in the laboratory, it is the measurement of all the isoforms of CK-MB. The total isoform of CK-MB consists of CK-MB1 and CK-MB2 (Omran et al., 2022).

While CK-MB can be useful in the diagnosis of myocardial infarction, the preferred cardiac biomarker is cardiac troponins due to the high sensitivity of cardiac troponins. As mentioned earlier, CK-MB was the cardiac biomarker used before the use of cardiac troponin. When cardiac troponins were introduced in the laboratory, CK-MB was not used as much. Furthermore, CK-MB can also be elevated in other cardiovascular diseases. These cardiovascular diseases include “myocarditis, pulmonary embolism, cardiac trauma, heart transplantation, chemotherapy-induced cardiotoxicity, and cardiac surgery” (Omran et al., 2022). While CK-MB is elevated in these other cardiovascular diseases, it does not help with the diagnose of these diseases. Additionally, there is elevation of CK-MB levels in non-cardiovascular diseases, such as “end stage renal failure, skeletal muscle trauma, muscular dystrophy, dermatomyositis, rhabdomyolysis, delirium tremens, and amyloidosis” (Omran et al., 2022). With the elevation of CK-MB in these non-cardiovascular diseases, it can lead to false-positive results (Omran et al., 2022).
The measurement of CK-MB is not as sensitive as cardiac troponins. This helps one to understand why cardiac troponins are mostly used in the diagnosis of myocardial infarction. Even though CK-MB may not be as sensitive as cardiac troponins, it can still be considered as a relevant cardiac biomarker.

**The Advantages and Disadvantages of Myoglobin**

Myoglobin is a protein that binds to oxygen. It is typically abundant in skeletal and cardiac muscle tissues. It is not found in any other tissue besides skeletal and cardiac muscle tissues (Thupakula et al., 2022). Myoglobin can be seen in the bloodstream when muscle damage has occurred. After understanding the other cardiac biomarkers, myoglobin is a much older cardiac biomarker. Before the introduction of cardiac biomarkers, such as CK-MB and cardiac troponins, myoglobin was used as a cardiac biomarker for the diagnosis of cardiovascular diseases. However, myoglobin is primarily used in the diagnosis of acute myocardial infarction (AMI). It is considered to be a sensitive biomarker for acute myocardial infarction rather than other cardiovascular diseases (Aydin et al., 2019).

When examining how myoglobin is measured in the laboratory, the levels of myoglobin increase in about 1 to 4 hours. It eventually peaks in number around 4 to 12 hours. The levels do not return back to its baseline until after 24 to 26 hours has passed (Dasgupta & Wahed et al., 2021). Because of how rapid myoglobin elevates, it is an important cardiac biomarker for early detection of cardiac injury. It helps to quickly detect whether or not a person is experiencing a cardiac injury. In patients with acute myocardial infarction, myoglobin elevates in number between 6 to 10 hours and peaks during the 12th hour (Aydin et al., 2019). This allows one to easily detect cardiac injury earlier rather than later. When comparing myoglobin to the other cardiac biomarkers, such as CK-MB and cardiac troponins, myoglobin increases more rapidly.
CK-MB and cardiac troponins typically increase after 4 to 9 hours. On the other hand, myoglobin increases only after 1 to 4 hours (Dasgupta & Wahed, 2021). This shows how quick and rapid myoglobin is detected after a cardiac injury has occurred.

Even though myoglobin can be easily detected after a cardiac injury has passed, it is considered an older cardiac biomarker that is no longer used in the laboratory (Dasgupta & Wahed, 2021). Similar to CK-MB, it lacks specificity in determining the type of cardiovascular disease (Thupakula et al., 2022). If the myoglobin is not specific enough, it makes it harder for the physician to use it as a way to diagnose the type of cardiovascular disease. Before the use of cardiac troponins and CK-MB, myoglobin was mainly used an early indicator of acute myocardial infarction. Currently, myoglobin is rarely used an early indicator for acute myocardial infarction due to the high sensitivity and specificity of cardiac troponins (Dasgupta & Wahed, 2021). Because of the lack of specificity, it is recommended that myoglobin is combined with other types of cardiac biomarkers. By combining with other types of cardiac biomarkers, it can allow one to better confirm and diagnose a patient with acute myocardial infarction (Thupakula et al., 2022).

Although myoglobin is more sensitive than the other cardiac biomarkers, it is important to understand that it is not as commonly used anymore.

The Advantages and Disadvantages of Other Cardiac Biomarkers

While the most commonly used cardiac biomarkers consist of cardiac troponins, creatinine kinase, CK-MB, and myoglobin, there can be other biomarkers that are used in the diagnosis of cardiovascular diseases. These other biomarkers may include lactate dehydrogenase (LDH), B-type natriuretic peptide (BNP), and C-reactive protein (CRP). Most of these other
biomarkers are not specific for evaluating for cardiovascular diseases, which makes it harder for diagnosis.

Lactate dehydrogenase is an enzyme that is found in most tissues of the human body. It was introduced as a biomarker in the 1970s with creatinine kinase (Dasgupta & Wahed, 2021). There are different diseases that can elevate the levels of lactate dehydrogenase because lactate dehydrogenase exists with multiple isozymes from LDH-1 to LDH-5. Because lactate dehydrogenase exists in five forms, it is commonly found in many diseases. These diseases include “liver disease, anemia, heart attack, bone fractures, muscle trauma, cancers, and infections such as encephalitis, meningitis, and HIV” (Farhana & Lappin, 2022). The idea of using lactate dehydrogenase for the diagnostic of cardiovascular diseases is very difficult due to the fact that it is hard to narrow down the possible causes. Because lactate dehydrogenase is present in many diseases, it makes it challenging for a physician to diagnose a cardiovascular diseases. With that in mind, lactate dehydrogenase is considered a biomarker that is not specific for detecting damage to cardiac muscles. Similar to myoglobin, it would need to be combined with another biomarker specific for cardiac injury, such as cardiac troponins (Farhana & Lappin, 2022).

B-type natriuretic peptide (BNP) is considered a natriuretic peptide. Natriuretic peptides (NPs) are proteins produced by the heart. The main function of these natriuretic peptides is to remove high amounts of sodium and potassium from urine (Dahiya, 2021). One of the natriuretic peptides include B-type natriuretic peptide, which is mostly found in the myocardium of the left ventricle. When the ventricles are stretched out from extra fluids, these proteins are released by the heart (Dahiya et al. 2021). B-type natriuretic peptide is used in the laboratory in assessing if a patient has heart failure (HF). In the blood, the normal concentration is 35 pg/mL (Dahiya et al.,
With patients that are experiencing heart failure, there are higher concentrations of B-type natriuretic peptide. In order to diagnose heart failure, a patient with a value less than 100 pg/mL is unlikely to have heart failure, while a patient with a value greater than 400 pg/mL is likely to have heart failure (Dahiya et al., 2021). While the measurement of B-type natriuretic peptide is valuable in diagnosing heart failure, there are still limitations involved. Similar to most of the other cardiac biomarkers, B-type natriuretic peptide is not considered specific enough in order to diagnose cardiovascular diseases. It is found in the “brain, lungs, kidneys, aorta, and adrenal glands” (Omran et al., 2022). As mentioned previously, the lack of specificity makes it harder to diagnose a particular disease.

C-reactive protein is considered an inflammatory biomarker. With cardiovascular diseases, there is typically elevated levels of C-reactive protein concentrations over a period of time (Luan & Yao, 2018). Unlike other inflammatory diseases, the levels of C-reactive protein do not spike up and fall down. It tends to remain elevated for some time before it drops back to its baseline. The elevated concentrations can help further diagnose atherosclerosis, which is the blockage of arteries due to the formation of plaques. C-reactive protein is mostly used in the prognosis of artery coronary syndrome (ACS). While it can be used in the prognosis of artery coronary syndrome, it is not specific or sensitive in detecting cardiac damage (Wang et al., 2020). There are also many inflammatory diseases that can be detected with C-reactive protein, which include type II diabetes, age-related macular degeneration, hemorrhagic stroke, Alzheimer’s disease and Parkinson’s disease (Luan & Yao, 2018). Once again, it makes it harder to narrow down certain diseases.

**Conclusion**
After understanding more about the functions of cardiac biomarkers, particularly cardiac troponins, CK-MB, and myoglobin, one is able to learn how important cardiac biomarkers are in diagnosing cardiovascular diseases. When looking at these cardiac biomarkers, it is best to select the cardiac biomarker that is most sensitive and most specific. By having a cardiac biomarker that is sensitive, it will allow for quick detection of cardiac damage. Additionally, having a cardiac biomarker that is specific allows for easier diagnosis of the particular disease. Out of the main cardiac biomarkers typically used in diagnosing cardiovascular diseases, cardiac troponins are considered the most powerful cardiac biomarker. While cardiac troponins may be considered the best cardiac biomarker in evaluating for cardiovascular diseases, it is also important to have additional biomarkers measured to further assist in the diagnosis of CVDs.

References


