

Cardiac biomarkers and prognosis in patients with COVID-19

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Prognostication has become a recurrent challenge in COVID-19. Rigorous risk stratification strategies may improve dedicated health care and logistics in the management of a truly systemic disease in the present state of pandemic.¹

Even though respiratory failure remains the landmark of and the main cause of death from moderate or severe COVID-19, several cardiovascular complications and numerous cases of thromboembolic disease have been reported.²

Controversy remains about how to use and interpret cardiovascular biomarkers in patients with COVID-19. Higher troponin and natriuretic peptide concentrations have been previously described in association with pneumonias caused by other respiratory pathogens and are strongly associated with the risk of death.^{3,4}

During the last 2 years, a growing body of research has focused on the assessment of cardiac biomarkers such as natriuretic peptides and high-sensitivity cardiac troponin (hs-cTn) in patients with COVID-19,³⁻⁹ as they have been viewed as promising predictors of the prognosis. Both biomarkers are commonly elevated in hospitalized patients with COVID-19 and their concentration correlates directly with disease-related complications and mortality during hospital stay.⁸⁻⁹ Thus, they may aid in the identification of patients at a higher risk for poor outcomes, and guide resource management. Even though there may be a linear relationship between concentrations of hs-cTn and N-terminal pro-B-type natriuretic peptide (NT-proBNP), they are associated with different facets of cardiovascular involvement during COVID-19 and may be complementary during the risk stratification process.

Early research during the pandemic identified myocardial injury as an adverse prognostic factor. However, the reason for the elevation of hs-cTn levels may be multifactorial as it may be caused by direct cytotoxic effects of SARS-CoV-2 as well as endothelial impairment, immune-mediated responses, a prothrombotic state, or

even the disbalance between oxygen demand and supply during acute illness.¹⁰

Natriuretic peptides are biomarkers reflecting myocardial stress, which increases during high-volume states associated with elevated filling pressures. They have become invaluable tools in the diagnosis, prognostication, and management of patients with heart failure. Despite being usually used by physicians to assess the cardiac function, they are nonspecific and their levels may increase during critical illness associated with some degree of cardiovascular involvement of right ventricular strain and higher intracavitary pressures due to increased afterload and hypoxemia. Their use may simplify the prognostic assessment in comparison with more complex risk scores, for example, among patients with thromboembolic disease and respiratory infections, both of which are conditions that may complicate COVID-19.

In the current issue of *Polish Archives of Internal Medicine*, Klocek et al¹¹ studied the association between cardiac biomarkers (NT-proBNP and hs-cTn) and clinical outcomes in a large cohort (n = 1729) of patients with SARS-CoV-2 infection, regardless of whether they had heart failure or not. They found that 41.5% and 81.5% of patients who had the levels of high-sensitivity cardiac troponin T (hs-cTnT) and NT-proBNP assessed on admission, respectively, had elevated concentrations of these biomarkers (defined as hs-cTnT ≥ 14 ng/ml and NT-proBNP > 125 pg/ml). Besides, both parameters showed a positive correlation.

As expected, median levels of hs-cTnT and NT-proBNP on admission were significantly higher in the patients with chronic heart failure than in those without a preceding chronic heart failure diagnosis. Both biomarkers were independently associated with mortality after adjusting for multiple relevant covariates. Receiver operating characteristic analysis showed that a hs-cTnT level equal to or above 142 ng/ml and an NT-proBNP level equal to or above 969 pg/ml were the optimal

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cutoff points to predict in-hospital mortality, with a sensitivity of 80% and 79%, respectively.

The study results confirm that mortality increases along with higher levels of cardiac biomarkers, after considering clinically relevant confounders such as chronic heart failure. This independence from chronic heart failure status underscores that natriuretic peptides are not specific for the diagnosis of heart failure, and suggests a potential role of other mechanisms, such as elevated pulmonary pressure due to microangiopathy, right ventricular dysfunction, and sepsis, all being associated with a worse prognosis.¹² The authors conclude that elevated NT-proBNP concentrations may discriminate short-term outcomes in COVID-19 patients with or without heart failure, and that systematic assessment of this biomarker in clinical practice may be useful to improve risk stratification.

The 2 most relevant limitations of this study, acknowledged by the authors, are the potential for a selection bias and the lack of possible generalizability of the results to nonhospitalized populations of COVID-19 patients. As the assessment of the cardiac biomarkers was not protocolized and left to the discretion of the treating physician, the patients with hs-TnT or NT-proBNP levels assessed (60.2% and 41.4% of the entire cohort, respectively) constituted a sicker population with more comorbidities. This may have biased the results towards poorer outcomes and reduced the external validity of the study conclusions. However, the fact that biomarker assessment was performed on admission (not after clinical deterioration) strengthens the prognostic value.

In agreement with the discussed study, we think that NT-proBNP and cardiac troponin should be included (in addition to inflammatory and thrombosis biomarkers) to dedicated COVID-19 laboratory panels to both simplify and improve the initial risk-stratification at first medical contact, regardless of prior history of cardiovascular disease. However, implications of in-hospital evolution of cardiac biomarkers, their specific relationships with cardiac complications of COVID-19, and the association between long-term prognosis and biomarker levels have not been adequately investigated yet. The usefulness of cardiac biomarkers may extend to follow-up, as they may aid in the selection of vulnerable patients that would benefit from specific surveillance programs after discharge from the hospital.¹³⁻¹⁵

The study by Kloczek et al¹¹ helps to fill a significant knowledge gap regarding the initial assessment and management of patients with COVID-19, and sets the path for future research regarding long-term outcomes of cardiac complications during acute illness and after hospital discharge.

ARTICLE INFORMATION

DISCLAIMER The opinions expressed by the author(s) are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

CONFLICT OF INTEREST None declared.

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REFERENCES

- 1 Caro-Codón J, Lip GYH, Rey JR, et al. Prediction of thromboembolic events and mortality by the CHADS2 and the CHA2DS2-VASc in COVID-19. *Europace.* 2021; 23: 937-947. [↗](#)
- 2 Rey JR, Caro-Codón J, Poveda Pineda D, et al. Arterial thrombotic complications in hospitalized patients with COVID-19. *Rev Esp Cardiol (Engl Ed).* 2020; 73: 769-771. [↗](#)
- 3 Mueller C, Giannitsis E, Jaffe AS, et al. Cardiovascular biomarkers in patients with COVID-19. *Eur Heart J Acute Cardiovasc Care.* 2021; 10: 310-319. [↗](#)
- 4 Duan J, Wu Y, Liu C, et al. Deleterious effects of viral pneumonia on cardiovascular system. *Eur Heart J.* 2020; 41: 1833-1838. [↗](#)
- 5 Lala A, Johnson KW, Januzzi JL, et al. Prevalence and impact of myocardial injury in patients hospitalized with COVID-19 infection. *J Am Coll Cardiol.* 2020; 76: 533-546. [↗](#)
- 6 Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol.* 2020; 5: 802-810. [↗](#)
- 7 O'Donnell C, Ashland MD, Vasti EC, et al. N-terminal pro-B-type natriuretic peptide as a biomarker for the severity and outcomes with COVID-19 in a nationwide hospitalized cohort. *J Am Heart Assoc.* 2021; 10: e022913. [↗](#)
- 8 Caro-Codón J, Rey JR, Buño A, et al. Characterization of myocardial injury in a cohort of patients with SARS-CoV-2 infection. *Medicina Clínica.* 2021; 157: 274-280. [↗](#)
- 9 Caro-Codón J, Rey JR, Buño A, et al. Characterization of NT-proBNP in a large cohort of COVID-19 patients. *Eur J Heart Fail.* 2021; 23: 456-464. [↗](#)
- 10 Sandoval Y, Januzzi JL Jr, Jaffe AS. Cardiac troponin for assessment of myocardial injury in COVID-19: JACC review topic of the week. *J Am Coll Cardiol.* 2020; 76: 1244-1258. [↗](#)
- 11 Kloczek M, Wojciechowska W, Terlecki M, et al. Cardiac biomarkers on admission and in-hospital mortality in COVID-19 patients with or without concomitant heart failure. *Pol Arch Intern Med.* 2022; 132: 16256. [↗](#)
- 12 Rey JR, Caro-Codón J, Rosillo SO, et al. Heart failure in COVID-19 patients: prevalence, incidence and prognostic implications. *Eur J Heart Fail.* 2020; 22: 2205-2215. [↗](#)
- 13 Al-Aly Z, Xie Y, Bowe B. High-dimensional characterization of post-acute sequelae of COVID-19. *Nature.* 2021; 594: 259-264. [↗](#)
- 14 Italia L, Tomasoni D, Bisegna S, et al. COVID-19 and heart failure: from epidemiology during the pandemic to myocardial injury, myocarditis, and heart failure sequelae. *Front Cardiovasc Med.* 2021; 8: 713560. [↗](#)
- 15 Scherrenberg M, Frederix I, De Sutter J, et al. Use of cardiac telerehabilitation during COVID-19 pandemic in Belgium. *Acta Cardiol.* 2021; 7: 773-776. [↗](#)