Are COVID-19 Patients Dying of or with Cardiac Injury?

Vasiliki Tsolaki, MD, George E. Zakynthinos, MD

Intensive Care Unit, University Hospital of Larissa, University of Thessaly Medical School, Faculty of Medicine, Larissa, Greece

Corresponding Author:

Vasiliki Tsolaki, MD

Intensive Care Unit,

University Hospital of Larissa,

University of Thessaly, Faculty of Medicine,

Larissa, Greece

Email: vasotsolaki@yahoo.com

tel: 00302413502961, fax: 00302413501018

Conflict of Interest: None

AJRCCM Articles in Press. Published May 20, 2020 as 10.1164/rccm.202004-1083LE

To the Editor,

We read with great interest the paper by Du and colleagues presenting the clinical characteristics of 85 patients in Wuhan dying of COVID-19.(1) Around 70% presented comorbidities (hypertension, diabetes and coronary heart disease) and thirteen patients (16%) died of cardiac problems, namely cardiac arrest, acute coronary syndrome (ACS) and malignant arrhythmia. (1) Cardiac involvement probably complicates SARS-COV-2 patients, but what is the true incidence (considering specific echocardiographic findings) and the attributable mortality, are aspects not well clarified yet.

Very few reports have used echocardiographic criteria beyond biomarkers to diagnose cardiac injury, but none has differentiated between myocarditis, cardiomyopathy (stress or septic), ACS and acute heart failure in the era of COVID-19. Acute cardiac injury was reported in 44.7% of the fatalities in Du et al report, but the specific echocardiographic abnormalities are not presented. (1) Did these "cardiac injuries" involve patients with myocarditis? Or were there features indicative of stress or even septic cardiomyopathy, mostly, reversible entities? Considering biomarkers, troponin levels are markedly increased in myocarditis and ACS. On the contrary, in Takotsubo and septic cardiomyopathy, there is a disparity between biomarker levels and the extent of myocardial dysfunction. In addition, hypo-akinesia usually does not correspond to a specific coronary artery territory. (5) Therefore, a reference on the nature of cardiac injury would be worthy.

A diagnosis of "cardiac injury" mainly relying on biomarker levels may be misleading. In a recent report involving 416 hospitalized patients from Wuhan, 19.7% presented "acute myocardial injury". The diagnosis relied on increased cardiac biomarker (hs-TnI) levels, regardless of the electrocardiographic and echocardiographic findings. (2) Du et al, presented a high percentage of patients with "cardiac injury"; only data on lactate dehydrogenase,

AJRCCM Articles in Press. Published May 20, 2020 as 10.1164/rccm.202004-1083LE

creatinine kinase and aspartate aminotransferase are reported, but not on cardiac specific enzymes.(1) On the other hand, cardiac specific biomarkers alone may not be diagnostic of cardiac damage. TnI is elevated in septic shock, pulmonary embolism and critically ICU patients. In "cardiac injury" patients, NT-proBNP levels were found elevated. (2) However, we have previously found that BNP is a biomarker that correlates with the severity of sepsis. (4) BNP may be elevated when SARS-COV-2 patients present septic shock resulting from a superinfection, even with normal cardiac function. Additionally, the troponin and BNP levels were normal in a 64-year-old female patient from our ICU, who acutely established pericarditis on the sixteenth day post COVID-19 diagnosis.

Moreover, in Figure 1C, Du et al present a CT image of a 23-year-old female patient with COVID-19. The cardiac structure seems greatly enlarged; considering the young age of the patient, this finding could correspond to true myocarditis (therefore, ground glass opacities could depict hydrostatic pulmonary edema). (1) It would be informative if the authors provided data on this aspect (increased cardiac dimensions on CT, a finding beyond the criteria used for "cardiac injury" diagnosis). Inciardi et al, reported a 53-year-old woman with COVID-19, who presented acute myopericarditis and cardiogenic shock with severe systolic dysfunction, confirmed with MRI. Noteworthy, the patient never presented signs of respiratory involvement. (6)

Finally, data on the attributable to cardiac injury mortality are totally lacking (1). The proportion of the "cardiac injury" patients who actually died due to cardiogenic shock, is not mentioned. Markers of perfusion, such as low $ScvO_2$, would add information on the contribution of cardiac dysfunction to the fatal outcome. Furthermore, did the patients, dying of malignant arrythmia and cardiac arrest, suffer from cardiac comorbidities? Did the arrhythmia occur on a substrate of "myocardial injury", or was this a complication of the

AJRCCM Articles in Press. Published May 20, 2020 as 10.1164/rccm.202004-1083LE

prescribed medications, i.e. chloroquine? All these issues need to be clarified, to thoroughly understand the “myocardial damage” that COVID-19 induces.

AJRCCM Articles in Press. Published May 20, 2020 as 10.1164/rccm.202004-1083LE

References

1. Du Y, Tu L, Zhu P, Mu M, Wang R, Yang P, Wang X, Hu C, Ping R, Hu P, Li T, Cao F, Chang C, Hu Q, Jin Y, Xu G. Clinical Features of 85 Fatal Cases of COVID-19 from Wuhan: A Retrospective Observational Study. *Am J Resp Crit Care Med* [online ahead of print] 03 April 2020; https://www.atsjournals.org/doi/abs/10.1164/rccm.202003-0543OC.

2. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, Gong W, Liu X, Liang J. Association ofcardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol.* Published online March 25, 2020 doi:10.1001/jamacardio.2020.0950.

3. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061-1069. doi:10.1001/jama.2020.1585

4. Papanikolaou J, Makris D, Mpaka M, Palli E, Zygoulis P, Zakynthinos E. New insights into the mechanisms involved in B-type natriuretic peptide elevation and its prognostic value in septic patients. *Crit Care* 2014;18(3):R94 doi:10.1186//cc13864

5. Pelliccia F, Kaski JC, Crea F, Camici P. Pathophysiology of Takotsubo Syndrome. *Circulation* 2017; 135(24):2426-2441

6. Inciardi R, Lupi L, Zaccone G, Italia L, Raffo M, Tomasoni D, Cani D, Cerini M, Farina D, Gavazzi E, Maroldi R, Adamo M, Ammirati E, Sinagra G, Lombardi C, Metra M. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). *JAMA Cardiol* published online March 27,2020 doi: 10.1001/jamacardio.2020.1096.

AJRCCM Articles in Press. Published May 20, 2020 as 10.1164/rccm.202004-1083LE