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**3**  
**Utility of cardiac bioenzymes in predicting cardiovascular outcomes in SARS-CoV-2**

Utility of cardiac bioenzymes in COVID-19

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**Abstract**

The relationship between COVID 19 and cardiovascular diseases has been an important issue. Therefore, cardiac biomarkers and cardiac imaging have an important place in the diagnostic phase. It is important to know the relationship of biomarkers in COVID-19 so that we can understand the diagnosis of the disease, the predicted course and results after diagnosis.

**Key Words:** cardiac bioenzymes; COVID-19; Treatment; Diagnosis; triple rule-out computed tomography angiography (TRO CTA); Dual Energy Computed Tomography (DECT)

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**Core Tip:** Recommends biomarkers, especially troponin, in patients with COVID-19-associated myocarditis and other myocardial damage; however, they have proven that in addition to traditional biomarkers, new cardiac bioenzymes such as prepesin, ST2 and copeptin also increase and significantly worsen the prognosis. Knowing this, evaluation together with other imaging methods is also important in diagnosis.

### TO THE EDITOR

We read with interest and attention the review written by Anjani Muthyala et. al<sup>[1]</sup>. One of the main effects <sup>2</sup> of the coronavirus disease 2019 (COVID-19) pandemic is on the cardiovascular system. Therefore, it is important to know and use cardiac biomarkers well, and to come to an advanced point in the diagnosis stage by combining them with cardiac imaging methods. Therefore, the authors discussed the importance of these biomarkers in COVID-19 in order to determine the ways to diagnose the disease, follow-up after diagnosis and treatment. Although biomarkers are important, we also mentioned them in our evaluation since it is important to evaluate them with imaging methods. We think that when we combine cardiac biomarkers and imaging methods, a very important point will be reached in the diagnosis.

Including troponin<sup>[2]</sup>, which provides us with information about the prognosis in the diagnosis of cardiac acute coronary syndromes and myocardial damage, as well as Brain Natriuretic Peptide (BNP)<sup>[3]</sup> and pro-BNP, which gives us an advantage in <sup>1</sup> the early detection of heart diseases and understanding the morbidity status of such diseases. Natriuretic peptides, especially natriuretic peptides, tend to be elevated and associated with poor

prognosis in patients with heart disease, which is independently thought to be associated with COVID-19 even though the patients have no history of cardiac disease. In this review, the authors summarized the role of biomarkers in determining and diagnosing the extent of involvement of heart damage in people with COVID-19, as well as the permanent damage they may cause in the future.

In the review, the researchers divided it into three main sections, considering the diagnosis, prognosis, and mortality in order to simplify the role of cardiac biomarkers in COVID-19 disease. These three sections are as follows; 1- The relationship between cardiac troponin and COVID-19-related myocardial disease, 2- The relationship between natriuretic peptides and COVID-19-related myocardial disease, 3- The rest of the biomarkers are associated with myocardial disease.

Troponin consists of three main proteins in a complex structure<sup>[4]</sup>; Troponin C binds calcium and regulates the work of thin filaments during contraction<sup>[5]</sup>. Troponin T provides the connection of troponin in a complex with tropomyosin<sup>[6]</sup>. Troponin I acts as an inhibitory unit, and troponin C prevents contraction in the absence of calcium<sup>[7]</sup>. The amount of troponin that rises during myocardial injury has been observed to be higher among patients with COVID-19 who died compared to those who survived. In studies concentrating on this subject, a significant relationship has been shown between troponin and mortality with additional patient and hospital-related conditions, even in patients without comorbidities<sup>[8,9,10]</sup>.

BNP is first proteolytically processed from its precursor proBNP to BNP. Afterwards, it is secreted from the heart as N-terminal proBNP (NT-proBNP), undivided proBNP and mature BNP and NT-proBNP in ventricular myocytes, and the amount of secretion increases in patients with heart failure<sup>[11]</sup>. In the review, it is concentrated that the main reason for the increase in natriuretic peptides in SARS-CoV-2 is some inflammatory

processes that can lead to fulminant myocarditis. However, heart damage and hypoxia are thought to be some of the important causes of the increase in natriuretic peptides.

However, the cardiac markers mentioned in the review alone cannot rule out cardiovascular disease. Although it is supported by ECG, it may show atypical symptoms. Therefore, the differential diagnosis of acute chest pain after the new types of COVID-19 has become complicated. The viscosity increase due to COVID-19 hypoxia also causes damage to endothelial cells, resulting in increases in coagulation. In cases where biomarkers and ECG are insufficient at this stage, TRO CTA provides us an advantage in examining the entire thoracic vascular system and detecting cardiovascular vascular diseases.

One of the important points of the new COVID-19 disease is that this disease has the potential to cause acute presentations. One of the most important of these tables is acute chest pain, which also includes respiratory tract diseases, which is the most common symptom of COVID-19. In these cases, one of the important causes of acute chest pain is diseases that affect the lung parenchyma or accompanying vascular pathologies in COVID-19 cases. In a study conducted in these cases, it is emphasized that TRO CTA is an important diagnostic method that is effective and does not require intervention to the patient in those who apply to the emergency department with sudden onset symptoms<sup>[12]</sup>.

One of the important points apart from acute presentations is the long-term effects of COVID-19. In one study, persistent long-term COVID symptoms such as shortness of breath, chest pain, cough, and muscle weakness were proven to be associated with CT severity values<sup>[13]</sup>. In this review, it is also emphasized that the relationship of CT with persistent symptoms yields better data than laboratory parameters. Knowing the relationship between CT

severity and long-term COVID symptoms can also help to identify at-risk patients and establish follow-up programs to support these cases.

COVID-19 damages the myocardium by various mechanisms. The review focused on multiple viral infections causing sympathetic activation, direct viral invasion and proinflammatory cytokines inducing heart failure. The main reason for the increase in natriuretic peptides increased as a result of myocardial damage is thought to be due to interleukin (IL)-1 $\beta$  and similar proinflammatory cytokines. Magnetic Resonance Imaging (MRI), which has an important place in the diagnosis of myocarditis, also has an important place in imaging in myocarditis formed in this way; however, Cardiac MRI has some disadvantages such as not being ubiquitous, high cost, claustrophobia, incompatibility with pacemaker and its application due to prostheses. In these cases, in a study conducted, Dual Energy Computed Tomography (DECT) has proven to be significantly superior to MRI<sup>[14]</sup>. The authors recommend natriuretic peptides such as troponin and BNP in patients with myocarditis and other myocardial damage mentioned in the study; however, they proved that in addition to traditional biomarkers, new cardiac bioenzymes such as prepro-BNP, ST2 and copeptin also increase and cause marked worsening of prognosis. In addition to biochemical markers, imaging methods, especially CT, have an important place in the diagnosis of myocardial damage and comorbidities in COVID-19 patients. To give an example, DECT is used in practice as an important imaging method in the diagnosis of myocarditis-like conditions with myocardial damage<sup>[14]</sup>. TRO CTA is a frequently used imaging method in the detection of hypercoagulation, which we can give as an example of comorbidity conditions<sup>[12]</sup>.

In summary, we have seen that there is a significant relationship between COVID-19 and cardiovascular system findings. After understanding this relationship, we learned that we should make the best use of the data we have

at the point of diagnosis. Here, we know that we need to proceed to diagnosis by combining many cardiac biomarkers such as laboratory values such as BNP and pro-BNP with imaging methods such as ECG, CT, DECT and TRO CTA. In conclusion, we should make the best use of all available methods for diagnosis and treatment in order to reduce cardiovascular-related mortality and morbidity rates and improve prognosis in these patients.

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SIMILARITY INDEX

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### PRIMARY SOURCES

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| 1 | Y Hirata. "Measurement of plasma brain natriuretic peptide level as a guide for cardiac overload", <i>Cardiovascular Research</i> , 08/15/2001<br><small>Crossref</small> | 14 words — 1% |
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