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New-generation antidiabetic agents in cardiac surgery: cardiovascular and renal benefits beyond glycemic control

Agentes antidiabéticos de nueva generación en cirugía cardíaca: beneficios cardiovasculares y renales más allá del control glucémico

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ABSTRACT

In recent years, new antidiabetic drugs have emerged, such as GLP-1 receptor agonists, sodium-glucose cotransporter 2 inhibitors, and dipeptidyl peptidase-4 inhibitors, which have gained relevance for offering benefits beyond glycemic control, especially in cardiovascular and renal protection. In this context, it is pertinent to examine their potential role in cardiac surgery. The manuscript aims to describe and analyze the positive and negative impact of these therapies on cardiovascular and renal outcomes in patients undergoing cardiac surgery, regardless of the presence of diabetes mellitus. A systematic search is conducted in PubMed, Scopus, and the Cochrane Library for studies published between 2020 and 2025. Studies evaluating the safety and efficacy of GLP-1 receptor agonists, sodium-glucose cotransporter 2 inhibitors, and dipeptidyl peptidase-4 inhibitors, and dipeptidyl peptidase-4 inhibitors were included. The outcomes analyzed are perioperative safety, glycemic control, cardiovascular complications, and renal function. GLP-1 receptor agonists improved perioperative glycemic control, reduced insulin requirements, and promoted cardiac recovery, without increasing hypoglycemia or serious adverse events. Sodium-glucose cotransporter 2 inhibitors demonstrated cardioprotective and nephroprotective effects, with a lower incidence of acute kidney injury, reduced inflammatory markers, and improved outcomes after coronary artery bypass grafting. In contrast, the evidence on dipeptidyl peptidase-4 inhibitors was inconsistent, with inconclusive

RESUMEN

En los últimos años han surgido nuevos fármacos antidiabéticos, como los agonistas del receptor de GLP1, los inhibidores del cotransportador sodio-glucosa tipo 2 y los inhibidores de la dipeptidil peptidasa-4, que han cobrado relevancia por ofrecer beneficios más allá del control glucémico, especialmente en la protección cardiovascular y renal. En este contexto, resulta pertinente examinar su papel potencial en la cirugía cardíaca. El objetivo de la presente revisión es describir y analizar el impacto positivo y negativo de estas terapias sobre los resultados cardiovasculares y renales en pacientes sometidos a cirugía cardíaca, independientemente de la presencia de diabetes mellitus. Se emplea una búsqueda sistemática en PubMed, Scopus y Cochrane Library de estudios publicados entre 2020 y 2025. Se incluyeron estudios que evaluaron la seguridad y eficacia de agonistas del GLP1, inhibidores del SGLT2 e inhibidores de DPP4. Los desenlaces analizados son seguridad perioperatoria, control glucémico, complicaciones cardiovasculares y función renal. Los agonistas del GLP1 mejoraron el control glucémico perioperatorio, redujeron los requerimientos de insulina y favorecieron la recuperación cardíaca, sin aumentar hipoglucemias ni eventos adversos graves. Los inhibidores del SGLT2 mostraron efectos cardioprotectores y nefroprotectores, con menor incidencia de lesión renal aguda, reducción de marcadores inflamatorios y mejores resultados tras cirugía de revascularización coronaria. En contraste, la evidencia sobre inhibidores del DPP-4 fue inconsistente, con beneficios poco

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benefits and even a possible risk of organ dysfunction. In summary, GLP-1 receptor agonists and odium-glucose cotransporter 2 inhibitors are emerging as safe and promising options in cardiac surgery, while routine use of dipeptidyl peptidase-4 inhibitors is not recommended due to limited and controversial evidence.

Keywords: cardiac surgery, GLP-1 agonists, SGLT2 inhibitors, DPP-4 inhibitors.

concluyentes e incluso un posible riesgo de disfunción orgánica. En conclusión, agonistas del GLP1 e inhibidores del SGLT2 se perfilan como opciones seguras y prometedoras en cirugía cardíaca, mientras que el uso rutinario de inhibidores del DPP4 no está recomendado por la evidencia limitada y controvertida.

Palabras clave: *cirugía cardíaca, agonistas GLP1, inhibidores SGLT2, inhibidores DPP4.*

Abbreviations:
AKI = acute kidney injury
CABG = coronary artery bypass grafting
CGM = continuous glucose monitoring
CPB = cardiopulmonary bypass
DM = diabetes mellitus
DPP-4i = dipeptidyl peptidase-4 inhibitors
GLP-1 RAs = glucagon-like peptide-1 receptor agonists
HF = heart failure
HFpEF = hearth failure with preserved ejection fraction
ICU = Intensive Care Unit
SGLT2i = sodium-glucose cotransporter type 2 inhibitors

INTRODUCTION

In recent years, new pharmacological agents have been developed for the management of diabetes mellitus (DM). These agents have demonstrated benefits that extend beyond glycemic control, contributing to both the prevention and treatment of cardiovascular diseases, thereby increasing their clinical relevance. Among these, the drugs with evidence of cardiovascular and renal protection, as well as positive effects in patients with heart failure (HF), stand out, namely, glucagon-like peptide-1 receptor agonists (GLP-1 RAs), dipeptidyl peptidase-4 inhibitors (DPP-4i), and sodium-glucose cotransporter type 2 inhibitors (SGLT2i).[1]

Emerging evidence suggests that these agents exert protective effects in various organs beyond glucose regulation. Furthermore, it has been proposed that they may confer benefits to patients undergoing cardiac surgery, both in those with and without DM, particularly in the context of HF. In this regard, GLP-1 analogs, DPP-4i, and SGLT2i have emerged as promising therapeutic alternatives, with a favorable safety profile during the perioperative period.[1]

Over the past decades, cardiac surgery rates have steadily increased. Approximately 1.5 million such procedures are performed worldwide each year, reflecting the substantial global burden of cardiovascular diseases, which remain among the leading causes of morbidity and mortality.[2] It is estimated that around 32% of patients with these conditions have a high likelihood of requiring surgical intervention. Among the most common procedures is coronary artery bypass grafting (CABG), in which the prevalence of diabetes mellitus ranges between 10 and 44%. Both HF and acute kidney injury (AKI) represent major postoperative complications, as they significantly increase morbidity and mortality rates in these patients.[1,3]

Within this context, the objective of the present review is to describe and analyze the positive and negative impacts of novel antidiabetic agents on cardiovascular and renal outcomes in patients undergoing cardiac surgery, irrespective of the presence of DM. The scope of this review focuses on the individual use of these drugs (rather than combination therapy) and on outcomes observed during the immediate postoperative period.

MATERIAL AND METHODS

A comprehensive literature review was conducted using the most current data available. The bibliographic search was performed across scientifically validated databases, including PubMed, Scopus, and the Cochrane Library, among others. Keywords related to both novel antidiabetic agents (GLP-1 RAs, SGLT2i, DPP-4i) and cardiac surgery interventions were used, such as *"Cardiac Surgical Procedures," "Benefits of new antidiabetics in surgery,"* and *"SGLT2 inhibitors and cardiac surgery"*. Boolean operators were applied to refine the search strategy, for example: *"Cardiac Surgical Procedures" [MeSH] OR "cardiac surgery" OR "CABG"* AND *"Sodium-Glucose Transporter 2 Inhibitors" [MeSH] OR SGLT2 inhibitors OR dapagliflozin OR empagliflozin*, among others.

Initially, 15 relevant studies were identified. After applying the selection criteria, 10 articles were included, focusing on those published within the last five years (2020-2025).

Inclusion criteria: studies that individually evaluated one of the three agents of interest (without combination therapy), included participants with or without diabetes mellitus, and had a sample size greater than 20 subjects, to ensure adequate statistical robustness and alignment with the study objective.

Exclusion criteria: studies involving combined treatments or published more than five years prior, as these fell outside the intended scope of this review.

Description of novel oral antidiabetic agents and their benefits

1. **Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 RAs).** GLP-1 is a 30–amino acid peptide hormone primarily produced in the intestine and, to a lesser extent,

in the hypothalamus.[4] Its main physiological role is the regulation of blood glucose; however, its half-life is short due to rapid degradation by the enzyme dipeptidyl peptidase-4 (DPP-4). GLP-1 exerts its effects through a high-affinity G protein-coupled receptor that stimulates insulin secretion and inhibits glucagon release, thereby promoting glucose homeostasis.[5]

GLP-1 analogs have been structurally modified to resist hydrolysis by DPP-4, which prolongs their therapeutic activity. This results in improved glycemic control and significant reductions in body weight. Moreover, cardiovascular outcome trials have demonstrated that these agents reduce the incidence of major adverse cardiovascular events, as well as overall mortality and hospitalization rates in the general population. It is noteworthy that these mortality benefits are primarily observed in patients without preexisting heart failure, whereas no significant effects have been reported in those with established HF.[1] Additionally, GLP-1 RAs have shown a clinically relevant impact on weight reduction.[6]

In the perioperative setting, the American Society of Anesthesiologists (ASA) and the American Gastroenterological Association (AGA) published a 2024 guideline supporting the safe use of these drugs in patients who are not at high risk for delayed gastric emptying or aspiration. The decision to continue or discontinue treatment during the preoperative period should be based on a multidisciplinary consensus among the surgical team.[1,7]

2. **Dipeptidyl Peptidase-4 Inhibitors (DPP-4i).** The catalytic enzyme dipeptidyl peptidase-4 (DPP-4), also immunologically known as CD26, is an exopeptidase that cleaves peptides after the second position of the amino-terminal end. It is expressed in multiple cell types, including hepatocytes, endothelial cells, and pancreatic islet endocrine cells. Inhibition of DPP-4 prevents the degradation of incretin hormones such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), thereby prolonging their half-life and enhancing insulin secretion while reducing glucagon release.[1,8]

   DPP-4 inhibitors are characterized by a lower risk of hypoglycemia and weight gain compared to other antidiabetic drugs, such as sulfonylureas. These agents have been reported to provide benefits in patients with DM and hearth failure with preserved ejection fraction (HFpEF), as they are associated with a reduced risk of cardiovascular death, HF hospitalization, and renal function decline. However, some studies have indicated that saxagliptin and alogliptin may increase the risk of serious heart failure events, possibly due to mechanisms involving sympathetic overactivity.[1,9]

   In this regard, the EXAMINE and SAVOR-TIMI 53 clinical trials reported a significant increase in heart failure hospitalizations among patients treated with saxagliptin compared with placebo, leading to contraindication of its use in this population.[10,11] In contrast, alogliptin may be considered in patients with DM and HF, provided that it is administered under close medical supervision. Currently, GLP-1 receptor agonists and SGLT2i are preferred agents for managing heart failure and preventing major adverse cardiovascular events.

   Regarding the perioperative management of DPP-4 inhibitors, there are two divergent perspectives: some authors recommend continuing their use on the day of surgery, while others advise discontinuation at least 24 hours before the procedure.[12,13]

3. **Sodium-Glucose Cotransporter Type 2 Inhibitors (SGLT2i).** It acts by blocking this transporter, located on the apical membrane of the proximal convoluted tubule, which is responsible for the reabsorption of sodium and glucose from urine into the bloodstream. Inhibition of this transporter increases urinary glucose excretion, lowers serum glucose levels, and is associated with a lower risk of hypoglycemia. Furthermore, the combination of natriuresis and osmotic diuresis induced by glucosuria produces hemodynamic benefits by reducing preload, afterload, and myocardial wall stress.[14,15]

   This class of drugs has the strongest clinical evidence regarding cardiovascular and renal benefits. The DELIVER trial (2022) demonstrated that dapagliflozin reduced the risk of worsening heart failure (HF) or cardiovascular death in patients with HF and preserved ejection fraction (LVEF >40%).[16] Similarly, the SOLOIST-WHF study (2020), conducted in hospitalized patients with DM experiencing acute HF exacerbation, showed that early post-discharge administration of sotagliflozin reduced cardiovascular mortality, hospital readmissions, and Intensive Care Unit (ICU) admissions compared with placebo.[17] Additionally, the CREDENCE trial (Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy) found that canagliflozin use led to a 30% relative risk reduction in the composite primary outcome of end-stage kidney disease, doubling of serum creatinine, or death from cardiovascular or renal causes. This renal protection was attributed to a reduction in intraglomerular pressure.[18]

   Based on these findings, the latest American Heart Association (AHA) guidelines include dapagliflozin and empagliflozin as first-line agents in the management of heart failure with preserved ejection fraction (HFpEF), marking them as the first drugs to demonstrate improved prognosis and survival in this condition.[19]

   In the perioperative context, expert consensus statements diverge regarding management. While some recommend

discontinuing SGLT2 inhibitors at least 24 hours before elective surgery or invasive procedures, clinical evidence supporting this recommendation remains limited.[1,20] Conversely, the U.S. Food and Drug Administration (FDA) advises interrupting therapy at least 72 hours before surgery due to the drugs' prolonged half-life.[1,21] Reintroduction may occur 24 hours after surgery, provided the patient is under close monitoring for potential adverse effects.

Novel antidiabetics and cardiac surgery

1. **GLP-1 analogs.** GLP-1 analogs have demonstrated cardioprotective effects in various contexts, raising the possibility that these benefits may also extend to patients undergoing cardiac surgery. Although evidence in this specific setting remains limited, some clinical trials have explored this relationship.
   A randomized trial in patients with DM undergoing cardiac surgery with cardiopulmonary bypass (CPB), aged 20–80 years, compared the use of liraglutide plus insulin versus insulin infusion alone for perioperative glycemic control. Sixty patients were included and evenly divided into two groups. The results showed that liraglutide combined with insulin achieved significantly lower perioperative glucose levels compared to insulin alone, with a mean difference of 15.9 mg/dl. Additionally, during the first postoperative hour, hyperglycemia incidence was lower in the combination group (43.75 vs. 67.85%; p = 0.061), an effect that persisted until postoperative day two (23.65 vs. 32.79 mg/dl; p = 0.018).[22] Similar findings were reported by Oosterom et al., in a study of 25 patients (with and without DM), where 13 received liraglutide and 12 received placebo. Continuous glucose monitoring demonstrated a significant improvement in perioperative glucose range, with an absolute difference of 25% (95% CI: −41.4 to −8.9; p = 0.004). Time in range was higher in the liraglutide-treated group (72 vs 47%).[23]
   Hulst et al., investigated not only glycemic control but also the effect of liraglutide on myocardial function after cardiac surgery. In this study, which included 261 patients, echocardiographic, hemodynamic, biomarker, and inotropic support requirements were evaluated. Findings showed that a higher proportion of patients treated with liraglutide maintained normal postoperative left ventricular systolic function (68 vs 53%; difference 15%, 95% CI: 0-30; p = 0.049). A higher mean heart rate was also observed in this group (83 ± 11 vs 77 ± 11 bpm; p < 0.001). No differences were noted in other hemodynamic parameters, vasoactive drug use, or serum biomarkers.[24]
   Exenatide has also been evaluated in a randomized, double-blind trial in patients undergoing CABG or aortic valve replacement. The study assessed its impact on mortality and major organ failure over a 5.9-year follow-up. No significant differences were observed compared to placebo regarding time to first event, though the authors noted that further research is needed to clarify its potential role in this context.[25]
2. **DPP-4 Inhibitors.** Research on DPP-4 inhibitors in the context of cardiac surgery is particularly relevant, not only due to their increasing prescription rates over recent decades but also because of controversies regarding their effects on heart failure, particularly with saxagliptin and alogliptin.
   In a clinical trial involving 182 adult patients with DM undergoing CABG, the efficacy of sitagliptin versus placebo for perioperative hyperglycemia prevention and management was evaluated. Treatment began one day prior to surgery and continued during hospitalization. The primary endpoint was the incidence of postoperative hyperglycemia. No significant differences were found in hypoglycemia frequency, daily mean glucose, surgery duration, ICU or hospital stay, vasopressor requirements, perioperative complications, reoperations, or readmissions. However, sitagliptin-treated patients required lower mean daily insulin doses after transfer to the regular ward compared to placebo (21.1 ± 18.4 vs 32.5 ± 26.3 units; p = 0.007).[1,26]
   Parker et al., assessed the impact of DPP-4 inhibitors in cardiac surgery and found that sitagliptin did not significantly improve glycemic control. Repeated measures analysis revealed similar mean blood glucose levels between groups (147.2 ± 4.8 mg/dl in the intervention group vs 153.0 ± 4.6 mg/dl in the control group; p = 0.388). Additionally, lower DPP-4 activity correlated with greater organ dysfunction and poorer outcomes in ICU patients after CPB. In a cohort of 46 patients undergoing CPB, an inverse correlation was observed between DPP-4 levels and biomarkers such as lactate and creatinine. Organ-protective effects associated with higher DPP-4 activity were particularly evident in postoperative renal function, an important consideration since acute kidney injury complicates up to 30% of cardiac surgery recoveries, highlighting the cardiorenal interaction.[27]
3. **SGLT2 Inhibitors.** Currently represent the oral antidiabetic class with the strongest evidence due to their well-established benefits in the prevention and treatment of cardiovascular and renal diseases. Their role in cardiac surgery is of particular interest.
   A multicenter study by Sardu et al., included 648 patients with ischemic heart disease, with and without DM, undergoing minimally invasive CABG with extracorporeal circulation (MiECC). The study assessed the effects of SGLT2 inhibitors on inflammatory response and clinical outcomes (all-cause mortality, cardiovascular mortality, nonfatal myocardial infarction, stroke, and need for repeat revascularization). After five years of follow-

up, non-diabetic patients showed lower inflammatory marker levels compared to diabetic patients. Within the DM group, those treated with SGLT2 inhibitors exhibited significantly lower levels of leukocytes, CRP, IL-1, IL-6, and TNF-α compared to untreated patients. At one year, SGLT2 users had lower rates of cardiovascular mortality and repeat revascularization ($p < 0.05$).[28]

Similarly, Snel et al., conducted a phase IV pilot trial in 55 patients undergoing cardiac surgery with CPB, who received empagliflozin (n = 25) or placebo (n = 30) starting three days before the procedure. The aim was to determine its impact on acute kidney injury (AKI), measured through biomarkers such as NGAL, KIM-1, HIF-1α, and their ratios with urinary creatinine. While serum NGAL levels on postoperative day two did not differ significantly, AKI incidence (KDIGO criteria) was markedly lower in the empagliflozin group (20 vs. 66.7%; $p < 0.001$). This group also showed lower glucose peaks, reduced hyperglycemia incidence, and decreased insulin requirements during the first 48 postoperative hours.[29]

Taghiyev et al. also documented a nephroprotective effect of SGLT2 inhibitors in patients undergoing cardiac surgery with CPB. Thirty-six hours after surgery, the estimated glomerular filtration rate (eGFR) was significantly higher in the treated group (mean difference 11.8 ml/min; 95% CI: 3.12-20.44; $p = 0.009$). Although albuminuria reduction was not statistically significant, a favorable trend toward lower urinary albumin concentrations was observed in the intervention group.[30]

Finally, Fardman et al., retrospectively evaluated the safety and effects of SGLT2 inhibitors in patients with left ventricular assist devices (LVADs). Among 138 patients, 29 received SGLT2 inhibitors post-implantation (23 empagliflozin, 6 dapagliflozin). Follow-up showed a significant reduction in daily furosemide dose (47 to 23.5 mg/day; mean difference 23.5 mg/day, 95% CI: 8.2-38.7; $p = 0.004$) and a decrease in body weight (−2.5 kg; 95% CI: 0.7-4.3; $p = 0.008$). Additionally, systolic blood pressure decreased by 5.6 mmHg compared to the control group (95% CI: 0.23-11; $p = 0.042$).[31]

DISCUSSION

Novel oral antidiabetic agents have gained significant relevance in recent years due to their cardiovascular benefits and their capacity to provide organ protection, particularly for the heart and kidneys, in addition to improving glycemic control. In the context of cardiac surgery, these effects are especially important, as they may contribute to both patient safety and prognosis. Within this group, SGLT2 inhibitors and GLP-1 analogs emerge as the agents with the strongest scientific support for perioperative use. In contrast, DPP-4 inhibitors show more controversial results: although they aid in glycemic control, some studies suggest a potential risk of organ dysfunction. The main characteristics and evidence of each pharmacological class are summarized in *Table 1*.

GLP-1 receptor agonists are considered a safe option for perioperative management, as they promote more stable glycemic control, reduce insulin requirements, and help preserve postoperative cardiac function. Furthermore, no increase in hypoglycemia incidence or adverse effects has been observed compared with conventional insulin therapy.

Although available evidence remains limited, several studies support these benefits. It is worth noting that two of the three trials evaluating liraglutide included relatively small populations; however, a favorable aspect is that both diabetic and non-diabetic patients were included. Specifically, the study by Oosterom et al., included only 25 patients and presented methodological limitations, such as bias in glucose measurement using continuous glucose monitoring (CGM) compared with reference arterial determinations. While CGM may take longer to detect hyperglycemic episodes, it offers a safety advantage by lowering the threshold for imminent hypoglycemia alarms. In this trial, CGM readings did not meet the strict ISO 15197:2013 criteria, achieving 62% of samples, although this percentage was higher than previously reported studies (41%).[20]

Hulst et al. reported improved echocardiographic function in the liraglutide-treated group compared with placebo. However, no differences were observed in postoperative serum biomarkers, likely because, in cardiac surgery, marker release is related to direct myocardial injury during the procedure, unlike in percutaneous coronary intervention studies where elevations are ischemia-driven.[21] An additional limitation was that only 170 patients underwent perioperative echocardiography to establish baseline status. Despite these constraints, findings suggest that preoperative administration of liraglutide may modestly improve postoperative cardiac function, alter immediate hemodynamic parameters (e.g., increased heart rate), and better preserve left ventricular function on follow-up echocardiography. These results support the need for larger clinical trials focusing on postoperative cardiovascular outcomes in patients undergoing cardiac surgery.[1,21]

Regarding DPP-4 inhibitors in cardiac surgery, evidence remains limited. In the previously mentioned study by Cardona et al., their use in type 2 diabetic patients undergoing CABG was associated with a significant reduction in mean daily insulin requirements. However, no differences in postoperative glucose levels in the ICU were observed, suggesting limited clinical benefit. Conversely, Noels et al., reported that DPP-4 inhibitors not only lack significant relevance for perioperative glycemic control but may even be harmful by promoting postoperative organ dysfunction. This finding is particularly relevant considering that, although experimental animal studies suggested potential

Table 1: Comparison of novel antidiabetic agents in the context of cardiac surgery.

Pharmacological Group	Main Benefits	Risks / Limitations	Evidence in Cardiac Surgery	Current Recommendation
GLP-1 Agonists (liraglutide, exenatide)	- Improved perioperative glycemic control - Reduced insulin requirements - Possible preservation of left ventricular function	- Modest effects on hemodynamic function - Small sample sizes in studies - Heterogeneous results	Small trials and some RCTs show improvements in glycemia and echocardiographic parameters	Promising and safe, but larger studies are needed
DPP-4 Inhibitors (sitagliptin, saxagliptin, alogliptin)	- Lower risk of hypoglycemia - Possible reduction in insulin doses	- Inconsistent evidence in glycemic control - Risk of heart failure with saxagliptin/alogliptin - Potential for organ dysfunction	Trials show conflicting results; some do not demonstrate significant differences in glycemia	Not routinely recommended in cardiac surgery
SGLT2 Inhibitors (empagliflozin, dapagliflozin, sotagliflozin)	- Cardioprotective and nephroprotective effects - Lower incidence of acute kidney injury (AKI) - Reduced perioperative inflammation - Lower cardiovascular mortality and revascularization rates	- Risk of ketoacidosis (low but present) - Evidence still limited in cardiac surgery - Several studies with small sample sizes	Pilot trials and retrospective studies show reduced AKI and improved long-term outcomes	Highly promising, with the highest level of current evidence; larger RCTs required

AKI = acute kidney injury. RCT = randomized controlled trial.

cardioprotective effects of DPP-4 inhibition, these results cannot be directly extrapolated to complex clinical scenarios such as human cardiac surgery.[25]

SGLT2 inhibitors represent the antidiabetic class with the most promising outcomes in cardiac surgery, as available studies suggest both cardioprotective and nephroprotective effects. Nevertheless, several methodological limitations should be noted. For example, the study by Snel et al., had a small sample size and an open-label design, introducing the possibility of chance influencing observed intergroup differences. While the findings align with the study's objectives, they should primarily be regarded as hypothesis-generating for future research. Moreover, the absence of ketoacidosis cases in this pilot study, although not definitive evidence of safety due to the low incidence of this complication, is an encouraging observation. It should also be noted that insulin-dependent type 2 diabetic patients were not included, although the glucose/insulin administration protocol would likely have mitigated the risk of ketoacidosis if it had occurred.[27]

In the Sardu et al., study, a notable consideration is that diabetic patients were already on chronic SGLT2 inhibitor therapy, and therapy allocation was not randomized. This lack of randomization and blinding could introduce bias and limit the validity of the results. Therefore, further studies in larger populations with robust methodological design and extended follow-up are recommended to definitively clarify the molecular, cellular, and clinical effects of SGLT2 inhibitors in diabetic patients undergoing CABG with MiECC.[26]

CONCLUSION

Although available information is limited, particularly regarding DPP-4 inhibitors, it can be concluded that both GLP-1 analogs and SGLT2 inhibitors are safe for perioperative use and provide cardiovascular and renal benefits in the postoperative period for patients undergoing various types of cardiac surgery, regardless of whether the patient has underlying DM.

Regarding DPP-4 inhibitors, due to mixed and controversial evidence, their perioperative use is recommended to be restricted, as there is insufficient evidence of glycemic control benefit and a potential risk of organ failure.

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