Commentary: Modern antihyperglycemic medications in the era of the frail cardiac surgical patient

Dustin Scott Kehler, MSc, PhD,^a and Rakesh C. Arora, MD, PhD, FRCSC, FACS^{b,c}

From the ^aDivision of Geriatric Medicine, Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada; ^bDepartment of Surgery, Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada; and ^cCardiac Sciences Program, St Boniface Hospital, Winnipeg, Manitoba, Canada.

No funding was provided for this editorial.

Disclosures: Authors have nothing to disclose with regard to commercial support.

Received for publication May 15, 2019; accepted for publication May 15, 2019; available ahead of print June 21, 2019.

Address for reprints: Dustin Scott Kehler, MSc, PhD, QEII Health Sciences Centre, Room 1314, Camp Hill Veterans Memorial Building, 5955 Veterans' Memorial Ln, Halifax, Nova Scotia B3H 2E1, Canada (E-mail: scott.kehler@dal.ca).

J Thorac Cardiovasc Surg 2019;158:1118-9

0022-5223/\$36.00

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<https://doi.org/10.1016/j.jtcvs.2019.05.034>

Dustin Scott Kehler, MSc, PhD (left), and Rakesh C. Arora, MD, PhD, FRCSC, FACS (right)

Central Message

Trials demonstrate superior outcomes with CABG relative to PCI in patients with diabetes. The perioperative surgical team should consider protective benefits with modern antihyperglycemic medications.

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Randomized trials comparing percutaneous coronary intervention and coronary artery bypass grafting show superior long-term outcomes with surgical revascularization.^{1,2} In turn, the number of patients requiring cardiac surgery with preexisting chronic conditions such as type 2 diabetes is likely to grow. The advantage of new antihyperglycemic agents glucagonlike peptide-1 receptor agonists (GLP-1RAs) and sodium glucose cotransporter-2 inhibitors (SGLTIs) relative to classic medications for patients with diabetes is the significant risk reduction for major adverse cardiovascular events (MACEs).^{3,4} In the coming years, we will understand the long-term effects of these medications for the secondary prevention of MACE in the surgical patient.

PROS AND CAUTIONS WITH MODERN ANTIHYPERGLYCEMIC AGENTS

In this issue of the *Journal*, Pagidipati and Lopes⁵ summarize clinical trials examining the impact SGLTI and GLP-1RA medications. The risk of MACEs during 2 to 4 years in patients with diabetes and cardiovascular disease relative to a group receiving placebo were 14% lower with the SGLTIs empagliflozin (hazard ratio [HR], 0.86; 95% confidence interval [CI], 0.74-0.99) and canagliflozin (HR, 0.86; 95% CI, 0.75-0.97). The SGLTI dapagliflozin did not reduce the risk of MACEs. For GLP-1RAs, MACE risk was reduced by 24% with semaglutide (HR, 0.74; 95% CI, 0.58-0.95) and 13% with liraglutide (HR, 0.87; 95% CI, 0.78-0.97); lixisenatide and exenatide did not reduce risk. Pagidipati and Lopes⁵ provide considerations for surgeons with the antihyperglycemic agents. Specifically, patients who underwent coronary artery bypass grafting 1 to 5 years before receiving empagliflozin and liraglutide had a MACE risk reduction similar to that of the entire intervention group. Pagidipati and Lopes⁵ also

indicate that the class of medication will be important when considering the individual patient: an SGLTI should be considered if the progression of heart failure and renal disease are concerns, whereas a GLP-1RA could be initiated postoperatively if there is fear of new or worsening cardiovascular disease.⁵ Furthermore, patients with significant renal function impairment should be closely monitored even when using SGLTIs or GLP-1RAs. Collectively, the considerations for surgeons proposed by Pagidipati and Lopes⁵ align with the most recent guidelines for diabetic treatment recommendations in patients with atherosclerotic cardiovascular disease.⁶

Pagidipati and Lopes⁵ indicate that the advantage of the new antihyperglycemic agents, particularly, SGLTIs, is their safety when combined with other secondary prevention medication regimens (eg, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, β -blockers, and statins) after cardiac surgery. Still, as we witness an era of older surgical patients who are receiving a multitude of medications unrelated to their cardiovascular disease symptoms and are presumably frailer than previous patients, appropriate discretion is needed. High levels of preoperative frailty increase the risk of MACE and poor functional survival after surgical intervention.^{7,8} Patients with higher levels of frailty may have more impaired kidney function and be prescribed more medications,⁹

particularly those requiring kidney clearance commonly prescribed in the surgical setting, such as digoxin.¹⁰ In turn, medication optimization may be an important postoperative treatment goal for the frailer surgical patient. We remain cautiously optimistic, however, regarding the advantage that has already been seen with SGLTIs and GLP-1RAs in the nonsurgical setting and in those with a history of surgical revascularization.

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