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SYSTEMATIC REVIEW

Current Trends in the Treatment of Heart Failure in Patients with Diabetes Mellitus and Ejection Fraction: An Analysis of the Relationship between SGLT2 and Heart Failure

Tendencias Actuales en el Tratamiento de la Insuficiencia Cardíaca en Pacientes con Diabetes Mellitus y Fracción de Eyección: Un Análisis de la Relación entre SGLT2 y la Insuficiencia Cardíaca

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ABSTRACT

Introduction: the use of glyflozines, a group of drugs, in the treatment of heart failure, diabetes mellitus and chronic kidney disease is analyzed. To highlight the pathophysiological mechanisms shared between these diseases and the increased risk of cardiovascular events in patients with these conditions. Glyflozines have shown benefits in all three diseases mentioned, surprising researchers for their cardiovascular effects. The article mentions the association between type 2 diabetes mellitus (DM2) and heart failure, as well as the increased risk of cardiovascular disease in patients with DM2. **Objectives:** to analyze the two isoforms of sodium-glucose transporters (SGLT1 and SGLT2) and the role of SGLT2 inhibitors in promoting osmotic diuresis and glucose excretion, in relation to treatment for heart failure, diabetes mellitus and chronic kidney disease.
Methods: a Systematic Review of the literature was performed, which will be governed according to PRISMA guidelines. The units of analysis will be abstracts and full text of articles with randomized clinical trial design or prospective or retrospective cohort, published in Scopus, Web of Science and Pubmed, without temporal restriction.
Results: the results of this review strongly support the inclusion of T2GLS in the management strategies of heart failure in patients with diabetes mellitus. Furthermore, they suggest that these drugs can have a positive clinical impact in patients with different profiles, making them a versatile option. However, further research is needed to deepen the mechanisms of action and to explore their efficacy in patients with heart failure and preserved ejection fraction, as well as in other subgroups of clinical interest. The incorporation of SGLT2 into current and future clinical practice may represent a significant advance in the treatment of heart failure and improve the quality of life of affected patients. Future research should focus on addressing outstanding questions and areas of uncertainty to better guide clinical decision making and improve outcomes for patients with heart failure and diabetes mellitus.

Keywords: Cardiovascular Events; Gliflozinas; Treatment Optimization; Systematic Review.

RESUMEN

Introducción: se analiza el uso de gliflozinas, un grupo de fármacos, en el tratamiento de la insuficiencia cardiaca, la diabetes mellitus y la enfermedad renal crónica. Destacar los mecanismos

fisiopatológicos compartidos entre estas enfermedades y el mayor riesgo de eventos cardiovasculares en pacientes con estas afecciones. Las gliflozinas han mostrado beneficios en las tres enfermedades mencionadas, sorprendiendo a los investigadores por sus efectos cardiovasculares. El artículo menciona la asociación entre diabetes mellitus tipo 2 (DM2) e insuficiencia cardiaca, así como el mayor riesgo de enfermedad cardiovascular en pacientes con DM2.

Objetivos: analizar las dos isoformas de los transportadores de sodio-glucosa (SGLT1 y SGLT2) y el papel de los inhibidores de SGLT2 en la promoción de la diuresis osmótica y la excreción de glucosa, en relación al tratamiento para la insuficiencia cardiaca, la diabetes mellitus y la enfermedad renal crónica.

Método: se realizó una Revisión Sistemática de la literatura, que se regirá de acuerdo con las directrices PRISMA. Las unidades de análisis serán los resúmenes y texto completo de artículos con diseño de ensayos clínicos aleatorizado o cohorte prospectiva o retrospectiva, publicados en Scopus, Web of Science y Pubmed, sin restricción temporal.

Resultados: los resultados de esta revisión respaldan firmemente la inclusión de los SGLT2 en las estrategias de manejo de la insuficiencia cardíaca en pacientes con diabetes mellitus. Además, sugieren que estos medicamentos pueden tener un impacto clínico positivo en pacientes con diferentes perfiles, lo que los convierte en una opción versátil. Sin embargo, se necesita más investigación para profundizar en los mecanismos de acción y para explorar su eficacia en pacientes con insuficiencia cardíaca y fracción de eyección preservada, así como en otros subgrupos de interés clínico. La incorporación de los SGLT2 en la práctica clínica actual y futura puede representar un avance significativo en el tratamiento de la insuficiencia cardíaca y mejorar la calidad de vida de los pacientes afectados. Las investigaciones futuras deben centrarse en abordar las preguntas pendientes y las áreas de incertidumbre para guiar mejor la toma de decisiones clínicas y mejorar los resultados de los pacientes con insuficiencia cardíaca y diabetes mellitus.

Palabras clave: Eventos Cardiovasculares; Gliflozinas; Optimización del Tratamiento; Revisión Sistemática.

INTRODUCTION

The great benefits demonstrated by SGLT2 receptor inhibitors or glyflozines are explained by their pharmacological mechanisms of action. The objective is to try to understand them in order to make our daily practice reasonable, logical and more beneficial for our patients.

We know that in patients with type 2 diabetes, there is a simultaneous hyperabsorption of glucose and sodium in the proximal tubules by SGLT2 (sodium and glucose cotransporters). This causes vasodilatation of the glomerular afferent arteriole leading to increased glomerular inflammation and fibrosis, ultimately leading to diabetic nephropathy. Glyflozines act by blocking sodium-glucose transport proteins3, which increases the diuresis of sodium and glucose, generating a decrease in the reabsorption of the former and increasing its concentration in the macula densa, specialized cells located in the distal tubules. This generates a feedback at the glomerular tubule level that activates adenosine receptors, triggering a constriction of the afferent artery of the glomerulus; this constriction reduces glomerular hyperfiltration and therefore prevents renal damage.

Another benefit of gliflozins at the renal level is the reduction of tubular work and its oxygen consumption, reducing the damage associated with hypoxia of the tubular cells and finally improving the synthesis of erythropoietin and improving the anemia associated with this pathology.

The beneficial cardiac effects are multiple, complex and often still not precisely determined. Below, we will mention them and explain what has been deciphered about them.

The use of glyflozines, a group of drugs, in the treatment of heart failure, diabetes mellitus and chronic kidney disease is analyzed.

To highlight the pathophysiological mechanisms shared between these diseases and the increased risk of cardiovascular events in patients with these conditions.

Glyflozines have shown benefits in all three diseases mentioned, surprising researchers for their cardiovascular effects.

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The article mentions the association between type 2 diabetes mellitus (DM2) and heart failure, as well as the increased risk of cardiovascular disease in patients with DM2.

It also discusses the role of hyperglycemia in the development of macrovascular complications and the discordant results of studies on tight glycemic control and cardiovascular events.

The use of SGLT2 inhibitors, a type of glyflozines, and their positive effects on congestion, renal function and glucotoxicity.

Glyflozines, a group of drugs, have practical implications in the treatment of heart failure, diabetes mellitus, and chronic kidney disease.

These drugs have demonstrated benefits in reducing cardiovascular events, hospitalizations for heart failure, and overall mortality.

They can be used in patients with advanced chronic renal failure, even with reduced renal function.

Glyflozines have diuretic and hemodynamic effects, leading to weight loss and improved blood pressure control.

They also have metabolic effects, such as reduced glucose toxicity and improved glycemic control.

In addition, glyflozins have anti-inflammatory properties, which may contribute to their cardiovascular benefits.

Practical implications of this research include optimizing treatment strategies for patients with heart failure, diabetes mellitus and chronic kidney disease by incorporating gliflozins into their therapeutic regimens.

These pathologies are also included in a "vicious circle" because they share pathophysiological mechanisms that predispose to their coexistence in the same patient, significantly increasing the risk of cardiovascular events.

Glyflozines, a group of drugs with benefits in the three aforementioned diseases, have recently been added to the therapeutic arsenal.

Knowing how research with these drugs was developed and their mechanisms of action is essential to optimize patient treatment.

The objective of this systematic review is to comprehensively analyze the available scientific evidence on the relationship between sodium-glucose cotransporter type 2 (SGLT2) inhibitors and heart failure in patients with diabetes mellitus, focusing on cardiac ejection fraction (EF) as a key factor.

METHODS

Study Design: a Systematic Review of the literature will be conducted, which will be governed according to the PRISMA guidelines (preferred reporting items for systematic reviews and meta-analyses).

Study Population:

Inclusion Criteria: Randomized clinical trials evaluating SGLT2 and heart failure and prospective or retrospective cohort studies.

Exclusion Criteria: Review Articles, Scientific Letters/Letters to the Editor, Case Reports, Editorials, Original Articles corresponding to Observational Studies.

Selection and Sample Size

The units of analysis will be the abstracts and full text of articles with randomized clinical trial design or prospective or retrospective cohort, published in Scopus, Web of Science and Pubmed, without time restriction.

Ethical and legal considerations

This study included secondary data sources and therefore does not correspond to an analysis from the ethical point of view, given that no experimentation or evaluations were performed on human beings/experimental animals.

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RESULTS

Study	Country	Aim	Intervention	Type of research	Sample	Main results	Clinical/practical implications
Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction	Estados Unidos, Reino Unido, Países Bajos, Singapur, Argentina, República Checa, España, Rumania, Polonia, México, Arabia Saudita.	We designed the Dapagliflozin Evaluation to Improve the Lives of Patients with Preserved Ejection Fraction Heart Failure (DELIVER) trial to test the hypothesis that the SGLT2 inhibitor dapagliflozin would reduce the risk of worsening heart failure or cardiovascular death among patients with a mildly reduced or preserved ejection fraction.	GE: dapagliflozin at a dose of 10 mg once daily GC: Placebo	We randomly assigned 6263 patients with heart failure and a left ventricular ejection fraction of more than 40 % to receive dapagliflozin (at a dose of 10 mg once daily) or matching placebo, in addition to usual therapy.	GE: 3131 GC: 3132	Dapagliflozin reduced the combined risk of worsening heart failure or cardiovascular death among patients with heart failure and a mildly reduced or preserved ejection fraction. - The primary outcome was a composite of worsening heart failure or cardiovascular death. The size of the boxes in Figure 2 is proportional to the number of patients in the subgroup, and arrows on the confidence interval bars indicate that the upper or lower boundary of the confidence interval is off the scale. - The primary outcome, the occurrence of worsening heart failure or cardiovascular death, was assessed in a time-to-event analysis. The trial aimed to detect a hazard ratio of 0,80 for the comparison of	- Dapagliflozin, an SGLT2 inhibitor, has shown efficacy in reducing the risk of hospitalization for heart failure and cardiovascular death in patients with chronic heart failure and a left ventricular ejection fraction of 40 or less . - The findings of the DELIVER trial suggest that dapagliflozin may also be effective in patients with a higher left ventricular ejection fraction, providing further evidence to support its use in a broader population of heart failure patients . - The use of dapagliflozin as essential therapy in patients with heart failure, regardless of the presence or absence of type 2 diabetes mellitus or left ventricular ejection fraction, is supported by these data .

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						dapagliflozin and placebo with respect to the primary outcome. - Among patients with heart failure and a mildly reduced or preserved ejection fraction, dapagliflozin resulted in a lower risk of the primary composite outcome, fewer worsening heart failure events and cardiovascular deaths, and a lower symptom burden, with no excess of adverse events. Findings were consistent across prespecified subgroups, including those defined according to left ventricular ejection fraction.	- These results have important implications for the management of heart failure, as dapagliflozin could be considered as a treatment option to reduce the risk of worsening heart failure and cardiovascular death in a wider range of patients .
Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction	Estados Unidos, Reino Unido, Países Bajos, Singapur, Argentina, República Checa, España, Rumania, Polonia, México,	We designed the DAPA-HF (Dapagliflozin and Pre-vention of Adverse Outcomes in Heart Failure) trial to prospectively evaluate the efficacy and safety of the SGLT2 inhibitor dapagliflozin in	GE: dapa-gliflozin at a dose of 10 mg once daily GC: Placebo	phase 3, placebo-controlled trial,	GE: 2373 GC: 2371	The primary outcome of the study was a composite of death from cardiovascular causes, hospitalization for heart failure, or an urgent visit resulting in intravenous therapy for heart failure. The cumulative incidences of the primary outcome were estimated using	The study found that patients who received dapagliflozin had a lower risk of worsening heart failure or death from cardiovascular causes compared to those who received placebo. The primary outcome of the study was a composite of death from cardiovascular

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	Arabia Saudita.	patients with heart failure and a reduced ejection fraction, regardless of the presence or absence of diabetes.		the Kaplan-Meier method, and hazard ratios were calculated using Cox regression models. Adverse events were monitored throughout the trial. Serious adverse events and adverse events associated with the discontinuation of treatment were recorded. Adverse events of interest, such as volume depletion, renal events, major hypoglycemic events, bone fractures, diabetic ketoacidosis, amputations, and Fournier's gangrene, were specifically analyzed. The trial aimed to detect a hazard ratio of 0,80 for the comparison between dapagliflozin and placebo. The prespecified safety analyses included serious adverse events, adverse events associated with treatment discontinuation, adverse events of interest, and laboratory findings.	causes, hospitalization for heart failure, or an urgent visit resulting in intravenous therapy for heart failure. The trial aimed to detect a hazard ratio of 0,80 for the comparison between dapagliflozin and placebo. The trial enrolled approximately 4500 patients, with an expected recruitment period of 18 months and an average follow-up period of approximately 24 months. The results showed a significant reduction in the risk of dying in patients who received dapagliflozin.

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						The trial enrolled approximately 4500 patients, with an expected recruitment period of 18 months and an average follow-up period of approximately 24 months.	
The SGLT2 inhibitor empagliflozin in patients hospitalized for acute heart failure: a multinational randomized trial	Paises bajos, Alemania, Estados Unidos, Australia, Polonia, Francia, Portugal, Singapur, China, España, Suecia, Belgica, Hungría, Japón, Noruega, Dinamarca, Republica checa, Italia.	evaluate the effects of empagliflozin on three fundamental goals of care in patients hospitalized for acute heart failure: improvement of survival, reduction of heart failure events, and improvement of symptoms.	GE: dapagliflozin at a dose of 10 mg once daily GC: Placebo	multicenter, randomized, double-blind, 90 day superiority trial to evaluate the effect on clinical benefit, safety and tolerability of once daily oral EMPagliflozin 10 mg compared with placebo	GE:265 GC: 265	It provides evidence that empagliflozin, an SGLT2 inhibitor, is effective and safe when initiated in patients with de novo hospitalization for acute heart failure who are not yet treated with background heart failure therapies. The study demonstrates that empagliflozin significantly reduces the risk of cardiovascular death or hospitalization for heart failure in patients with both reduced and preserved left ventricular ejection fraction. shows that empagliflozin is well-tolerated, with fewer serious adverse events compared to placebo, and has a clinical benefit that is	SGLT2 inhibitors, including dapagliflozin, have shown promising results in reducing the risk of cardiovascular death or hospitalization for heart failure in patients with chronic heart failure

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						apparent within 90 days of treatment initiation.	
Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure	Estados Unidos, Grecia, Canada, Japón, Brasil, India, Mexico, Belgica, China, España, Países Bajos, Hungría, Argentina, Polonia, Italia, Francia, Republica Checa.	provides evidence that empagliflozin is associated with a lower combined risk of cardiovascular death or hospitalization for heart failure compared to placebo in patients with chronic heart failure and reduced ejection fraction, regardless of the presence or absence of diabetes.	GE: dapagliflozin 10 mg/dayli GC: Placebo	double-blind trial, we randomly assigned 3730 patients with class II, III, or IV heart failure and an ejection fraction of 40 % or less	GE: 1863 GP: 1867	The total number of hospitalizations for heart failure was lower in the empagliflozin group than in the placebo group (hazard ratio, 0,70; 95 % CI, 0,58 to 0,85; P<0,001). The annual rate of decline in the estimated glomerular filtration rate was slower in the empagliflozin group than in the placebo group (–0,55 vs. –2,28 ml per minute per 1,73 m 2 of body-surface area per year, P<0,001), and empagliflozin-treated patients had a lower risk of serious renal outcomes. Uncomplicated genital tract infection was reported more frequently with empagliflozin.	n the Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure (DAPA-HF) trial, dapagliflozin demonstrated a reduction in the risk of cardiovascular death or hospitalization for heart failure in patients with mild-to-moderate degrees of left ventricular systolic dysfunction.
Empagliflozin in Patients With Heart Failure, Reduced Ejection Fraction, and Volume Overload	Estados Unidos, Alemania, Reino Unido.	show a reduction in heart failure events during long-term treatment with SGLT2 inhibitors	GE: dapagliflozin 10 mg/dayli GC: placebo	double-blind randomized trial.	GE: 1139 GP:1110	Empagliflozin, an SGLT2 inhibitor, was found to reduce the composite risk of cardiovascular death or hospitalization for heart failure, decrease total hospitalizations for	Patients with an ejection fraction of 30 or less were particularly responsive to empagliflozin treatment in terms of reducing the risk of cardiovascular

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						heart failure, and improve health status and functional class in patients with heart failure and reduced ejection fraction. These benefits were observed in patients with and without recent volume overload, and there was no significant difference in the magnitude of these benefits between the two groups. Changes in body weight, hematocrit, and natriuretic peptides did not closely track each other or correlate with the clinical benefits of empagliflozin, suggesting that diuresis may not be the dominant mechanism of action for SGLT2 inhibitors in heart failure patients.	death and hospitalizations for heart failure
Renal and Cardiovascular Effects of SGLT2 Inhibition in Combination With Loop Diuretics in Patients With Type 2 Diabetes and Chronic Heart Failure	Estados Unidos	Explore the effects of the SGLT2 inhibitor empagliflozin on diuresis and natriuresis and on the interaction between loop diuretics and SGLT2 inhibitors.	GE: Empagliflozin 25 mg/dayli GC: Placebo	double-blind randomized trial.	GE: 23 GC: 23	Empagliflozin caused a significant increase in 24-hour urine volume without an increase in urinary sodium when used in combination with loop diuretic.	These results suggest empagliflozin may have an advantageous diuretic profile in patients with type 2 diabetes and heart failure in addition to loop diuretics, with only a short, transient natriuresis.

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Dapagliflozin Effects on Biomarkers, Symptoms, and Functional Status in Patients With Heart Failure With Reduced Ejection Fraction	Estados Unidos.	examining the early effects of SGLT-2i on clinically important end points in patients with heart failure and reduced ejection fraction.	GE: empagliflozin 10 mg/dayli GC: placebo	randomized, double-blind, placebo-controlled trial.	GE:131 GC:132	In patients with heart failure and reduced ejection fraction, use of dapagliflozin over 12 weeks did not affect mean NT-proBNP but increased the proportion of patients experiencing clinically meaningful improvements in HF-related health status or natriuretic peptides. Benefits of dapagliflozin on clinically meaningful HF measures appear to extend to patients without type 2 diabetes mellitus.	These findings suggest that dapagliflozin may have a favorable effect on improving disease-specific health status (symptoms, function, and quality of life) after 12 weeks of treatment in patients with heart failure and reduced ejection fraction
Effects of canagliflozin in patients with type 2 diabetes and chronic heart failure: a randomized trial (CANDLE)	Japon	Compared the effect of canagliflozin with glimepiride, based on changes in N-terminal pro-brain natriuretic peptide (NT-proBNP), in that patient population.	GCanagliflozin: canagliflozin 100 mg dayli GGlimepiride: glimepiride 0,5mg dayli	multicentre, prospective, randomized, open-label, blinded-endpoint trial	GCanagliflozin: 113 GGlimepiride: 120	This study did not meet the predefined primary endpoint of changes in NT-proBNP levels, with 24 weeks of treatment with canagliflozin vs. glimepiride. Further research is warranted to determine whether patients with heart failure with preserved ejection fraction, regardless of diabetes status, could potentially benefit from treatment with SGLT2 inhibitors.	canagliflozin showed a significant improvement in NYHA classes in the subgroup with a baseline LVEF <50

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Association of Empagliflozin Treatment With Albuminuria Levels in Patients With Heart Failure	Francia, Portugal, Estados Unidos, Gracia, Reino Unido, Alemania, Polonia.	Analyze the association of empagliflozin with study outcomes across baseline levels of albuminuria and change in albuminuria in patients with HF across a wide range of ejection fraction levels	GE: Empagliflozin, 10 mg/dayli GC: Placebo	randomized in a double-blind.	GE:4860 GC: 4858	Empagliflozin treatment was associated with a reduction in albuminuria levels in patients with heart failure (HF) across a wide range of ejection fraction levels. No relevant differences were detected between patients in the placebo vs empagliflozin groups in terms of adverse events, adverse events leading to discontinuation, serious adverse events, and acute kidney failure events.	empagliflozin treatment was associated with a reduction in albuminuria levels in patients with HF. This suggests that empagliflozin may have a beneficial effect on the structural damage of the glomerular filtration barrier and could potentially improve kidney and cardiovascular outcomes in these patients.
Effects of empagliflozin on erythropoiesis in heart failure: data from the Empire HF trial	Estados Unidos.	investigate the early effect of empagliflozin on erythropoiesis and iron metabolism in patients with heart failure with reduced ejection fraction (HFrEF) after 12 weeks of treatment.	GE: Empagliflozin, 10 mg/dayli GC: Placebo	double-blind, randomized, placebo-controlled trial	GE:95 GC:95	empagliflozin increases erythropoiesis and augments early iron utilization in patients with HFrEF. These mechanisms may contribute to the cardioprotective properties of empagliflozin	Empagliflozin therapy increases erythropoiesis and augments iron utilization, but further research is needed to determine the long-term clinical outcomes in patients with HFrEF
The effects of canagliflozin compared to sitagliptin on cardiorespiratory fitness in type 2	Estados Unidos, Canada.	The objective of the study was to investigate whether canagliflozin, an SGLT2 inhibitor, improved	Sitagliptin: 100mg/dayli Canaglifozin: 100mg/dayli	double-blind randomized controlled trial	Sitagliptin: 19 Canaglifozin: 17	in patients with T2DM and HFrEF canagliflozin was associated with improvements in several measures of	The study measured the ventilatory efficiency using the minute ventilation/carbon dioxide production (VE/VCO2) slope as

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diabetes mellitus and heart failure with reduced ejection fraction: The CANA-HF study		cardiorespiratory fitness (CRF) in patients with type 2 diabetes mellitus (T2DM) and heart failure with reduced ejection fraction (HFrEF) compared to sitagliptin, a DPP4 inhibitor. The study aimed to assess the effects of canagliflozin on peak oxygen consumption (VO2) and ventilatory efficiency, independent of glycemic control.				CRF such as lean peak VO2, VAT and RER-matched VO2, and an improvement in the MLHFQ score reflecting a reduced HF symptom burden compared to sitagliptin, despite no significant differences in glycemic and hemodynamic control	one of the co-primary endpoints. However, there were no significant changes in VE/VCO2 slope between the canagliflozin and sitagliptin groups canagliflozin patients tended to have lower respiratory exchange ratio (RER) at follow-up, this did not negatively affect the peak VO2, indicating that canagliflozin did not impair ventilatory efficiency
The SGLT2 inhibitor empagliflozin reduces tissue sodium content in patients with chronic heart failure: results from a placebo-controlled randomised trial	Estados Unidos, Reino Unido.	The objective of the study was to investigate the effect of empagliflozin, an SGLT2 inhibitor, on tissue sodium content in patients with chronic heart failure (CHF) .	GE: empagliflozin 10 mg once daily GC: Placebo	double-blind, randomised (2:1), placebo-controlled.	GE: 48 GC: 26	After 1 and 3 months of treatment with empagliflozin, there was a significant decrease in skin sodium content (p = 0,039 and p = 0,013, respectively) compared to placebo. No significant changes were observed in muscle sodium and muscle water content. The decrease in skin sodium content may reflect a decrease in subclinical micro-oedema or/and in non-osmotic bound tissue sodium, both of	The reduction of extravascular sodium content, as seen with empagliflozin treatment, may contribute to improved left ventricular function by reducing myocardial interstitial oedema, which causes systolic and diastolic cardiac dysfunction and increased stiffness of the left ventricle.

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						which have been reported to impair left ventricular function.	
Canagliflozin for Japanese patients with chronic heart failure and type II diabetes	Japon	The study aimed to assess the changes in fat areas, markers of glycemic control, renal function, oxidative stress, lipid parameters, atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), flow-mediated dilation (FMD), and echocardiographic left ventricular function after 12 months of canagliflozin treatment.	GE: 100 mg/day for 12 months.	prospective controlled trial of canagliflozin in outpatients with chronic heart failure and diabetes	GE:35	Canagliflozin treatment for 12 months resulted in a significant decrease in all fat areas (subcutaneous, visceral, and total) in Japanese patients with chronic heart failure and type II diabetes. ANP and BNP levels also decreased significantly, along with improvements in renal function, oxidized LDL, and FMD. Canagliflozin demonstrated cardiac and renal protective effects, as well as improvements in oxidative stress, diastolic function, and endothelial function. It was found to be effective in patients with heart failure with preserved ejection fraction and could potentially be a first-line therapy for such patients with diabetes.	Canagliflozin treatment resulted in a significant decrease in body weight and body mass index, as well as a lower prevalence of metabolic syndrome. It also led to a decrease in hs-CRP levels, indicating reduced inflammation. These effects highlight the potential of canagliflozin in managing weight and metabolic parameters in patients with chronic heart failure and type II diabetes The study provides evidence for the beneficial effects of canagliflozin on cardiovascular and metabolic parameters in Japanese patients with heart failure and type II diabetes. These findings have important clinical implications for the management of patients with these

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							conditions, suggesting that canagliflozin could be a valuable addition to the treatment regimen, potentially improving outcomes and reducing the risk of cardiovascular events
Combined effects of ARNI and SGLT2 inhibitors in diabetic patients with heart failure with reduced ejection fraction	Corea del Sur, Emiratos Árabes Unidos.	investigate whether the combination of an angiotensin receptor-neprilysin inhibitor (ARNI) and a sodium-glucose co-transporter-2 inhibitor (SGLT2i) could be more effective in improving cardiac function and disease prognosis in diabetic patients with heart failure with reduced ejection fraction (HFrEF).	G1: ARNI + SGLT2i G2: ARNI only G3: SGLT2i only GC:	The study was conducted retrospectively, analyzing data from diabetic patients with heart failure with reduced ejection fraction (HFrEF) who were prescribed an angiotensin receptor-neprilysin inhibitor (ARNI) and/or a sodium-glucose co-transporter-2 inhibitor (SGLT2i) .	G1:51 G2:52 G3:52 GC: 51	diabetic patients with heart failure with reduced ejection fraction (HFrEF) who received a combination of angiotensin receptor-neprilysin inhibitor (ARNI) and sodium-glucose co-transporter-2 inhibitor (SGLT2i) (group 1) had a lower risk of hospitalization for heart failure (HHF) and cardiovascular mortality compared to other treatment groups (group 2: ARNI only, group 3: SGLT2i only, group 4: neither ARNI nor SGLT2i) Patients in group 1 also showed more pronounced improvements in left ventricular ejection fraction and E/e' (a measure of diastolic	The combination therapy of ARNI and SGLT2 inhibitors has shown significant improvements in left ventricular ejection fraction and E/e' compared to individual medications or no medication, indicating enhanced myocardial function The concurrent use of ARNI and SGLT2 inhibitors may have additive or synergistic effects in improving cardiac function and prognosis in diabetic patients with heart failure with reduced ejection fraction (HFrEF) The combination therapy of ARNI and SGLT2 inhibitors has been associated

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						function) compared to the other groups	with a lower risk of hospitalization for heart failure (HHF) and cardiovascular mortality compared to treatment with either ARNI or SGLT2 inhibitors alone or no medication .
Effect of Empagliflozin on Hemodynamics in Patients With Heart Failure and Reduced Ejection Fraction	Estados Unidos.	This study aimed to investigate the effects of sodium-glucose cotransporter-2 inhibitor empagliflozin on central hemodynamics in patients with HF and HFrEF.	GE: empagliflozin 10mg/dayli GC:Placebo	double-blinded, placebo-controlled, randomized trial.	GE:35 GC:35	The study found that there was no significant treatment effect of empagliflozin on the ratio of pulmonary capillary wedge pressure (PCWP) to cardiac index (CI) at peak exercise after 12 weeks. However, when considering hemodynamics over the full range of exercise loads, empagliflozin significantly reduced PCWP but did not have an effect on CI. This reduction in PCWP was consistent among patients with and without type 2 diabetes.	Empagliflozin significantly reduced PCWP over the full range of exercise loads in patients with stable heart failure and reduced ejection fraction (HFrEF), regardless of whether they had type 2 diabetes or not. This reduction in PCWP was observed after 12 weeks of treatment with empagliflozin. The effects of empagliflozin on PCWP were consistent across pre-specified subgroup analyses, suggesting that the reduction in PCWP is a consistent effect of empagliflozin in patients with HFrEF
Effect of Empagliflozin on Blood Volume	Estados Unidos.	determine whether inhibition of the sodium-glucose cotransporter-2	GE: Empagliflozin, 10 mg/day GC: placebo	Double-blinded, placebo-controlled,	GE: 35 GC:35	The analysis showed that empagliflozin treatment significantly reduced stressed blood volume	Empagliflozin induced a modest reduction in estimated SBV, suggesting a salutary

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Redistribution in Patients With Chronic Heart Failure and Reduced Ejection Fraction: An Analysis From the Empire HF Randomized Clinical Trial		(SGLT2) with empagliflozin could favorably affect SBV in these patients. The study conducted a post hoc analysis of a randomized trial and evaluated the change in estimated SBV after 12 weeks of empagliflozin treatment compared to placebo. The analysis included right heart catheterization at rest and during exercise to assess the effect of empagliflozin on SBV over the full range of exercise loads. The study found that empagliflozin treatment significantly reduced SBV compared to placebo in patients with stable chronic heart failure and reduced ejection fraction during submaximal exercise		randomized trial.		(SBV) compared to placebo after 12 weeks of treatment in patients with stable chronic heart failure and reduced ejection fraction during submaximal exercise.	effect on venous capacitance in patients with heart failure and reduced ejection fraction
Dapagliflozin effects on lung	Estados Unidos,	determine if dapagliflozin	GE: dapagliflozin 10 mg daily	multicentre, randomized,	GE: 41 GC: 44	There was no significant difference	Dapagliflozin reduces the risk of

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fluid volumes in patients with heart failure and reduced ejection fraction: Results from the DEFINE-HF trial	Canada, Australia.	could directly impact LFV as a potential mechanism for the observed benefits of SGLT2 inhibitors in reducing the risk of cardiovascular death or worsening heart failure and improving symptoms, physical function, and quality of life in patients with HFrEF	GC: placebo	placebo-controlled trial in 263 HF patients		in mean adjusted lung fluid volume (LFV) at 12 weeks between dapagliflozin and placebo groups. However, significantly fewer dapagliflozin-treated patients experienced no change or deterioration in LFV, and a greater proportion of dapagliflozin-treated patients had improvement in LFV The study provided the first direct evidence that SGLT2 inhibitors, like dapagliflozin, may facilitate osmotic diuresis and reduce interstitial fluid, resulting in congestion relief with minimal impact on blood volume.	cardiovascular death or worsening heart failure, leading to improved symptom burden and physical function Dapagliflozin facilitates osmotic diuresis and reduces interstitial fluid, resulting in congestion relief and improved symptoms . Patients who experienced improvement in lung fluid volumes (LFVs) with dapagliflozin had a significantly greater improvement in Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS), indicating better quality of life
Dapagliflozin Improves Heart Failure Symptoms and Physical Limitations Across the Full Range of Ejection Fraction: Pooled Patient-Level Analysis	Estados Unidos.	determine whether the benefits of SGLT2 inhibitors, specifically dapagliflozin, on symptoms and physical limitations vary across the full range of ejection	GE: dapagliflozin 10 mg/dayli GC:placebo	randomized in a double-blind fash-ion, 1:1 to oral dapagliflozin 10 mg or matching placebo once	GE: 293 GC: 294	The study included a total of 587 participants, with a median age of 67 years. Most participants had previously been hospitalized for heart failure, and there was a high prevalence of obesity among the	There is a dearth of efficacious therapies that improve health status (symptoms, physical limi-tations, and quality of life) in individuals with HF regardless of EF.

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From DEFINE-HF and PRESERVED-HF Trials	fraction (EF) in patients with heart failure (HF)		participants. The median NT-proBNP level was elevated at baseline, indicating heart failure severity, while the median estimated glomerular filtration rate (eGFR) was 59 mL/min per 1,73m2. The majority of patients were treated with loop diuretics, ACE inhibitors/angiotensin receptor blockers/angiotensin receptor-neprilysin inhibitors, and beta blockers. The baseline Kansas City Cardiomyopathy Questionnaire-Clinical Summary Score (KCCQ-CSS) was 67 points, indicating a moderate impact of heart failure symptoms and physical limitations. The median ejection fraction (EF) was 50 %, with patients distributed across EF categories of ≤40 %, >40-≤60 %, and >60 %. Effects of Dapagliflozin on KCCQ-CSS: Dapagliflozin significantly improved the KCCQ-CSS at 12 weeks compared to	

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			placebo, with a placebo-adjusted difference of 5,0 points. This improvement was consistent across all EF categories (≤40 %, >40-≤60 %, and >60 %) and when EF was analyzed as a continuous variable. The benefits of dapagliflozin on KCCQ-CSS were also consistent when analyzing other KCCQ domains and in responder analyses. These findings suggest that dapagliflozin improves symptoms and physical limitations in patients with heart failure, regardless of their EF. Additional Subgroup Analysis: An additional subgroup analysis specifically examined the effects of dapagliflozin versus placebo on KCCQ-CSS at 12 weeks in patients with an EF of 65 and above. The effects of dapagliflozin on other KCCQ domains (Total Symptom Score, Physical Limitations Score, and Overall Summary Score) were	

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						also evaluated. The analysis found no significant differences in the effects of dapagliflozin versus placebo on these outcomes across the full range of baseline EF, including in patients with an EF of 65 and above.	
The effect of luseogliflozin and alpha-glucosidase inhibitor on heart failure with preserved ejection fraction in diabetic patients: rationale and design of the MUSCAT-HF randomised controlled trial	Japan	The objective of the paper is to describe the rationale and design of the MUSCAT-HF randomized controlled trial.	Luseoglizofi: 2,5mg/dayli Voglibose: 0,2mg/ 3 times a day	multi-centre, prospective, open-label, randomised controlled trial	190 patients	the differences between the luseogliflozin and voglibose groups in parameters such as the ratio of early mitral inflow velocity to mitral annular early diastolic velocity (Ee'), left ventricular ejection fraction, body weight, and HbA1c at 12 weeks. These will also be analyzed using ANCOVA in the FAS population. Prespecified subgroup analyses will be performed on the primary outcome using ANCOVA in various subgroups, including baseline age, HbA1c, BNP, renal function, use of thiazolidine, body weight, and presence or absence of atrial fibrillation/flutter at	Significant reduction in BNP levels with luseogliflozin compared to voglibose, it could suggest a potential therapeutic option for managing HFpEF in T2DM patients

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						baseline. Exploratory analyses will also be conducted in subgroups based on blood pressure, heart rate, waist circumference, cardiovascular risk factors, alcohol consumption, regular medication, and serum lipid levels. Safety Analysis: The safety analysis will be performed in the safety analysis set (SAFETY), which includes all patients who receive at least one dose of the study drug. Analysis of serious adverse events (MACE, hypoglycemia, urinary tract infection) will be conducted using the Cochran-Mantel-Haenszel test with stratification factors.	
Effect of canagliflozin on N-terminal pro-brain natriuretic peptide in patients with type 2 diabetes and chronic heart failure according to baseline use of glucose-lowering	Japan	Assess the effect of canagliflozin, compared to glimepiride, on N-terminal pro-brain natriuretic peptide (NT-proBNP) concentration in patients with type 2 diabetes (T2D) and chronic heart failure (CHF)	Canaglifloin: 100mg/dayli Glimepirlde: 0,5mg/dayli	investigator-initiated, multicenter, open-label, randomized, controlled trial.	Canaglifloin:122 Glimepirlde:123	The CANDLE trial assessed the effect of canagliflozin on N-terminal pro-brain natriuretic peptide (NT-proBNP) concentration in patients with type 2 diabetes (T2D) and chronic heart failure (CHF) based on their baseline use of	the use of canagliflozin, an SGLT2 inhibitor, in patients with type 2 diabetes (T2D) and chronic heart failure (CHF) may have beneficial effects on N-terminal pro-brain natriuretic peptide (NT-proBNP) concentration, a marker of heart

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agents		based on their baseline use of other glucose-lowering agents.				glucose-lowering agents. The analysis showed that the effect of canagliflozin on NT-proBNP concentration was similar in both the naïve and non-naïve subgroups Additionally, there was no significant difference in the impact of canagliflozin on systolic blood pressure, body mass index, and extracellular volume between the naïve and non-naïve subgroups. However, canagliflozin treatment improved New York Heart Association (NYHA) class only in patients who had not been taking glucose-lowering agents.	failure severity, regardless of the baseline use of other glucose-lowering agents.
Effect of Sotagliflozin on Early Mortality and Heart Failure-Related Events	Estados Unidos, Canada, Francia, Países Bajos, Suecia.	Evaluate the efficacy of sotagliflozin versus placebo in decreasing mortality and heart failure-related events among patients with type 2	GE: Sotagliflozin 200mg/dayli GC: placebo	phase III, international, double-blind, randomized, placebo-controlled trial.	GE: 290 GC:306	SOLOIST-WHF trial showed that starting sotagliflozin before discharge in patients with type 2 diabetes hospitalized for worsening heart failure (WHF) significantly decreased	sotagliflozin significantly reduced all-cause mortality at 90 days after discharge (HR: 0,39 [95 % CI: 0,17-0,88]; P = 0,024) The analysis also showed that over

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		diabetes who began study treatment on or before discharge from their index hospitalization for worsening heart failure (WHF). The main endpoint of interest was cardiovascular death or HF-related event occurring within 90 and 30 days after discharge for the index WHF hospitalization.				cardiovascular deaths and HF events through 30 and 90 days after discharge. Sotagliflozin reduced the main endpoint of cardiovascular death or HF-related event at 90 days after discharge (HR: 0,54 [95 % CI: 0,35-0,82]; P = 0,004) and at 30 days (HR: 0,49 [95 % CI: 0,27-0,91]; P = 0,023). It also reduced all-cause mortality at 90 days (HR: 0,39 [95 % CI: 0,17-0,88]; P = 0,024)	the entire postdischarge follow-up period, sotagliflozin decreased the risk of the main endpoint (cardiovascular death or HF-related event) by 31 % (HR: 0,69 [95 % CI: 0,51-0,94]; P = 0,017) sotagliflozin decreased the relative risk of a composite of cardiovascular mortality and HF-related events in patients who received the study drug before or at the time of discharge from their index event
Design and rationale of the EMPA-VISION trial: investigating the metabolic effects of empagliflozin in patients with heart failure	Reino Unido, Alemania, Estados Unidos.	investigate the effects of empagliflozin treatment on cardiac energy metabolism and physiology in patients with heart failure (HF). The study aimed to elucidate the mechanisms behind the positive outcomes observed in previous trials,	GE: Empagliflozin 10mg/dayli GC: placebo	double-blind, randomized, placebo-controlled design.	GE: 43 GC: 43	Treatment with empagliflozin reduced the risk of death from cardiovascular (CV) causes by 38 % and HF hospi-talization by 35 %, in patients with T2DM and established CV disease. 12 In the trial, the reduction in the composite primary outcome (3-point major adverse CV	the effects of empagliflozin on cardiac energy metabolism may pave the way for the development of targeted therapies that specifically modulate energy metabolism in HF patients. novel treatments could potentially improve cardiac function, reduce HF

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	such as reductions in HF hospitalization and cardiovascular mortality. The trial employed various assessments, including magnetic resonance spectroscopy (MRS) and cardiovascular magnetic resonance (CMR), to evaluate the metabolic effects of empagliflozin. The primary endpoint of the study was the change in resting phosphocreatine-to-adenosine triphosphate (PCr/ATP) ratio, as measured by 31 Phosphorus-MRS. The results of the EMPA-VISION trial are expected to shed light on the mechanistic action of empagliflozin in patients with HF and provide further insights into its safety and efficacy outcomes		events) was specifically driven by a reduction of endpoints associated with the pro-gression of HF.	hospitalizations, and enhance overall patient outcomes in HF, regardless of the presence or absence of type 2 diabetes mellitus

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		observed in previous trials.					
Rationale and design of the Dapagliflozin after Transcatheter Aortic Valve Implantation (DapaTAVI) randomized trial	España	the clinical benefit and safety of the SGLT-2 inhibitor dapagliflozin in patients undergoing TAVI.	GE: apagliflozin 10 mg once daily GC: placebo	independent pragmatic, controlled, prospective, randomized, open-label blinded endpoint, multicentre trial	GE:510 GC:510	assess the clinical benefit and safety of the SGLT-2 inhibitor dapagliflozin in patients undergoing transcatheter aortic valve implantation (TAVI) The results of the DapaTAVI trial may inform clinical decision-making and potentially lead to the incorporation of SGLT-2 inhibitors, such as dapagliflozin, into the standard care for patients undergoing TAVI	The use of dapagliflozin in this population may reduce the risk of heart failure hospitalization, which is a common complication after TAVI
Dapagliflozin Influences Ventricular Hemodynamics and Exercise-Induced Pulmonary Hypertension in Type 2 Diabetes Patient	Japon	The objective of the study was to investigate the impact of dapagliflozin, a sodium-glucose cotransporter-2 inhibitor (SGLT2-i), on left ventricular (LV) systolic and diastolic function, as well as the elevation of LV filling pressure (LVFP) and right ventricular systolic pressure (RVSP) during exercise in patients with type	GE: 5 mg dapagliflozin/dayli GC: placebo	double-blind, placebo-con-trolled.	GE:36 GC:28	Sodium-glucose cotransporter-2 inhibitors (SGLT2-i) have been shown to reduce all-cause mortality, cardiovascular mortality, and rehospitalization for heart failure (HF) in patients with type 2 diabetes mellitus (T2DM) during a 6-month period Dapagliflozin can improve left ventricular (LV) systolic and diastolic function, suppress the elevation of LV filling	dapagliflozin, an SGLT2-i, may have potential clinical implications in improving cardiovascular outcomes and reducing the risk of heart failure in patients with T2DM. Further research and clinical trials are warranted to validate these findings and explore the long-term effects of SGLT2-i treatment in this patient population.

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		2 diabetes mellitus (T2DM) and cardiovascular risk. The study aimed to assess whether dapagliflozin could improve cardiac response during exercise and potentially provide cardioprotective effects independent of glucose-lowering effects				pressure (LVFP), and reduce right ventricular systolic pressure (RVSP) on echocardiography, both at rest and during exercise, in T2DM patients with cardiovascular risk	
Effects of the SGLT2 inhibitor dapagliflozin on cardiac function evaluated by impedance cardiography in patients with type 2 diabetes. Secondary analysis of a randomized placebo-controlled trial	Italia	Evaluate whether treatment with the SGLT2 inhibitor dapagliflozin affected cardiac function in patients with type 2 diabetes using impedance cardiography (ICG) in a randomized placebo-controlled trial.	GE: dapagliflozin 10 mg/dayli GC: placebo	double-blind, placebo-con-trolled.	GE:15 GC:15	Despite strong evidence that SGLT2i prevent HF in T2D with or without prior HF episodes, we found no effects of dapagliflozin on parameters of cardiac function measured by ICG.	Clinicians should consider the overall cardiovascular benefits of SGLT2 inhibitors, such as reduced hospitalization for heart failure, when prescribing these medications to patients with type 2 diabetes, rather than expecting direct improvements in cardiac function
Effect of dapagliflozin on cardiac function in people with type 2 diabetes and albuminuria – A double blind randomized	Dinamarca	Aimed to investigate whether treatment with the SGLT2i dapagliflozin on top of renin angiotensin	GE: dapagliflozin 10 mg/dayli GC: placebo	double-blind, randomized, placebo-controlled crossover trial.	GE: 20 GC: 20	The results showed no significant changes in left ventricular ejection fraction (LVEF), global longitudinal strain, E/e', and tissue Doppler velocity e'.	The study found that dapagliflozin, an SGLT2 inhibitor, may have minor effects on diastolic function in people with type 2 diabetes, albuminuria, and

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placebo-controlled crossover trial	aldosterone system (RAAS) blocking treatment can 1. improve cardiac function measured by echocardiography and cardiac risk prediction based on N-Terminal pro-Brain Natriuretic Peptide (NTproBNP), Troponin I (TnI), MidRegional pro-ADrenoMedullin (MRproADM) and MidRegional proAtrial Natriuretic Peptide (MRproANP) 2.		However, a composite score showed a 19,8 % improvement in diastolic function with dapagliflozin treatment.	preserved left ventricular ejection fraction (LVEF) . These findings suggest that dapagliflozin could potentially be beneficial in improving diastolic function in this patient population . However, it is important to note that there were no significant changes observed in other measures of cardiac function, such as LVEF, global longitudinal strain, and tissue Doppler velocity .

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DISCUSSION

In this systematic review, we have analyzed a series of studies and clinical trials that investigated the relationship between sodium-glucose cotransporter type 2 (SGLT2) inhibitors and heart failure in patients with diabetes mellitus, paying special attention to cardiac ejection fraction (EF). The results obtained from these studies provide valuable information on the impact of SGLT2 on the prevention and treatment of heart failure in diabetic patients.

One of the key findings of this review is that T2GLS, such as dapagliflozin and empagliflozin, have been shown to be effective in reducing the combined risk of worsening heart failure or cardiovascular death in patients with heart failure and a mildly reduced or preserved cardiac ejection fraction. These results are consistent with several clinical trials that have investigated different SGLT2s and their beneficial effects in heart failure, independent of ejection fraction.

Accumulating evidence suggests that SGLT2s not only reduce heart failure events and cardiovascular death, but also improve patients' quality of life by reducing symptom burden and the need for hospitalization. Moreover, these benefits appear to be consistent across a variety of patient subgroups, including those with different cardiac ejection fractions, suggesting that SGLT2s may be a promising therapeutic option in a broad spectrum of heart failure patients.

However, it is important to note that this review has also identified some limitations and areas for improvement in the current evidence. In particular, more research is needed to fully understand the underlying mechanisms of how SGLT2s improve cardiac function in patients with diabetes mellitus and sometimes without diabetes. In addition, most studies focused on heart failure patients with reduced ejection fraction, and further exploration is needed in patients with preserved ejection fraction.

Interestingly, the promising role of sodium-glucose cotransporter type 2 (SGLT2) inhibitors in the prevention and treatment of heart failure in patients with diabetes mellitus and cardiac ejection fraction is noteworthy. Despite some methodological limitations and areas of uncertainty, the results support the idea that SGLT2s can improve quality of life and reduce symptom burden in these patients. These findings have significant implications for clinical practice and justify the need for future research to expand our understanding of this relationship and its applicability in different heart failure patient populations.

Based on the systematic review of available studies, we can affirm that sodium-glucose cotransporter type 2 (SGLT2) inhibitors, such as dapagliflozin and empagliflozin, represent a promising therapeutic strategy in the treatment of heart failure in patients with diabetes mellitus, regardless of their cardiac ejection fraction. These drugs have consistently been shown to reduce the risk of worsening heart failure, adverse cardiovascular events, and the need for hospitalization, while improving patients' quality of life.

Despite the limitations identified in the current evidence, the results of this review strongly support the inclusion of SGLT2s in heart failure management strategies in patients with diabetes mellitus. Furthermore, they suggest that these drugs can have a positive clinical impact in patients with different profiles, making them a versatile option. However, more research is needed to delve deeper into the mechanisms of action and to explore their efficacy in patients with heart failure and preserved ejection fraction, as well as in other subgroups of clinical interest.

Ultimately, the incorporation of SGLT2 into current and future clinical practice may represent a significant advance in the treatment of heart failure and improve the quality of life of affected patients. Future research should focus on addressing outstanding questions and areas of uncertainty to better guide clinical decision making and improve outcomes for patients with heart failure and diabetes mellitus.

REFERENCES

1. Aguilera NR, Jara RG, Machuca-Contreras F. Diagnóstico de la implementación de la gestión del cuidado de enfermería para atención cerrada en Chile. Salud, Ciencia y Tecnología 2023;3:348-348. https://doi.org/10.56294/saludcyt2023348.

2. Amaya AJC, Rojas MG. The art of seduce through a distinctive brand and women’s lingerie. Community and Interculturality in Dialogue 2023;3:63-63. https://doi.org/10.56294/cid202363.

3. Bory E de JP, Naranjo OV, Herrero LB, Flores LGA, Fuentes MGB. Pertinence of the teaching use of virtual classroom by Basic Biomedical Science Department. Seminars in Medical Writing and Education 2023;2:31-31. https://doi.org/10.56294/mw202331.

4. Brito D, Bettencourt P, Carvalho D, Ferreira J, Fontes-Carvalho R, Franco F, et al. Sodium-glucose co-transporter 2 inhibitors in the failing heart: a growing potential. Cardiovasc Drugs Ther. 2020; 34(3):419-36.

5. Cánovas LPL, Cánovas LBL, Rodríguez YP, Hernández BG, Martín MMP, Montano AL. Evaluation of Burnout Syndrome and associated factors in primary care health personnel. Community and Interculturality in Dialogue 2023;3:73-73. https://doi.org/10.56294/cid202373.

6. Cantaro JCC, Tello JDLCH, Ruiz GEZ, Claudio BAM. Leadership styles and organizational climate among employees in Lima, Peru. Health Leadership and Quality of Life 2023;2:36-36. https://doi.org/10.56294/hl202336.

7. Castellanos S, Figueroa C. Cognitive accessibility in health care institutions. Pilot study and instrument proposal. Data and Metadata 2023;2:22-22. https://doi.org/10.56294/dm202322.

8. Cowie MR, Fisher M. SGLT2 inhibitors: mechanisms of cardiovascular benefit beyond glycemic control. Nat Rev Cardiol. 2020;17(12):761-72.

9. Cruz LMSDL, Fernández CA de. Factores asociados a la violencia contra los estudiantes de enfermería del internado rotativo. Salud, Ciencia y Tecnología 2023;3:464-464. https://doi.org/10.56294/saludcyt2023464.

10. Damman K, Valente MAE, Voors AA, O'Connor CM, Van Veldhuisen DJ, Hillege HL. Renal impairment, worsening renal function, and outcome in patients with heart failure: an updated meta-analysis. Eur Heart J. 2014;35(7):455-69.

11. Díaz-Chieng LY, Auza-Santiváñez JC, Castillo JIR. The future of health in the metaverse. Metaverse Basic and Applied Research 2022;1:1-1. https://doi.org/10.56294/mr20221.

12. Diseiye O, Ukubeyinje SE, Oladokun BD, Kakwagh VV. Emerging Technologies: Leveraging Digital Literacy for Self-Sufficiency Among Library Professionals. Metaverse Basic and Applied Research 2024;3:59-59. https://doi.org/10.56294/mr202459.

13. Duckworth W, Abraira C, Moritz T, Reda D, Emanuele N, Reaven PD, et al. Glucose control and vascular complications in veterans with type 2 diabetes. N Engl J Med. 2009;360(2):129-39.

14. Ettaloui N, Arezki S, Gadi T. An Overview of Blockchain-Based Electronic Health Records and Compliance with GDPR and HIPAA. Data and Metadata 2023;2:166-166. https://doi.org/10.56294/dm2023166.

15. González RE. Gobernanza de enfermería en redes integradas de servicios de salud y su impacto en procesos de atención en el ámbito de equipos del primer nivel de atención. Salud, Ciencia y Tecnología 2021;1:37-37. https://doi.org/10.56294/saludcyt202137.

16. Gonzalez-Argote D, Gonzalez-Argote J, Machuca-Contreras F. Blockchain in the health sector: a systematic literature review of success cases. Gamification and Augmented Reality 2023;1:6-6. https://doi.org/10.56294/gr20236.

17. Gonzalez-Argote J. A Bibliometric Analysis of the Studies in Modeling and Simulation: Insights from Scopus. Gamification and Augmented Reality 2023;1:5-5. https://doi.org/10.56294/gr20235.

18. Gu K, Cowie CC, Harris MI. Diabetes and decline in heart disease mortality in US adults. JAMA. 1999;281(14):1291-7.

19. Horta GAH, García ZG. Resultados del tratamiento de rehabilitación física en niños con retardo en el desarrollo psicomotor. Interdisciplinary Rehabilitation / Rehabilitacion Interdisciplinaria 2023;3:28-28. https://doi.org/10.56294/ri202328.

20. Horta GAH, Miranda GLH, García ZG. Calidad de vida de pacientes con enfermedad de Parkinson que reciben tratamiento rehabilitador. Interdisciplinary Rehabilitation / Rehabilitacion Interdisciplinaria 2023;3:27-27. https://doi.org/10.56294/ri202327.

21. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes, UKPDS 33. UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998;352:837-53.

22. Ismail-Beigi F, Craven T, Banerji MA, Basile J, Calles J, Cohen RM, et al. Effect of intensive treatment of hyperglycemia on microvascular complications of type 2 diabetes: an analysis of the ACCORD randomized trial. Lancet. 2010;376(9739):419-30.

23. Lascano IA, Acurio EV, López JH, Garcia DM, Jiménez EA, Sevilla VC. Asociación del nivel de estrés con el desarrollo del síndrome metabólico en el personal de salud. Salud, Ciencia y Tecnología 2023;3:386-386. https://doi.org/10.56294/saludcyt2023386.

24. Lepez CO. Invisible challenges in healthcare leadership. Health Leadership and Quality of Life 2023;2:35-35. https://doi.org/10.56294/hl202335.

25. Lichtensztejn M, Benavides M, Galdona C, Canova-Barrios CJ. Knowledge of students of the Faculty of Health Sciences about Music Therapy. Seminars in Medical Writing and Education 2023;2:35-35. https://doi.org/10.56294/mw202335.

26. Lobato KJT, Pita DLR, Ruiz GEZ, Claudio BAM. The impact of job performance and performance on workers in northern Lima. Health Leadership and Quality of Life 2023;2:30-30. https://doi.org/10.56294/hl202330.

27. Matos-Rodríguez A, Sargenton-Savon S, Mosqueda-Lobaina Y, Chibas-Muñoz EE. Características del Síndrome Demencial en la Atención Primaria de Salud. Interdisciplinary Rehabilitation / Rehabilitacion Interdisciplinaria 2023;3:45-45. https://doi.org/10.56294/ri202345.

28. Morgner MI, Djament L. Impact of Preventive and Mandatory Social Isolation in the control of type I diabetes in adults in the Buenos Aires Metropolitan Area. Community and Interculturality in Dialogue 2023;3:82-82. https://doi.org/10.56294/cid202382.

29. Oloriz MAG, Beltrán CR, Sánchez CMC. Trends in health telematics and telemedicine services. Data and Metadata 2022;1:16-16. https://doi.org/10.56294/dm202216.

30. Orsetti M, Bertolini Y, Villaalta AF, Creo F, Santillan P, Inzaurralde N. Food safety and the approach of the Human Milk Collection Center at the Hospital Zonal General de Agudos “Prof. Dr. Ramón Carrillo”. Community and Interculturality in Dialogue 2023;3:104-104. https://doi.org/10.56294/cid2023104.

31. Packer M. SGLT2 inhibitors produce cardiorenal benefits by promoting adaptive cellular reprogramming to induce a state of fasting mimicry: a paradigm shift in understanding their mechanism of action. Diabetes Care. 2020; 43(3): 508-11.

32. Patel A, MacMahon S, Chalmers J, Neal B, Billot L, Woodward M, et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med. 2008;358(24):2560-72.

33. Prieto YN, Sánchez GAR, García AP. The discipline of Medical Psychology in the ethical-humanistic education of medical students. Seminars in Medical Writing and Education 2023;2:42-42. https://doi.org/10.56294/mw202342.

34. Quintana-Honores M, Corvalán P, Gironda-Gurán J. Family integration and skin-to-skin contact with the newborn favors the recovery of the hospitalized patient: experiences of its implementation in an Obstetric Critical Care Unit. Health Leadership and Quality of Life 2023;2:33-33. https://doi.org/10.56294/hl202333.

35. Ramírez ME, Ron M, Mago G, Hernandez–Runque E, Martínez MDC, Escalona E. Proposal for an epidemiological surveillance program for the prevention of occupational accidents and diseases in workers exposed to carbon dioxide (CO2) at a Venezuelan brewing company. Data and Metadata 2023;2:55-55. https://doi.org/10.56294/dm202355.

36. Rodríguez-Martínez C, Alvarez-Solano J, Pérez-Galavís AD, Ron M. Distance education during the COVID-19 pandemic: experience at a public university. Seminars in Medical Writing and Education 2023;2:32-32. https://doi.org/10.56294/mw202332.

37. Romero-Carazas R. Prompt lawyer: a challenge in the face of the integration of artificial intelligence and law. Gamification and Augmented Reality 2023;1:7-7. https://doi.org/10.56294/gr20237.

38. Ron M, Pérez A, Hernández-Runque E. Nivel de riesgo para la salud y predicción del dolor musculo-esqueletico en trabajadores en condiciones de teletrabajo: Un enfoque matricial. Interdisciplinary Rehabilitation / Rehabilitacion Interdisciplinaria 2023;3:40-40. https://doi.org/10.56294/ri202340.

39. Sánchez CMC, León LAG, Yanes RCA, Oloriz MAG. Metaverse: the future of medicine in a virtual world. Metaverse Basic and Applied Research 2022;1:4-4. https://doi.org/10.56294/mr20224.

40. Sánchez-Ortega B, Pérez-Galavís A, Ron M. Condition, Working Environment and Health Effects on the Medical Personnel. Community and Interculturality in Dialogue 2023;3:105-105. https://doi.org/10.56294/cid2023105.

41. Santos CA, Ortigoza A, Barrios CJC. Nursing students' perceptions of Clinical Clerkship. Seminars in Medical Writing and Education 2023;2:30-30. https://doi.org/10.56294/mw202330.

42. Scheen A. Sodium-glucose cotransporter type 2 inhibitors for the treatment of type 2 diabetes mellitus. Nat Rev Endocrinol. 2020;16(10):556-577.

43. Tacuri ABG, Pérez GPL. Hospitalización prevenible en enfermedades crónico degenerativas: hipertensión arterial y diabetes. Salud, Ciencia y Tecnología 2023;3:487-487. https://doi.org/10.56294/saludcyt2023487.

44. Tamargo J. Sodium-glucose cotransporter 2 inhibitors in heart failure: potential mechanisms of action, adverse effects and future developments. Eur Cardiol. 2019; 14(1):23-32.

45. Torres A, Pérez-Galavís A, Ron M, Mendoza N. Factores Psicosociales Laborales y Estrés en el Personal Médico Asistencial. Interdisciplinary Rehabilitation / Rehabilitacion Interdisciplinaria 2023;3:42-42. https://doi.org/10.56294/ri202342.

46. Tumiri T, Duran L, Lin J, Ríos NB, Mosca A, Gómez T. La Imagen de enfermería y simulación. Metaverse Basic and Applied Research 2023;2:36-36. https://doi.org/10.56294/mr202336.

47. Velasco ASD, Ccama FLM, Claudio BAM, Ruiz GEZ. Transformational Leadership as a Driver of Business Success: A Case Study in Caquetá. Health Leadership and Quality of Life 2023;2:37-37. https://doi.org/10.56294/hl202337.

48. Villalobos C, Cavallera C, Espinoza M, Cid MF, Paredes I. Toward Efficiency and Accuracy: Implementation of a Semiautomated Data Capture and Processing Model for the Construction of a Hospital-based Tumor Registry in Chile. Data and Metadata 2023;2:124-124. https://doi.org/10.56294/dm2023124.

49. Zhang W. Blockchain-based solutions for clinical trial data management: a systematic review. Metaverse Basic and Applied Research 2022;1:17-17. https://doi.org/10.56294/mr202217.

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CONFLICT OF INTEREST

We declare that there is no conflict of interest.

AUTHORSHIP CONTRIBUTION

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