

Cardiovascular drug therapy and surrogate COVID-19 outcomes: which is the impact of the “miraculous” sodium-glucose co-transporter-2 inhibitors? Author’s reply

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We would like to thank for the interest in our article. It has been confirmed in numerous studies that COVID-19 can lead to increased risk of a poor outcome, which is particularly expressed in patients with older age and co-existing cardiometabolic comorbidities [1]. We confirmed in our study that older age, type 2 diabetes mellitus (DM), and heart failure were associated with worse in-hospital prognosis in patients hospitalized for COVID-19 [2].

We must admit that still there is a lack of specific therapy for COVID-19, despite the fact that numerous drugs have been studied. Since the beginning of the pandemic, the safety and efficacy of drugs dedicated to patients with cardiometabolic comorbidities have attracted interest. In our analysis, we confirmed that in patients hospitalized for COVID-19, prior treatment with renin-angiotensin system blockers, statins, antiplatelet drugs, or beta-blockers was associated with a significant decrease in the odds of in-hospital death [2], however, due to the observational nature of the study, it does not prove the causal association.

During several months of the pandemic, we have witnessed the change in the treatment standards of COVID-19 which have resulted in lower rates of complications (i.e. low-molecular-weight heparin in the prevention of thromboembolic events, steroids in patients requiring oxygen therapy, etc.). However, there is still a profound need to improve the standard of care in order to achieve faster and more complete recovery with an additional reduction of cases with fatal outcomes.

We agree with Patoulas et al. that theoretically there might be a place for sodium-glucose

co-transporter-2 (SGLT-2) inhibitors in the management of patients with COVID-19 [3]. SGLT-2 inhibitors are not only antidiabetic drugs but it has been proven that this group improves prognosis in populations similar to those at risk for COVID-19 worse outcome, i.e. patients with DM and in subjects with heart failure, chronic kidney disease, and atherosclerotic cardiovascular disease [1, 4]. Treatment using SGLT-2 inhibitors is recommended by the latest 2021 Acute and Chronic Heart Failure Guidelines of the European Society of Cardiology. Therefore, investigation of the efficacy and safety profile of these agents in patients with COVID-19 is warranted.

In our study, we analyzed clinical data from 1729 patients. In this cohort, there were only 26 patients (1.5% of the entire cohort) with prior treatment with SGLT-2 inhibitors. We must acknowledge that it is insufficient to draw reliable conclusions. However, currently, we have available data of a larger group, i.e., 3391 patients hospitalized in our hospital for COVID-19. In this cohort, there were 65 patients (1.9%) treated with SGLT-2 inhibitors. In this group: 60 (92.3%) patients had DM, 9 (13.8%) had heart failure, 13 (30.0%) had ischemic heart disease, and 2 (3.1%) had chronic kidney disease.

If we take into consideration the highly beneficial impact of SGLT-2 inhibitors in patients with pre-existing cardiometabolic disorders, we must acknowledge that the prescription rate of these drugs in real life was lower than should have been expected. Of note, a low proportion of patients with diabetes on SGLT-2 inhibitors should be attributed mainly to a very limited reimbursement of these drugs in Poland, thus,

most type 2 diabetes patients have to pay for them out of pocket. At the beginning of the pandemic there was a concern about the safety profile of SGLT-2 inhibitors in patients with COVID-19, however, currently, there are data confirming their satisfactory safety profile in patients infected with SARS-CoV-2 [5].

In our cohort, we observed better outcomes among patients treated with SGLT-2 inhibitors ($n = 65$), as compared to non-treated ($n = 3326$). There were no in-hospital deaths in patients treated with SGLT-2, while in the rest of the cohort 354 (10.4%) patients died. We found lower frequency of need for mechanical ventilation (2 [0.1%] vs 351 [10.3%]; $P = 0.027$) in patients treated with SGLT-2 inhibitors. There was no significant difference in the need for intensive care unit hospitalization between SGLT-2 inhibitors users and non-users (5 [0.2%] vs 402 [11.8%]; $P = 0.19$). The low number of patients treated by SGLT2 inhibitors, the retrospective, observational nature of our analysis makes it prone to typical methodological problems, for example, selection bias related to higher eGFR among SGLT2 inhibitor users due to the SPC details in 2020 and beginning of 2021. Thus, the presented results should be treated with caution.

However, looking at our results, we should at least consider the continuation of SGLT-2 inhibitors in subjects with pre-existing indications for those medications. The mechanism of SGLT-2 inhibitor's action, the results of prior studies, and our findings indicate that further exploration is needed to fully establish the role of SGLT-2 inhibitors on COVID-19 course and outcome.

Article information

Conflict of interest: None declared.

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