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ORIGINAL RESEARCH ARTICLE

Eligibility of outpatients with chronic heart failure for sodium–glucose co-transporter-2 inhibitors

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Abstract

Aims Sodium–glucose co-transporter-2 inhibitors (SGLT2i) have been shown to have a relevant role in the prevention of hospitalizations for heart failure and improvement in the life expectancy of patients with diabetes and outpatients with chronic heart failure (CHF) with reduced left ventricular ejection fraction, independently from the presence of type 2 diabetes mellitus (T2DM). The aim of our study was to evaluate in a real-world population the number of outpatients with CHF who meet the enrolment criteria of the main randomized controlled trials (RCT) published in the last 5 years and consequently identify the percentage of patients who could potential benefit from SGLT2i therapy.

Methods and results We retrospectively evaluated all consecutive outpatients referred for CHF. The diagnosis of T2DM was according to the latest European Society of Cardiology Guidelines. Clinical characteristics considered for the enrolment in the RCTs were recorded. We enrolled 515 patients, 384 (75%) of whom had a left ventricular ejection fraction (LVEF) $\leq$ 40%, 82 (16%) had pre-diabetes, and 187 (36%) had diabetes. Most of the patients with LVEF $\leq$ 40% met the criteria for the DAPA-HF trial (65%), and this percentage was even higher if the serum level of *N*-terminal pro-brain natriuretic peptide was not considered. A high percentage of patients with diabetes and LVEF $>$ 40% met the criteria for the DECLARE (39%), CANVAS (47%), and EMPA-REG (30%) trials. Patients meeting the enrolment criteria of RCTs evaluating SGLT2i were also characterized by a high risk of heart failure events during follow-up.

Conclusions In spite of a low number of patients actually treated with SGLT2i, we observed that a high prevalence of patients with CHF met the clinical characteristics of RCTs that have demonstrated a beneficial effect of SGLT2i.

Keywords Type 2 diabetes mellitus; Sodium–glucose co-transporter inhibitor; Therapy; Heart failure

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Introduction

The co-presence of chronic heart failure (CHF) and type 2 diabetes mellitus (T2DM) is associated with a worse prognosis.[1,2] In recent years, a class of antidiabetic drugs, namely type 2 sodium–glucose co-transporter inhibitors (SGLT2i), has been demonstrated to significantly modify the risk of heart failure (HF) events in patients with T2DM.[3–7] A recent systematic review and meta-analysis of randomized, placebo-controlled, cardiovascular (CV) outcome trials of SGLT2i in patients with T2DM showed a significant decrease in hospitalization related to HF (HF hospitalization) as well as a reduction in progression of chronic kidney disease (CKD).[7] On the basis of these data, the updated European Guidelines on Diabetes, Pre-Diabetes and Cardiovascular Diseases developed in collaboration with the European Association for the Study of Diabetes recommend the use of this SGLT2i as first-line therapy in patients with T2DM.[8]

The next step in recommending the use of SGLT2i should include patients affected by heart failure with a reduced

ejection fraction (HFrEF) regardless of the presence of T2DM. The DAPA-HF[9] and EMPEROR-reduced[10] randomized controlled trials (RCTs) recently demonstrated the beneficial effect of dapagliflozin and empagliflozin in patients affected by HFrEF both with and without diabetes.

The aim of this study is to evaluate in a real-world population the number of outpatients with CHF who meet the enrolment criteria of the main RCTs published during the last 5 years and thus identify the percentage of patients who could potentially benefit from SGLT2i therapy.

Methods

Patients

We retrospectively evaluated 515 consecutive patients referred to our CHF outpatients' clinic between 2014 and 2019. At the time of enrolment, they were clinically stable for at least 30 days (i.e. no significant changes in haemodynamic status and in medical therapy) and received conventional medical and electrical therapy. We excluded patients with acute decompensated HF, previous heart transplantation, or mechanical circulatory assist devices.

The study conforms to the principles outlined in the Declaration of Helsinki.[11] This is a secondary analysis of a prospective study; main results have already been published.[12] The retrospective analysis relative to the present study was approved by the ethics committee of Policlinic University Hospital of Bari, Italy. Informed consent was obtained from all participants in the study.

Eligibility criteria

We evaluated the eligibility of patients meeting the current indications of the European Medicines Agency/Italian National Health System and adhering to the main enrolment criteria of the following RCTs published in the past 5 years:

- EMPA-REG OUTCOME trial.[3] Age $\geq$ 18 years, diagnosis of T2DM, body mass index $\leq$ 45 kg/m^2, history of coronary artery disease, stroke, or peripheral artery disease. Exclusion criteria: uncontrolled hyperglycaemia with a glucose level $>$ 240 mg/dL ($>$13.3 mmol/L) after an overnight fast during placebo run-in and confirmed by a second measurement (not on the same day), impaired renal function defined as a glomerular filtration rate (GFR) $<$ 30 mL/min during screening or run-in, acute coronary syndrome, stroke, or transient ischaemic attack within 2 months of informed consent, medical history of cancer, and/or treatment for cancer within the last 5 years.
- CANVAS trial.[4] Patients with T2DM with Hb1Ac ranging between 53 and 91 mmol/mol, age $\geq$ 30 years with a history of a CV event or age $\geq$ 50 years with two or more of the following: systolic blood pressure $>$ 140 mmHg despite therapy, cigarette smoker, microalbuminuria or macroalbuminuria, or history of hyperlipidaemia with high-density lipoprotein $<$ 38.8 mg/dL, GFR $>$ 30 mL/min/1.73 m^2.
- DECLARE trial.[5] Patients with T2DM with Hb1Ac ranging between 48 and 108 mmol/mol, age $\geq$ 40 years with a history of a CV event or $\geq$55-year-old men and $\geq$60-year-old women plus at least one of the following: dyslipidaemia, hypertension, or current smoking. Exclusion criteria: diagnosis of type 1 diabetes mellitus, chronic cystitis and/or recurrent urinary tract infections, and pregnant or breast-feeding patients.
- CREDENCE trial.[6] Estimated GFR between $\geq$30 and $\leq$90 mL/min/1.73 m^2, diagnosed with T2DM, urine albumin to creatinine ratio $>$ 300 and $\leq$5000 mg/g. Exclusion criteria: history of diabetic ketoacidosis or type 1 diabetes mellitus, renal disease that required treatment with immunosuppressive therapy, current or a history of New York Heart Association (NYHA) class IV HF, blood potassium level $>$ 5.5 mEq/L.
- DAPA-HF trial.[9] Age $\geq$ 18 years, established documented diagnosis of symptomatic HFrEF, NYHA functional class II–IV, left ventricular ejection fraction (LVEF) $\leq$ 40%, increased *N*-terminal pro-brain natriuretic peptide (NT-proBNP) levels ($\geq$600 pg/mL or $\geq$400 pg/mL if sinus rhythm present and hospitalization for HF in the last 12 months; $\geq$900 pg/mL if atrial fibrillation present), and eGFR $\geq$ 30 mL/min/1.73 m^2. Exclusion criteria: intolerance of an SGTL2 inhibitor, type 1 diabetes mellitus, symptomatic hypotension, or systolic blood pressure $<$ 95 mmHg, current acute decompensated HF or hospitalization due to decompensated HF $<$ 4 weeks before enrolment, myocardial infarction, unstable angina, stroke or transient ischaemic attack within 12 weeks of enrolment, severe, unstable, or rapidly progressing renal disease.
- EMPEROR-reduced.[10] Age $\geq$ 18 years, established documented diagnosis of symptomatic HFrEF, NYHA functional class II–IV, LVEF $\leq$ 40%, increased NT-proBNP levels ($\geq$600 pg/mL if sinus rhythm present and LVEF $\leq$ 30% or hospitalization for HF in the last 12 months; $\geq$1200 pg/mL if atrial fibrillation present and LVEF $\leq$ 30% or hospitalization for HF in the last 12 months; $\geq$1000 pg/mL if sinus rhythm present and LVEF ranged between 31% and 35%; $\geq$2000 pg/mL if atrial fibrillation present and LVEF ranged between 31% and 35%; $\geq$2500 pg/mL if sinus rhythm present and LVEF $>$ 35%; $\geq$5000 pg/mL if atrial fibrillation present and LVEF $>$ 35%). Exclusion criteria: intolerance of an SGTL2 inhibitor, type 1 diabetes mellitus, symptomatic hypotension or systolic blood pressure $<$ 100 mmHg, current acute decompensated HF, myocardial infarction, unstable angina, stroke or transient ischaemic attack within 90 days of

enrolment, and severe renal disease (eGFR <20 mL/min/1.73 m^2 by the Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] equation).

Clinical and laboratory parameters

The baseline evaluation was considered as the first recorded medical visit at which the patient's medical history was taken. Physical examination, 12-lead electrocardiogram, one-dimensional and two-dimensional echocardiographic evaluations were performed, and peripheral blood samples were taken. At the medical visit, the presence of ischaemic cardiomyopathy, cerebrovascular disease or stroke, arterial hypertension, atrial fibrillation, diabetes mellitus, and dyslipidaemia were recorded as well as HF, NYHA class, and antidiabetic therapy.

Echocardiographic recordings were performed using a phased-array echo-Doppler system (Vivid 7, GE, Madison, WI, USA) to evaluate left ventricular end-diastolic and end-systolic volume by the Simpson method. LVEF was then calculated. Right ventricular systolic function was evaluated by assessing tricuspid annulus systolic excursion. Finally, mitral and tricuspid regurgitation (arbitrary units from 0 to 4) and estimated pulmonary systolic arterial pressure were evaluated.

Fasting plasma glucose (FPG, mg/dL), haemoglobin A1c (HbA1c, mmol/mol), NT-proBNP (pg/mL), sodium (mEq/L), potassium (mEq/L), creatinine serum concentrations (mg/dL), and haemoglobin (g/dL) levels were measured at the baseline evaluation. The GFR (mL/min) was calculated using the CKD-EPI formula.[13]

The diagnosis of diabetes was based on medical records. A new diagnosis of diabetes was made in the presence of HbA1c $\geq$ 48 mmol/mol and FPG $\geq$ 126 mg/dL.[8] The diagnosis of pre-diabetes was made in the presence of a FPG level ranging between 100 and 125 mg/dL in the presence of an HbA1c level ranging from 44 to 48 mmol/mol.[8] Normo-glycaemia was defined as FPG $<$ 100 mg/dL and HbA1c $<$ 44 mmol/mol. The diagnosis of T2DM was made according to the latest European Society of Cardiology Guidelines.[8]

Follow-up

The patients were followed-up with scheduled visits according to the protocol of our HF Unit: monthly for patients waiting for heart transplantation, every 2 or 3 months for patients with advanced HF, every 6 months for other patients, and as soon as possible for patients with worsening of symptoms and signs of HF.

During follow-up, death from all causes, CV death, and hospitalization due to acute decompensated HF during follow-up up to 24 months were recorded.

The management of patients with T2DM was followed by their referral diabetic centre. To evaluate how antidiabetic therapy was modified after the introduction of SGLT2i, we analysed how the baseline therapy changed until the end of follow-up in a subgroup of 62 patients with T2DM enrolled from 2014 to 2015.

Statistical analysis

For continuous variables, the results are presented as means ± standard deviation; categorical variables are expressed as percentages. All variables with normal distribution were compared by using Student's *t*-test; otherwise, non-parametric tests were used. The χ^2 test was used for dichotomic variables. For each group of patients meeting enrolling criteria of all considered trials, the 2 years rate of each CV event evaluated during follow-up was calculated and expressed as percent values.

Statistical tests were considered significant with a P value $<$ 0.05. Statistical analyses were performed using Statistica software, Version 6.1 (StatSoft Inc., Tulsa, OK, USA).

Results

Characteristics of patients and eligibility for sodium–glucose co-transporter inhibitors therapy

We enrolled 515 patients: 82 (16%) with pre-diabetes and 187 (36%) with diabetes. *Table 1* shows the demographic and clinical characteristics of the patients enrolled according to the presence of LVEF $\leq$ 40%. Patients with a lower LVEF were more frequently male, affected by ischaemic cardiomyopathy, with a worse NYHA class and greater serum levels of NT-proBNP. They also showed a greater left ventricular end-diastolic and mitral regurgitation. Finally, they were also more frequently taking mineral corticoid receptor antagonists and diuretics and had an implanted cardioverter defibrillator.

Table 2 shows the eligibility for SGLT2i therapy according to the major inclusion and exclusion criteria from the RCTs in the whole sample patients with LVEF $\leq$ 40% with and without diabetes and in with patients LVEF $>$ 40% and diabetes. Most of the patients suitable for SGLT2i therapy met the DAPA-HF criteria, and most of those without considering NT-proBNP serum levels. As shown in *Figure 1*, this was the main criterion leading to exclusion from DAPA-HF eligibility. The influence of the NT-proBNP criterion

Table 1 Characteristics of the patients at the time of enrolment

Characteristic	All patients	LVEF ≤ 40%	LVEF > 40%	*P*
Number of patients	515	384	131	
Age (years)	62 ± 13	62 ± 13	62 ± 14	0.853
Male, *n* (%)	410 (80)	325 (85)	85 (65)	<0.001
Pre-diabetes, *n* (%)	128 (25)	98 (26)	30 (23)	0.549
Diabetes, *n* (%)	186 (36)	143 (37)	43 (33)	0.364
Ischaemic cardiomyopathy, *n* (%)	185 (36)	155 (40)	30 (23)	<0.001
Dyslipidaemia, *n* (%)	269 (52)	207 (54)	62 (47)	0.193
Arterial hypertension, *n* (%)	325 (63)	248 (65)	81 (62)	0.571
Body mass index (kg/m^2)	29 ± 7	28 ± 5	29 ± 6	0.016
NYHA class, *n* (%)				<0.001
I	4 (1)	0 (0)	4 (3)	
II	285 (55)	198 (52)	87 (66)	
III	226 (44)	186 (48)	40 (31)	
Systolic arterial pressure (mmHg)	122 ± 17	121 ± 17	127 ± 17	<0.001
Atrial fibrillation, *n* (%)	76 (15)	55 (14)	21 (16)	0.634
LVEDV (mL)	159 ± 66	174 ± 67	113 ± 37	<0.001
LVEF (%)	34 ± 10	29 ± 7	47 ± 5	<0.001
TAPSE (mm)	18 ± 4	18 ± 4	20 ± 4	<0.001
MR (a.u.)	1.7 ± 0.9	1.8 ± 0.9	1.4 ± 0.7	<0.001
TR (a.u.)	1.7 ± 0.9	1.7 ± 0.9	1.6 ± 1.0	0.347
PAPs (mmHg)	37 ± 14	37 ± 14	36 ± 14	0.623
Creatinine (mg/dL)	1.22 ± 0.9	1.22 ± 0.8	1.26 ± 1.4	0.626
GFR (mL/min/1.73 m^2)	72 ± 26	70 ± 25	73 ± 27	0.359
GFR < 30 mL/min/1.73 m^2, *n* (%)	27 (5)	20 (5)	7 (5)	0.952
Fasting glucose (mg/dL)	116 ± 45	116 ± 47	114 ± 41	0.671
Hb1Ac (mmol/mol)	44 ± 14	45 ± 14	44 ± 14	0.646
NT-proBNP (pg/mL)	2577 ± 5272	2948 ± 5463	1529 ± 4525	0.007
HF therapy				
ACEi/ARBs/ARNi, *n* (%)	414 (80)	311 (81)	103 (79)	0.556
β-Blockers, *n* (%)	497 (97)	374 (97)	123 (94)	0.059
MRA, *n* (%)	403 (78)	284 (74)	77 (59)	0.001
Diuretics, *n* (%)	474 (92)	359 (93)	115 (88)	0.049
ICD, *n* (%)	418 (73)	341 (89)	77 (58)	<0.001
CRT, *n* (%)	139 (27)	104 (27)	35 (27)	0.935

ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, ARB with neprylisin inhibitor; CRT, cardiac resynchronization therapy. GFR, glomerular filtration rate by EPI formula; Hb1Ac, glycated haemoglobin; ICD, implanted cardioverter defibrillator; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; MRA, mineral corticoid receptor antagonist; NYHA class, New York Heart Association class; NT-proBNP, *N*-terminal brain natriuretic peptide; PAPs, estimated pulmonary arterial systolic pressure; TAPSE, tricuspid annulus systolic excursion; TR, tricuspid regurgitation.

Table 2 Patients meeting the main inclusion criteria of the RCTs trials

		LVEF ≤ 40%		LVEF > 40%
	All patients	Patients without diabetes	Patients with diabetes	Patients with diabetes
Number of patients	515	241	143	43
Indications according to the main criteria of the RCTs*				
DECLARE, *n* (%)	59 (11)	—	42 (30)	17 (39)
CANVAS, *n* (%)	72 (14)	—	52 (36)	20 (47)
CREDENCE, *n* (%)	8 (2)	—	6 (4)	2 (5)
EMPA-REG-OUTCOME, *n* (%)	77 (15)	—	64 (45)	13 (30)
DAPA-HF, *n* (%)	249 (48)	153 (63)	96 (67)	—
DAPA-HF without NT-proBNP criterion, *n* (%)	348 (68)	219 (91)	129 (90)	—
EMPEROR-reduced (%), *n*	202 (39)	116 (48)	86 (60)	—
EMPEROR-reduced without NT-proBNP criterion, *n* (%)	348 (68)	213 (88)	135 (94)	—

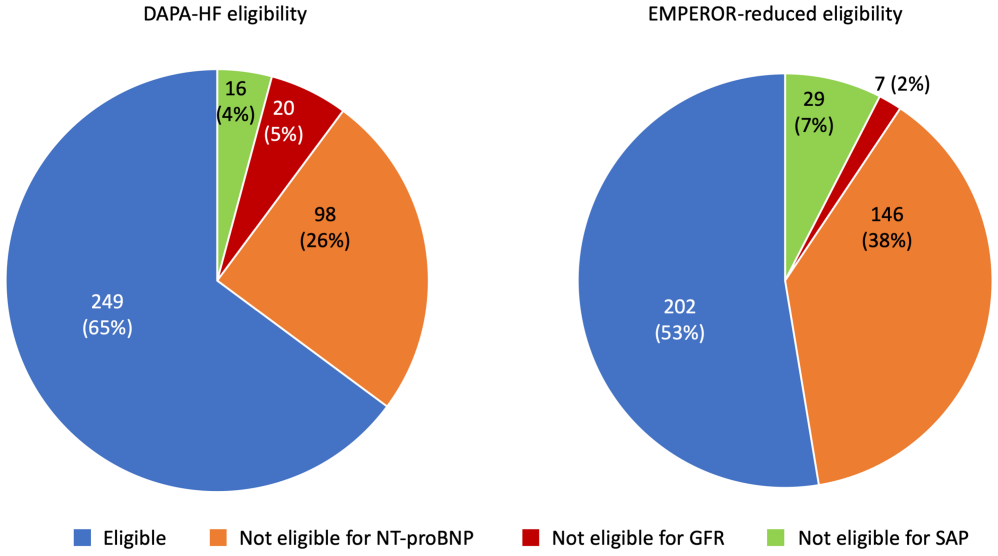
LVEF, left ventricular ejection fraction; NT-proBNP, *N*-terminal brain natriuretic peptide; RCT, randomized controlled trial.

was even more evident when EMPEROR-reduced was considered.

Patients in our series meeting the DAPA-HF and EMPEROR-reduced criteria were slightly different from those enrolled in the two trials (Supporting Information, *Table S1*); they were characterized by a worse NYHA class and greater NT-proBNP serum levels.

N-terminal pro-brain natriuretic peptide serum levels changed according to the eligibility for the different RCTs: for patients meeting criteria of DECLARE 1655 ± 2086,

Figure 1 Eligibility and rate of exclusion criteria for DAPA-HF (left) and EMPEROR-reduced (right) in our series of patients with left ventricular ejection fraction ≤ 40%. GFR, estimated glomerular filtration rate; NT-proBNP, amino-terminal pro-brain natriuretic peptide; SAP, systolic arterial pressure.



3166 ± 3936 for those of EMPAREG-outcome, 2502 ± 4295 for those of CANVAS, 2246 ± 2573 for those of CREDENCE, 3166 ± 3936 for those of DAPA-HF, and 3729 ± 4327 for those of EMPEROR-reduced.

Follow-up

During 24 months of follow-up, 57 (11%) patients died, 50 (10%) due to CV causes, and 134 (26%) experienced at least one hospitalization due to acute decompensated HF.

Figure 2 shows the rate of adverse events (death, CV death, and hospitalization due to worsening HF) in the subgroups of patients with diabetes (A) and those with LVEF ≤ 40% (B) and the correspondent RCTs. For patients with LVEF ≤ 40%, the rate of adverse events was greater among patients eligible for DAPA-HF and EMPEROR-reduced compared with those who were not eligible.

Diabetic therapy and changes over time

At the baseline evaluation, of the patients with diabetes, 60 (32%) were taking biguanides, 46 (24%) were on short acting insulin, 42 (23%) were on insulin glargine, 1 (1%) was on thiazolidinediones, 11 (6%) were on dipeptidyl-peptidase 4 (DPP4) inhibitors, 14 (8%) were on sulfonylurea, 4 (2%) were on SGLT2i, and 10 (5%) were on glucagon-like peptide-1 receptor agonists.

In a subgroup of 62 patients enrolled between 2014 and 2015, we compared the changes in antidiabetic therapy between baseline and last follow-up between 2018 and 2019. At baseline, none of these patients were on SGLT2i therapy. During follow-up, SGLT2i was prescribed in 10% of patients. Glucagon-like peptide-1 and dipeptidyl-peptidase 4 prescriptions also increased (from 3% to 13% and from 5% to 10%, respectively), whereas sulfonylurea decreased from 6% to 2%. Similar prescription rates were observed for metformin, glynides, and insulin. In none of the non-diabetic patients, SGLT2i was prescribed during the duration of our study.

Discussion

The main finding of this study is that a large number of patients affected by CHF meet the eligibility criteria for SGLT2i therapy according to the main RCTs published in the last 5 years. The number of eligible patients is even higher when considering patients with LVEF ≤ 40%. However, in our sample, only a small number of patients were prescribed SGLT2i, highlighting a gap between eligibility for SGLT2i therapy and actual prescription of this class of drugs.

In recent RCTs, the beneficial effect of SGLT2i in reducing HF-related events was demonstrated in patients with T2DM and known CV disease[3] and with both high CV risk and coronary artery disease.[4,5] SGLT2i significantly reduced the risk of HF hospitalization as well as progression of CKD, although a small percentage of patients had a history of CHF. Moreover, DAPA-HF and EMPEROR-reduced RCTs demonstrated the role of dapagliflozin and empagliflozin in reducing HF hospitalization in patients with HFrEF with and without T2DM. The significant reduction in the primary endpoint, over placebo, was consistent regardless of background therapy, thus suggesting

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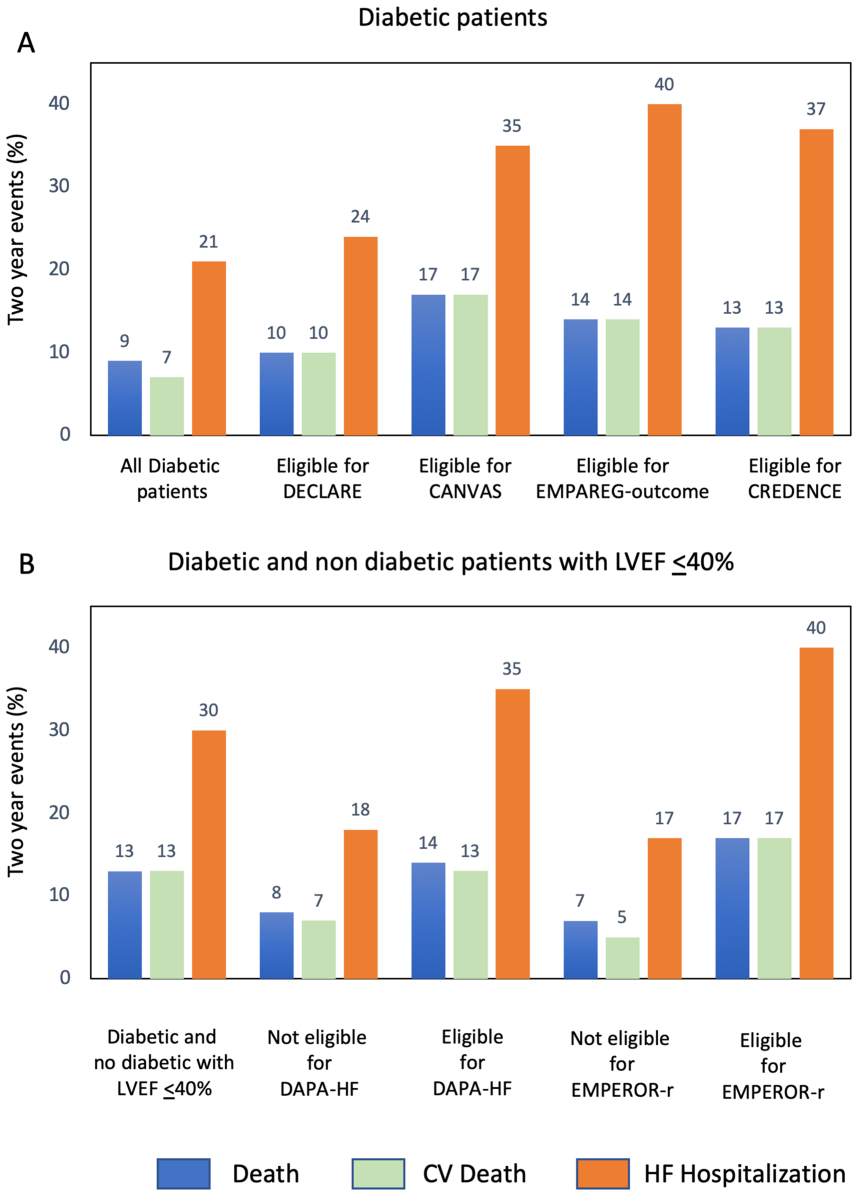
Figure 2 Rate of adverse events among patients with diabetes (A) and those with left ventricular ejection fraction ≤ 40% (B) and in the related subgroups of patients meeting the main criteria for SGLT2i RCTs. CV death, cardiovascular death; HF hospitalization, hospitalization due to worsening heart failure; LVEF, left ventricular ejection fraction; RCT, randomized controlled trial.



an incremental and complementary effect to conventional therapies for HFrEF.[9,10,14,15] In addition, in the DAPA-HF study, a significant reduction in CV death and death from all causes was observed. On the basis of these data, SGLT2i should be added to the current recommended therapy to further improve the prognosis of patients with HFrEF.

Here, we tried to identify the number of patients eligible for SGLT2i therapy in a real-world population. Our patients were in a stable clinical condition and under conventional therapy, mainly with LVEF ≤ 40%. A large number of our patients with LVEF ≤ 40% met the enrolment criteria for the DAPA-HF and EMPEROR-reduced studies. However, compared with the population enrolled in DAPA-HF and EMPEROR-reduced, our patients had a worse NYHA functional class and a greater level of NT-proBNP. These characteristics also explain the high rate of CV events we observed in our population, which further strengthens the potential usefulness of SGLT2i in these patients.

The number of patients suitable for SGLT2i therapy according to the DAPA-HF and EMPEROR-reduced criteria could be

even larger if NT-proBNP is not considered. NT-proBNP serum levels were used in DAPA-HF and EMPEROR-reduced to select a population with a greater probability of events, thus reducing the sample size. The NT-proBNP criterion was even stricter in EMPEROR-reduced than in DAPA-HF, thus explaining the lower number of our patients who were potentially eligible for this trial compared with DAPA-HF. This observation raises the question if NT-proBNP serum levels should be used to select patients suitable for SGLT2i therapy. However, the rate of adverse events in our patients not eligible for DAPA-HF and EMPEROR-reduced was still relevant (*Figure 2B*). Moreover, baseline NT-proBNP levels do not influence the beneficial effect of dapagliflozin.[16] Finally, the use of SGLT2i reduced the number of HF events throughout the CV continuum.

This observation also leads to another question, that is, should SGLT2i also be used in patients with LVEF $>$ 40%? In our sample, among patients with diabetes and LVEF $>$ 40%, some could be suitable for SGLT2i therapy.[3–6] The recent SOLOIST trial enrolled patients with characteristics different from those of our population, because with recent admission for acute decompensated HF, including both patients with reduced and preserved LVEF and comparing sotaglifozin with placebo.[17] The results of the trial first demonstrated the possible usefulness of SGLT2i also among patients with LVEF $>$ 40%. Ongoing trials will provide evidence in this clinical setting in the near future.[18] However, according to the current guidelines, SGLT2i should be prescribed in patients with T2DM regardless of LVEF.[8]

Although SGLT2i is the first class of hypoglycaemic drugs able to reduce hospitalizations for HF among patients with T2DM and reduce HF hospitalization in patients with HFrEF with and without diabetes, they are still underused in daily practice.[19] The first reason for this under prescription is related to the current European Medicines Agency/Italian National Health System indications, which are now being revisited, but which limited the use of SGLT2i according to GFR, mainly due to their hypoglycaemic efficacy in these conditions. The second reason is probably related to the lack of shared therapeutic pathways between HF specialists and diabetologists. In our study, the increase in the prescription of SGLT2i was mainly related to interaction with the referral diabetologists, who are the only ones who can prescribe this class of drugs according to NHS indications.

Limitations

This study is limited by its retrospective approach, and single centre setting, and our data should be considered in light of these factors.

Conclusions

We observed that a high number of outpatients with CHF were eligible for SGLT2i therapy according to their clinical characteristics. The results of the RCTs should encourage the prescription of SGLT2i, particularly among patients with HFrEF, among which dapagliflozin and empagliflozin are able to improve prognosis. An appropriate rate of prescription could be obtained by closer cooperation between HF specialists and diabetologists.

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Conflict of interest

None declared.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Clinical characteristics of patients meeting the enrolment criteria of DAPA-HF and patients treated with placebo or dapaglifozin in the DAPA-HF trial.

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