

## Postdischarge antidiabetic treatment in patients with type 2 diabetes and acute coronary syndrome: time for a change?

**To the editor** We read with interest the 2018 annual report of the Polish Registry of Acute Coronary Syndromes (PL-ACS) and the significant observations concerning a total of 7323 patients with type 2 diabetes mellitus (T2DM) admitted to the hospital due to acute coronary syndrome (ACS).<sup>1</sup> Despite the fact that glycemic control was relatively good among patients with T2DM, a closer look at baseline characteristics reveals that these patients had a significantly greater burden of cardiovascular disease (CVD) compared with nondiabetic patients, while they experienced significantly more in-hospital adverse outcomes (including death), except for stroke/transient ischemic attack.<sup>1</sup> Interestingly, a significant proportion of patients with T2DM were either prescribed insulin or no antidiabetic treatment at discharge, with left ventricular systolic dysfunction status playing a catalytic role for final decision.<sup>1</sup>

Since 2018, the year of data collection from the PL-ACS, the publication of a number of trials on the cardiovascular safety and efficacy of newer antidiabetics, namely sodium-glucose co-transporter-2 (SGLT-2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1RAs) has introduced a new era in the management of patients with concomitant T2DM and CVD. Recent meta-analytic data suggest that administration of SGLT-2 inhibitors in patients with established atherosclerotic CVD decrease the risk of major adverse cardiovascular events by 14% and the risk of cardiovascular death or hospitalization for heart failure (HF) by 24%, with patients having pre-existing HF experiencing the greatest reduction of 29%.<sup>2</sup> In addition, similar data document that administration of GLP-1RAs in the same population decreases the risk of major adverse cardiovascular events by 14%, with favorable effects on hospitalization for HF and all-cause mortality as well.<sup>3</sup>

Thus, according to the recently published 2019 guidelines on diabetes, prediabetes, and cardiovascular diseases developed by the European Society of Cardiology in collaboration with the European Association for the Study of Diabetes, major SGLT-2 inhibitors and GLP-1RAs are recommended for patients with T2DM and CVD (class I, level A), while insulin-based glycemic control should be cautiously considered in patients with ACS and significant hyperglycemia (>180 mg/dl) (class IIa, level C).<sup>4</sup> Importantly, it has also been demonstrated that insulin treatment in patients with T2DM and concomitant HF is associated with an increase in all-cause death by 27% and in HF hospitalization by 23%, while, in the administrative strategy, insulin prescription is related to significantly worse outcomes, as well.<sup>5</sup>

To sum up, it seems that there is enough evidence now to optimize postdischarge treatment in patients with T2DM and a recent ACS—especially in those with left ventricular systolic dysfunction—switching from classic antidiabetics to novel ones. Of course, individualization of treatment strategy, incorporating patients' needs and preferences and financial cost, is always required before making the final decision.

### ARTICLE INFORMATION

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**Authors' reply** We would like to thank Patoulias et al<sup>1</sup> for interest in our work and relevant comments. We also consider sodium-glucose co-transporter-2 (SGLT-2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1RAs) as promising options for patients with cardiovascular diseases, including left ventricular systolic dysfunction (LVSD) or heart failure (HF). In the past years, only few new drugs for patients with LVSD or HF were introduced, as many trials failed to prove benefits of the new molecules (ie, rolofylline, aliskiren, tolvaptan, tezosentan). We are sure that these drugs will be administered more often than we showed in our study in patients in 2018.<sup>2</sup> Unfortunately, the delay between the implementation study and plateau of usage in the real-life population is expected. In our opinion, the most important obstacle to provide treatment to all patients with appropriate indications is the cost of new drugs. At the same time, the newly introduced drugs are rarely reimbursed or the indications for refunding include only a small group of patients. Thus, the cost of therapy with new agents should be always discussed with the patient, as the compliance plays a pivotal role in the therapeutic process. The second issue regarding the low percentage of the SGLT-2/GLP-1RAs use in the Polish Registry of Acute Coronary Syndromes (PL-ACS), is that most of patients had no history of HF before myocardial infarction (MI) (82.3% in diabetic and 91.1% in non-diabetic group). On the other hand, more than 80% of patients were discharged with  $\beta$ -blocker and more than 75% with angiotensin-converting enzyme inhibitors.<sup>2</sup> It should therefore be assumed that the majority of patients had LVSD/HF treatment initiated

during the MI hospitalization. It raises the important clinical question, how LVSD/HF and antidiabetic therapies should be initiated and escalated during the hospital stay associated with MI.

The last issue that should be discussed concerns the specifics of retrospective analyses and registries. All results should be interpreted with caution, as most of the statistical methods are able to show the association between some variables, but not the cause and effect relationship. Some drugs are administered in patients with advanced stages of disease (ie, dobutamine in advanced HF or glycoprotein IIb/IIIa inhibitors as a bailout therapy in the treatment of MI). The same phenomenon may be observed in patients with HF and diabetes treated with insulin. In our opinion, in such cases, the worse prognosis may be an effect of the patient's clinical status and disease severity rather than the effect of the drug itself. Thus, some conclusions drawn based even on the advanced statistical methods (ie, propensity score matching or meta-analysis) should be interpreted with caution.

To conclude, the new drugs are the light at the end of the tunnel for many patients and physicians. Each patient should be treated individually, in the modern way according to the holistic assessment including patient compliance and resources.

## ARTICLE INFORMATION

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