Cardiac biomarkers are highly prognostic of in-hospital mortality in patients with COVID-19: what is the effect of renin-angiotensin system blockers without baseline heart failure on these biomarkers?

Authors' reply In his letter to the editor, Dr. D. Patoulias rightly and very accurately pointed out the issue of prior pharmacological treatment of patients admitted to the hospital for COVID-19 and the impact of particular drugs on their prognosis. It is still a burning issue, because over the past 2 years of the pandemic, a number of papers have addressed the effects of medications in the renin-angiotensin system inhibitor (RASI) family, especially angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), with some debate on their importance. The severity of COVID-19 depends on many factors, the most important ones being age and pre-existing comorbidities, including cardiovascular diseases.[1] In our study, published in the current issue of *Polish Archives of Internal Medicine*,[2] we showed that the levels of high-sensitivity cardiac troponin T (hs-cTnT) and N-terminal pro–B-type natriuretic peptide (NT-proBNP)—easy-to-obtain markers of cardiac injury assessed on admission—could be used as predictors of in-hospital death in patients with COVID-19. The linear relation between higher levels of hs-cTnT or NT-proBNP and mortality was seen both for patients with and without a history of chronic heart failure (CHF). Thus, it is important to determine whether the observed effect could have been influenced by the RASI treatment before admission to the hospital.

Our study included a total of 1729 patients with COVID-19. Of those, 1550 had no history of CHF, and only 378 individuals (24.4%) previously used RASIs. The median NT-proBNP level measured on admission did not differ between the patients who previously used RASIs and those who did not (370 pg/ml [interquartile range, IQR, 138.8–1253.5] vs 314.5 pg/ml [IQR, 103.8–1395.5]; P = 0.37, respectively). However, when analyzing subgroups of patients without concomitant CHF, differences in the NT-proBNP concentration were found. First, a difference was noted in the group of patients previously treated for arterial hypertension (816 cases, of whom 338 [41.4%] were using RASIs); the median NT-proBNP levels were 400.5 pg/ml (IQR, 147.8–1294.5) in the RASI users and 685 pg/ml (182–2884.8) in the nonusers (P = 0.011). Among the 816 patients with hypertension, 105 died during hospitalization: 82 of them (78%) had not been previously treated with RASIs, while 23 (22%) had received previous RASI treatment (P <0.01). The second group with differences in NT-proBNP levels were the patients with a prior history of coronary artery disease (CAD). There were 195 cases with CAD in our study; among them, 93 (47.7%) were previously treated with RASIs. The median NT-proBNP level in the RASI users with CAD was 479 pg/ml (IQR, 206.5–1380.5), and in the nonusers it was 1937.5 pg/ml (IQR, 421.3–4708) (P = 0.012). Among the 195 patients with CAD, 35 died during hospitalization: 25 of them (71%) had not been previously treated with RASIs, whereas 10 (29%) had received such a treatment (P = 0.02). Finally, we found no differences in the NT-proBNP concentration in the subgroups of patients with coexisting diabetes or atrial fibrillation. We can conclude that the individuals with hypertension or CAD who had not used RASIs prior to contracting COVID-19 had significantly higher levels of NT-proBNP on admission and higher in-hospital mortality than those who had received RASIs. Moreover, the same results were obtained for the hs-cTnT concentration: the patients admitted to the hospital for COVID-19 without a history of CHF, previously using RASIs for hypertension or CAD, had significantly lower values of hs-cTnT and lower in-hospital mortality. This observation

can be considered an indirect evidence of the protective effect of RASIs in the prevention of potential heart damage in the course of COVID-19, at least in some cardiovascular diseases.

When considering the role of RASIs in hypertensive individuals with concomitant COVID-19, the results of a recently published observational study of consecutive patients treated in the hospital in Bergamo, Italy[3] are worth mentioning. The researchers found, in a similarly aged cohort of 688 patients with arterial hypertension and COVID-19, that 67% of the study population had used ACEIs or ARBs before admission to the hospital. In this study, previous use of RASIs, either ACEIs or ARBs, was associated with lower all-cause mortality, whether in-hospital or shortly after discharge, in a population aged over 68 years but not in younger patients. As can be seen, there is still a need for research, preferably of prospective nature, that would assess the impact of treatment with RASIs both before and during hospitalization for COVID-19, taking into account the age of patients and comorbidities. However, at this stage of knowledge, we can advise patients (and their treating physicians) not to stop their current RASI treatment when they develop COVID-19, especially if they have hypertension, CAD, or HF.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

HOW TO CITE Klocek M, Terlecki M, Wojciechowska W, et al. Cardiac biomarkers are highly prognostic of in-hospital mortality in patients with COVID-19: what is the effect of renin-angiotensin system blockers without baseline heart failure on these biomarkers? Authors' reply. Pol Arch Intern Med. 2022; 132: 16294. doi:10.20452/pamw.16294

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