NARRATIVE REVIEW

SGLT-2 Inhibitors in the Management of Chronic Kidney Disease in Non-Diabetic Patients

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ABSTRACT

Introduction: Chronic kidney disease (CKD) is one of the most prevalent conditions worldwide and is projected to become a leading cause of morbidity and mortality in the coming decades. Until a few decades ago, the only established therapies shown to modify disease progression were renin–angiotensin system (RAS) inhibitors. However, newer agents such as sodium–glucose cotransporter 2 (SGLT-2) inhibitors have become a cornerstone of CKD management in both diabetic and non-diabetic patients, due to their protective effects on renal and cardiovascular outcomes.

Current evidence: SGLT-2 inhibitors reduce renal glucose reabsorption, leading to glucosuria. In addition, they lower intraglomerular pressure, thereby protecting the kidney from hyperfiltration-related damage, and promote natriuresis, which reduces plasma volume and blood pressure. Multiple studies have demonstrated their efficacy in preventing or delaying CKD progression, reducing cardiovascular mortality, hospitalizations, and heart failure, and improving quality of life in selected patients. However, their protective effects have not been consistently demonstrated in patients with prior stroke.

Conclusion: To date, SGLT-2 inhibitors are among the most effective therapies for slowing CKD progression. Their benefits have been consistent across multiple subgroups, particularly in patients with proteinuric CKD, both in diabetic and non-diabetic populations, as supported by randomized clinical trials and meta-analyses.

Keywords: Diabetes mellitus, Kidney Failure, Chronic, heart failure, Sodium-glucose cotransporter 2 inhibitors. (MeSH).

Inhibidores de la SLGT-2 en el manejo de enfermedad renal crónica en pacientes no diabéticos

RESUMEN

Introducción: la enfermedad renal crónica (ERC) es una de las entidades con mayor prevalencia y se proyecta que en el futuro sea una de las principales causas de enfermedades crónicas. Hasta hace un par de décadas, el único tratamiento conocido para modificar su curso eran los inhibidores del sistema renina-angiotensina. Sin embargo, las nuevas terapias como los inhibidores del cotransportador de sodio-glucosa tipo 2 (iSLGT-2) se han convertido en la piedra angular del tratamiento de esta entidad

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tanto en pacientes diabéticos como no diabéticos, debido a su efecto protector sobre la función renal y cardiovascular.

Estado del arte: los iSLGT-2 son fármacos que reducen la reabsorción renal de glucosa, generando glucosuria. Además, disminuyen la presión intraglomerular, protegiendo al riñón del daño asociado con la hiperglucemia y provocan natriuresis, lo que reduce el volumen plasmático y la presión arterial. Varios estudios han demostrado su eficacia para prevenir o retrasar el deterioro renal, la mortalidad cardiovascular, las hospitalizaciones y la insuficiencia cardíaca (IC), mejorando la calidad de vida en algunos pacientes. Sin embargo, los efectos protectores no son consistentes en pacientes con accidente cerebrovascular (ACV).

Conclusión: hasta la fecha, los iSLGT-2 son el tratamiento más eficaz para retrasar la progresión de la ERC. Sus beneficios han mostrado ser consistentes en diversos subgrupos particularmente en pacientes con ERC con proteinuria, tanto en aquellos diabéticos como no diabéticos, según ensayos clínicos y metanálisis.

Palabras clave: diabetes mellitus, insuficiencia renal crónica, insuficiencia cardíaca, inhibidores del cotransportador de sodio-glucosa 2, glifozinas (DeCS).

INTRODUCTION

Chronic kidney disease (CKD) represents one of the most prevalent conditions worldwide. To date, the only drugs proven to slow the progression of renal function decline are angiotensin-converting enzyme inhibitors (ACE inhibitors) and angiotensin II receptor blockers (ARBs)[1], which has limited therapeutic options in non-diabetic CKD. In this context, SGLT-2 inhibitors have emerged as a promising alternative, positioning themselves as safe and effective treatments in this population[2].

The 2024 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines highlight the fundamental role of SGLT-2 inhibitors in the treatment of CKD, both in patients with type 2 diabetes mellitus (T2DM) and in those without this condition[1].

The present review aims to describe the efficacy and safety of SGLT-2 inhibitors in the treatment of CKD in non-diabetic patients. The search was conducted in PubMed and Cochrane using the following MeSH terms: ((“sglt2”[All Fields]) OR (“SGLT2 inhibitor”[All Fields]) OR (“SGLT-2 inhibitor”[All Fields]) OR (“dapagliflozin”[All Fields]) OR (“empagliflozin”[All Fields]) OR (“canagliflozin”[All Fields]) OR (“ertugliflozin”[All Fields])) AND ((“kidney disease”[All Fields]) OR (“chronic kidney disease”[All Fields]) OR (“CKD”[All Fields])) AND ((“non diabetic”[All Fields]) OR (“non-diabetic”[All Fields]) OR (“without diabetes”[All Fields]) OR (“non diabetes”[All Fields])), applying the following filters: systematic reviews, meta-analyses, and randomized controlled trials, without date restriction, including articles published up to October 31, 2024. A total of 31 articles were identified, of which 3 meta-analyses and 2 randomized controlled trials evaluated renal effects in non-diabetic patients. Studies were selected based on the assessment of outcomes related to CKD progression and cardiovascular events. A second search was conducted on February 17, 2025, to include ongoing clinical trials registered in ClinicalTrials.gov, where 8 studies were identified whose purpose was to evaluate the renal effects of SGLT-2 inhibitors.

This work corresponds to a narrative review; no systematic assessment of methodological quality or risk of bias of the included studies was performed, and therefore its conclusions should be interpreted within this descriptive scope. During the final drafting of the manuscript, ChatGPT was used as a tool for punctuation review and grammatical correction in approximately 30% of the text, without altering the content of the article.

STATE OF THE ART

Mechanism of action of SGLT-2 inhibitors

The sodium-glucose cotransporter (SGLT) family comprises six isoforms identified in humans; the most studied are SGLT-1 and SGLT-2. SGLT-2 is predominantly expressed in the apical brush border of the renal proximal tubule, specifically in the S1 and S2 segments, and is responsible for approximately 90% of filtered glucose reabsorption. This cotransporter facilitates glucose entry into renal tubular cells against its concentration gradient through a mechanism coupled to sodium entry, whose gradient is maintained by the sodium/potassium ATPase pump[3].

Since SGLT-2 is a sodium–glucose cotransporter, its inhibition not only impacts glycemic control but also produces relevant effects on systemic hemodynamics. The decrease in sodium reabsorption reduces activation of the renin–angiotensin–aldosterone system (RAAS), as macula densa sensors, upon detecting an increased sodium chloride load, inhibit renin release into the bloodstream.

In addition, it is postulated that this reduction in sodium reabsorption induces natriuresis, promoting increased water excretion, which results in a diuretic effect and a decrease in plasma volume. Taken together, these mechanisms explain how SGLT-2 inhibitors contribute to reductions in preload, afterload, and blood pressure[4].

In the cardiovascular setting, empagliflozin has been shown to reduce left ventricular mass in patients with type 2 diabetes mellitus (T2DM) and coronary artery disease, which may reflect an improvement in cardiac remodeling. This finding, observed by magnetic resonance imaging in the EMPA-HEART[5] CardioLink-6 study, suggests a direct benefit on cardiac structure that may contribute to the cardioprotective effects observed with SGLT-2 inhibitors.

Furthermore, SGLT-2 inhibitors reduce intrarenal pressure by decreasing sodium reabsorption in the proximal tubule. This results in an increased sodium load reaching the thick ascending limb of Henle and the macula densa, activating tubuloglomerular feedback –a mechanism involved in autoregulation– leading to vasoconstriction of the afferent arteriole and, consequently, a decrease in intraglomerular pressure. This mechanism contributes to reducing glomerular hyperfiltration, one of the key factors in the progression of diabetic CKD[3].

The reduction in sodium and glucose reabsorption in the proximal tubule decreases tubular workload, which may improve renal oxygenation. It has been proposed that this more favorable environment promotes the restoration of erythropoietin (EPO) production by peritubular interstitial fibroblasts, which are sensitive to hypoxia. By improving oxygenation, these cells exhibit greater viability, which may favor a sustained increase in hematocrit. In the EMPA-REG OUTCOME study, an increase in hematocrit was observed with empagliflozin, and it has been suggested that this change may mediate, at least in part, the reduction in cardiovascular mortality observed with treatment[3].

Another proposed theory is that SGLT-2 inhibitors induce a metabolic state similar to fasting, promoting gluconeogenesis and enhanced ketogenesis. This effect is linked to the activation of molecular pathways such as SIRT1, PGC-1α, and FGF21 (sirtuin-1, peroxisome proliferator-activated receptor gamma coactivator 1-alpha, and fibroblast growth factor 21, respectively), which are considered sensors of energy deprivation. These mechanisms have been shown to exert protective effects at the cellular level by reducing oxidative stress, improving mitochondrial function, and promoting autophagy, with potential neuroprotective and cardiometabolic benefits[6].

CURRENT USES OF SGLT-2 INHIBITORS

SGLT-2 inhibitors as cardiovascular protectors

Regarding cardiovascular (CV) protection, several clinical trials have been conducted, including EMPA-REG OUTCOME (ERO), CANVAS, and DECLARE TIMI 58[7-9], which used empagliflozin, canagliflozin, and dapagliflozin in individuals with diabetes mellitus (DM), albeit with different baseline characteristics. Notably, in the DECLARE TIMI 58 study, most participants had multiple cardiovascular risk factors.

The composite outcome of these trials (MACE) was reduced by 11% compared with placebo (HR 0.89; 95% CI: 0.83-0.96; p = 0.0014), with stronger evidence driven by a reduction in hospitalizations for heart failure (HF).

In a meta-analysis, the protective role of SGLT-2 inhibitors on stroke in patients with diabetic kidney disease was evaluated, without finding statistical significance for the prevention of total ischemic stroke (RR 0.95 [95% CI: 0.79-1.13]; p = 0.585) or fatal stroke (RR 0.87; 95% CI: 0.60-1.27; p = 0.482). In the case of ischemic stroke, a neutral effect was observed (RR 0.99; 95% CI: 0.88-1.11; p = 0.952).

On the other hand, in patients who experienced hemorrhagic stroke, active treatment with SGLT-2 inhibitors was associated with a significant reduction in events (RR 0.49; 95% CI: 0.30-0.82; p = 0.007)[10]. In those with atrial fibrillation (AF) / atrial flutter (HR 0.81; 95% CI: 0.71-0.93), particularly in patients with estimated glomerular filtration rate (eGFR) < 45 mL/min/1.73 m² (HR 0.50; 95% CI: 0.31-0.79), these findings suggest a potential preventive role for hemorrhagic and thrombotic stroke in patients with AF and low eGFR.

Regarding the secondary outcome of CKD progression in subjects at high cardiovascular risk, a reduction in cardiovascular events was also observed in patients without HF and with an estimated glomerular filtration rate (eGFR) > 60 mL/min/1.73 m², with this effect maintained down to eGFR levels between 40 and 45 mL/min/1.73 m². [11]

Recently, the safety of these medications on cardiac function has been evaluated in patients with T2DM and pre-HF. The Ertu-GLS trial is a randomized, double-blind study with a duration of 24 weeks. It evaluated the use of ertugliflozin (5 mg daily) versus placebo in patients with left ventricular hypertrophy (E/e' ratio > 15) or impaired left ventricular global longitudinal strain (LVGLS), assessed by cardiac Doppler, but without symptoms consistent with HF.

Ertugliflozin showed improvement in LVGLS (mean difference [MD] −15.5 ± 3.1% to −16.6 ± 2.8%, p = 0.004) compared with the placebo group (MD −16.7 ± 2.7% to −16.4 ± 2.6%, p = 0.509), with a significant between-group difference (p = 0.013). As secondary outcomes, a reduction in left ventricular mass index (p = 0.034) and a significant improvement in ejection fraction (p = 0.010) were observed. Other evaluated parameters, such as glycated hemoglobin, LDL cholesterol, lipoprotein(a), and proteinuria, also showed significant improvement[9].

SGLT-2 inhibitors and their role in HF

In recent years, most studies on the use of SGLT-2 inhibitors have focused on the paradigm of HF management. Several clinical trials have been conducted; however, four studies have shown the most robust results to date: EMPEROR-Reduced[12] and DAPA-HF[13] in patients with reduced ejection fraction (EF < 40%), and EMPEROR-Preserved[13] and DELIVER[14] in those with preserved EF (> 50%).

In the EMPEROR-Preserved and DELIVER studies, a 20% reduction in the primary composite outcome (death or first hospitalization for HF) was observed (HR 0.80; 95% CI: 0.73-0.87), with reductions in both components:

cardiovascular death (HR 0.88; 95% CI: 0.77-1.00) and first hospitalization for HF (HR 0.74; 95% CI: 0.67–0.83)[15]. In studies involving patients with reduced EF, a 25% reduction was observed (HR 0.75; 95% CI: 0.65-0.85) in the primary composite outcome of cardiovascular death or hospitalization for HF.

Furthermore, both studies demonstrated robust benefits in reducing hospitalizations for HF (EMPEROR-Reduced HR 0.69; 95% CI: 0.59-0.81 and DAPA-HF HR 0.70; 95% CI: 0.59-0.83). However, EMPEROR-Reduced did not achieve a reduction in cardiovascular mortality, although it did show a significant slowing of eGFR decline in a particularly vulnerable population[12].

EFFECTS OF SGLT-2 INHIBITORS IN CKD

Initially, the studies with gliflozins that began to demonstrate beneficial renal effects were ERO, the CANVAS study, and DECLARE TIMI 58; however, all study populations had diabetes mellitus (DM)[7-9], and renal outcomes were evaluated as secondary endpoints. In the ERO trial, a lower incidence or progression of nephropathy was observed (12.7% vs. 18% compared with placebo; $p < 0.001$), representing a 39% relative risk reduction[15].

Additionally, a 44% reduction in the risk of doubling of serum creatinine and a 55% reduction in the initiation of renal replacement therapy (RRT) were observed. On the other hand, there were no significant differences in early albuminuria.

In the CANVAS study, the association of canagliflozin with progression of albuminuria and reduction in eGFR was analyzed, showing a 40% reduction in major renal outcomes (decline in eGFR, death from renal causes, and need for RRT), although without statistical significance[8]. The DECLARE-TIMI 58 trial conducted with dapagliflozin had as a secondary renal endpoint a ≥ 40% decline in eGFR to below 60 mL/min/1.73 m², need for RRT, or death from renal or cardiovascular causes. No statistically significant differences were observed in composite renal outcomes[15].

One of the first studies in which the primary outcome was a renal endpoint in patients with DM was the CREDENCE trial[16]. It showed that in patients with type 2 diabetes and albuminuria, the use of canagliflozin reduced the primary composite outcome (doubling of serum creatinine, death from renal or cardiovascular causes) by 34% and reduced initiation of RRT by 32%. The benefits were greater in patients with higher eGFR. Furthermore, it is noteworthy that the benefits observed in the trials mentioned thus far were independent of baseline eGFR and of the range of certain indices such as the albumin-to-creatinine ratio (ACR)[15].

At present, several studies have evaluated the use of SGLT-2 inhibitors in populations with and without diabetes mellitus (DM), with CKD as a secondary outcome. However, two studies have established the use of SGLT-2 inhibitors in patients with CKD (including etiologies other than diabetic nephropathy) and CKD progression as the primary outcome.

The first of these was the DAPA-CKD trial[2]. The use of dapagliflozin 10 mg was evaluated in patients with an eGFR of 25 to 75 mL/min/1.73 m² and an albumin-to-creatinine ratio (ACR) of 200 to 5000 mg/g. The results showed a significant reduction (HR 0.72; 95% CI: 0.64-0.82; $p < 0.001$) in the primary composite outcome (sustained decline in eGFR of more than 50%, need for renal replacement therapy [RRT], or death from renal or cardiovascular causes). A subgroup of patients continued receiving dapagliflozin or placebo after initiating dialysis, demonstrating a relative risk reduction of up to 21% in cardiovascular mortality and heart failure (HF), even in post-transplant patients. Subsequently, the EMPA-KIDNEY trial evaluated the use of empagliflozin 10 mg in patients with CKD at high risk of progression, regardless of population type[17]. Unlike DAPA-CKD, this trial included patients with an eGFR greater than 20 mL/min/1.73 m² and an ACR of up to 200 mg/g. The results showed a 28% reduction in CKD progression or cardiovascular mortality (HR 0.72; 95% CI: 0.64-0.82; $p < 0.001$)[15].

In subgroup analyses according to CKD etiology, the EMPA-KIDNEY study found evidence supporting the use of empagliflozin in patients with diabetic nephropathy for the primary outcome (HR 0.65; 95% CI: 0.53-0.80), glomerular disease (HR 0.77; 95% CI: 0.60-0.98), hypertensive/renovascular disease (HR 0.82; 95% CI: 0.61–1.11), and other or unknown causes (HR 0.73; 95% CI: 0.54-1.00). However, in the latter two groups, the difference was not statistically significant[17].

On the other hand, according to the presence of proteinuria, a reduction in HR was observed in patients with an ACR greater than 300 (HR 0.67; 95% CI: 0.58-0.78), whereas this trend was not observed in patients with an ACR between 30 and 300 or below 30 (HR 0.91; 95% CI: 0.65-1.26; HR 1.01; 95% CI: 0.66-1.55, respectively).

On the other hand, in the DAPA-CKD study[2], patients with diabetic nephropathy who received dapagliflozin showed a greater risk reduction compared with placebo in the primary outcome (HR 0.64; 95% CI: 0.52-0.79). This superiority was also observed in patients with CKD of non-diabetic etiology (HR 0.50; 95% CI: 0.35-0.72). However, the study excluded patients with type 1 diabetes mellitus (T1DM), polycystic kidney disease, lupus nephritis, ANCA-associated vasculitis, and those who had received immunotherapy within the six months prior to the intervention, which limits the applicability of the results to these subgroups in clinical practice. Table 1 summarizes the differences between the DAPA-CKD and EMPA-KIDNEY studies.

A recently published meta-analysis and meta-regression showed that the renal impact of different SGLT-2 inhibitors was a determining factor in the stabilization of HF. It was significantly associated, after the initial decline in eGFR, with the composite outcome ($p = 0.017$), and each 1 mL/min/1.73 m² improvement was associated with a 14% reduction in hospitalizations for HF[18]. In another meta-analysis, the effect of SGLT-2 inhibitors on renal outcomes was evaluated in a non-diabetic population (n = 15,605) with a mean eGFR

Tabla 1. Differences between pivotal trials (DAPA-CKD vs. EMPA-KIDNEY) in the subgroup of patients with chronic kidney disease without diabetes

Characteristic	DAPA-CKD	EMPA-KIDNEY
Drug and dose	Dapagliflozin 10 mg	Empagliflozin 10 mg
Design and sample size Inclusion criteria	Randomized controlled trial (RCT), double-blind, placebo-controlled; N = 4304 eGFR 25–75 mL/min/1.73 m²; UACR 200–5000 mg/g	Randomized controlled trial (RCT), double-blind, placebo-controlled; N = 6609 A. eGFR 20–<45 mL/min/1.73 m² B. eGFR 45–<90 mL/min/1.73 m² with elevated UACR C. eGFR >45 mL/min/1.73 m²; UACR >200 mg/g
Primary outcome (definition, composite)	Sustained decline in eGFR >50%, ESKD, renal or cardiovascular death	CKD progression (ESKD, eGFR <10, sustained decline in eGFR >40%, renal death), cardiovascular death
Follow-up (median)	2.4 years	2 years
eGFR (mean ± SD)	43.2 ± 12.3 vs. 43.0 ± 12.4	37.4 ± 14.5 vs. 37.3 ± 14.4
UACR (median, IQR)	965 (472–1903) vs. 934 (482–1868)	331 (46–1061) vs. 327 (54–1074)
Non-diabetic population (n)	1398	1779
Primary outcome (overall HR, 95% CI)	0.61 (0.51–0.72; p < 0.001)	0.72 (0.64–0.82; p < 0.001)
Non-diabetic subgroup (events/total)	45/694 vs. 83/701; HR 0.50 (0.35–0.72)	214/1779 vs. 252/1790; HR 0.64 (0.68-0.99)
CKD etiology		
Hypertensive/renovascular disease	—	82/706 vs. 96/739; HR 0.82 (0.61–1.11)
Glomerular disease	—	117/853 vs. 142/816; HR 0.77 (0.60–0.98)
Other/unknown	—	72/713 vs. 97/725; HR 0.73 (0.54–1.00)

eGFR: estimated glomerular filtration rate; UACR: urinary albumin-to-creatinine ratio; ESKD: end-stage kidney disease; HR: hazard ratio; CI: confidence interval; RCT: randomized controlled trial; IQR: interquartile range; CKD: chronic kidney disease.

range of 37-85 mL/min/1.73 m² (DAPA-HF, EMPEROR-Reduced, DELIVER, EMPEROR-Preserved, DAPA-CKD, EMPA-KIDNEY). Compared with placebo, the risk of CKD progression was significantly reduced by 37% (RR 0.63; 95% CI: 0.58-0.69), with similar RRs in patients with and without diabetes. In the four CKD trials (CREDENCE, SCORED, DAPA-CKD, EMPA-KIDNEY), RRs were similar regardless of the primary CKD diagnosis; additionally, the risk of acute kidney injury was reduced by 23% (RR 0.77; 95% CI: 0.70-0.84)[19].

Based on the available evidence, the KDIGO 2024 guidelines recommend the use of SGLT-2 inhibitors in patients with CKD (eGFR > 20 mL/min/1.73 m² and ACR > 200 mg/g), regardless of etiology and level of albuminuria (1A), and in patients with eGFR 20-45 mL/min/1.73 m² and ACR < 200 mg/g (2B)[1].

FUTURE PERSPECTIVES

It is worth noting that most clinical trials conducted to date with SGLT-2 inhibitors have excluded patients with eGFR < 20 mL/min/1.73 m², patients on dialysis, and kidney transplant recipients. As previously mentioned, post hoc analyses suggest that this class of drugs may be useful in preventing cardiovascular outcomes, including in patients with advanced CKD or transplant recipients.

Currently, multiple studies are underway to evaluate the use of SGLT-2 inhibitors in patients with CKD. Among them, the RENAL LIFECYCLE study[20] aims to assess the efficacy and safety of dapagliflozin in patients with advanced CKD (eGFR < 25 mL/min/1.73 m²), without discontinuation of treatment at the initiation of dialysis (at least 3 months after starting dialysis) or following kidney transplantation (eGFR ≤ 45 mL/min/1.73 m² at least 6 months after transplantation). The study aims to determine whether dapagliflozin is superior to placebo in terms of all-cause mortality as the primary outcome, as well as hospitalization for HF, reduction in the incidence of end-stage CKD, and reduction in the composite outcome of advanced CKD, dialysis, and kidney transplantation. Additionally, it will analyze renal effects

(energy metabolism and mitochondrial morphology) and cognitive effects of the intervention. Another important aspect is that it will evaluate the incidence of type 2 diabetes mellitus (T2DM) in patients with CKD.

Other ongoing studies include GLUTREPO[21], which aims to determine the effects of SGLT-2 inhibitors over six months on markers of senescence, inflammation, and tubulointerstitial damage in patients with CKD, with and without diabetes. Likewise, the study by Srisawat[22] is evaluating the nephroprotective effects of empagliflozin compared with placebo in patients with stage 2 to 3 acute kidney injury (AKI), assessing the primary composite outcome of mortality due to AKI, RRT, newly established CKD, and CKD stage progression. The trial by Mohsen[23] explores the impact of SGLT-2 inhibitors on CKD progression (eGFR 25-75 mL/min/1.73 m^2) in non-diabetic patients and the potential negative impact on bone and mineral metabolism using quantitative CT. Additionally, a study conducted at the National Taiwan University Hospital[24] is investigating whether SGLT-2 inhibitors may represent a therapeutic option for AKI and their potential to prevent progression to CKD, using changes in albuminuria levels compared with baseline as the outcome measure. The trial led by Mavrakanas[25] aims to characterize the pharmacokinetics, pharmacodynamics, and efficacy of canagliflozin in patients with advanced CKD, including those undergoing hemodialysis.

Regarding studies focused on specific CKD etiologies, the trial by Fehr and Hofmann[26] investigates the role of SGLT-2 inhibitors in electrolyte management in patients with autosomal dominant polycystic kidney disease. Similarly, the study by Yap[27] examines the effects of SGLT-2 inhibitors on the progression of renal function in patients with lupus nephritis and CKD, based on a significant correlation between circulating memory B cells and SGLT-2 expression in patients with lupus nephritis.

CONCLUSION

Studies conducted to date demonstrate that SGLT-2 inhibitors delay CKD progression in patients with diabetic nephropathy. This finding has led to the exploration of their effects in patients with CKD of other etiologies, and studies are currently underway investigating their potential utility in acute kidney injury (AKI) and in patients undergoing dialysis or renal replacement therapy (RRT). Although the mechanisms underlying nephroprotection are not yet fully understood, ongoing protocols aim to better characterize these protective pathways. In conclusion, initiation of treatment with SGLT-2 inhibitors in patients with CKD is considered safe and recommended for those with an eGFR of 20-45 mL/min/1.73 m^2 and an ACR > 200 mg/g, and their indication is expected to expand to include patients with CKD of diverse etiologies, such as polycystic kidney disease or lupus nephritis, as well as those in advanced stages of the disease.

Author contributions: Conceptualization, Data curation, Methodology, Investigation, Project administration, Supervision, Validation, Visualization, Writing—original draft, Writing—review and editing (AME, JCGP, GO).

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