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Brief Report

Preventing Heart Failure Admission with Sodium-Glucose Cotransporter-2 Inhibitors versus Angiotensin Receptor-Neprilysin Inhibitor: A Target Trial Emulation Study

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Little is known on the real-world comparative effectiveness of sodium-glucose cotransporter-2 inhibitors (SGLT2i) versus angiotensin receptor-neprilysin inhibitor (ARNi) used for heart failure (HF) management. This study used South Korea's nationwide claims data from 2015 to 2020 to construct a population-based cohort of new users of SGLT2is or ARNi. Individuals were followed from the first prescription date of SGLT2is or ARNi until outcome occurrence, treatment switch or discontinuation, death, or end of the study period. Within the 1:1 propensity score-matched cohort, we estimated hazard ratios (HR) with 95% confidence intervals (CI) for the risk of HF admission with SGLT2is compared with ARNi using proportional subdistribution hazards model of Fine and Gray. We identified 496 propensity-score matched patient-pairs of SGLT2is and ARNi; with a mean age of 72.5 years and a male representation of 57.6%. Incidence rate of HF admission was 27.3 and 35.6 per 100 person-years in SGLT2is and ARNi group. When comparing the risk of HF admission associated with SGLT2is group with ARNi group, HR was 0.71 (95% CI 0.48-1.04). Effect modifications were observed by history of hospitalization for HF (p-for-interaction=0.002) and by recent use of renin-angiotensin-system inhibitors (p-for-interaction=0.005). With future studies using more recent data warranted to corroborate our study results, these preliminary findings support current guideline recommendations for HF management and further, suggest similar effectiveness between SGLT2is and ARNi in routine care settings.

Keywords: SGLT2i, ARNi, heart failure, target trial emulation, real-world evidence

Introduction

Sodium-glucose cotransporter-2 inhibitors (SGLT2is) are the recent addition to guideline-directed medical therapy in heart failure (HF) (McDonagh et al. 2021; Bayés-Genís et al. 2022; Heidenreich et al. 2022). SGLT2is are recommended for managing comorbid conditions and addressing the varying severity levels of HF alongside another relatively novel class of HF medication, angiotensin receptor-neprilysin inhibitor (ARNi), along with conventional HF medications such as renin-angiotensin-system inhibitors and beta-blockers (McDonagh et al. 2021; Bayés-Genís et al. 2022; Heidenreich et al. 2022). Although the absolute usage remains lower than other conventional medications, the utilization of SGLT2is and ARNis are increasing rapidly. Notably, SGLT2is primarily target renal

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reabsorption, reducing fluid accumulation and promoting beneficial cardiac structural changes, while ARNis aim to improve neurohormonal balance and alleviate symptoms. This divergence in mechanisms raises questions about potential differences in their effectiveness in preventing HF admission. However, despite these guideline updates and the distinct mechanisms of action, the direct comparative effectiveness of SGLT2is versus ARNi in routine clinical practice remains unexplored.

Previous data comparing their effectiveness are primarily based on indirect comparisons of randomized controlled trials through network meta-analysis, which have reported inconsistent results. Two studies showed non-differential risk of HF admission (hazard ratio [HR] 0.87, 95% CI 0.75-1.02) (Aimo et al. 2021) or composite of cardiovascular death or HF admission (HR 0.93, 95% CI 0.82-1.06) (Yan et al. 2021) associated with SGLT2is compared to ARNi, whereas one study found modest lower risk of composite of cardiovascular death or HF admission associated with ARNi compared to SGLT2is (HR 0.86, 95% CI 0.75-0.98) (Teo et al. 2022). Uncertainty remains on the comparative effectiveness of SGLT2is versus ARNi in preventing HF admission. Challenges also exist in generalizing and translating results from ideal trial settings to real-world settings (Dhruva and Redberg 2008). This study aimed to explore the potential effectiveness of SGLT2 inhibitors compared to ARNi in decreasing the risk of HF admission, providing insights into these new treatment options for managing HF in real-world settings. To focus our investigation while addressing potential confounding by indication, we have restricted our study population to patients with both type 2 diabetes and HF, as SGLT2is are indicated for both conditions, whereas ARNi is indicated exclusively for HF.

Materials and Methods

We emulated a hypothetical target trial using South Korea's nationwide health insurance claims data between 1 January 2015 and 31 December 2020 (Supplementary Table 1) (Kim et al. 2017; Matthews et al. 2022). Individuals newly prescribed a SGLT2i or an ARNi from 1 January 2020 to 31 December 2020 were eligible for entry into the study cohort, given the publication of DAPA-HF (dapagliflozin and prevention of adverse outcomes in HF) trial results in late 2019; we assumed that SGLT2is were likely to have been considered for HF management after this landmark trial.

Cohort entry was defined as the date of the first prescription for either a SGLT2i (dapagliflozin, empagliflozin, ipragliflozin, ertugliflozin) or an ARNi (sacubitril/valsartan) during this period. Of these eligible patients, we excluded patients aged <18 years or prescribed both study drugs of interest at cohort entry, and those meeting any of the following criteria before cohort entry: not diagnosed with HF or type 2 diabetes; not prescribed conventional HF medications (e.g., renin-angiotensin-system inhibitors, beta-blockers, mineralocorticoid receptor antagonists); diagnosed with type 1 diabetes; prescribed insulin as monotherapy; had contraindication to SGLT2is, which is end-stage renal disease or received dialysis; or received cardiac surgery (Supplementary Fig. 1).

The outcome of interest was time to first HF admission, defined by hospital admission with primary or secondary diagnosis of HF, which has shown positive predictive value of 82.1%. Patient were followed from the date of cohort entry until the earliest of outcome occurrence, switch to a comparator drug, treatment discontinuation (no successive prescription within 30 days from the end of the day supply), death, or end of the study (31 December 2020).

To address the potential confounding between groups and obtain comparability, we conducted 1:1 greedy nearest neighborhood matching without replacement within caliper width of 0.05 in propensity scores. The propensity score was generated by including all baseline characteristics in the multivariable logistic regression model: age at cohort entry date, sex, history of hospitalization of HF, comorbidities, use of medications, baseline diabetes treatment (drug classes and the number of classes), baseline HF treatment (drug classes and the number of classes), and healthcare utilization (Table 1). Baseline comorbidities, use of medications, treatment for diabetes and HF, and healthcare utilization were assessed within a year before cohort entry. We also assessed recent diabetes and HF treatment within a month before and at the date of cohort entry and included in the propensity score model to minimize confounding by indication.

Within the propensity score matched cohort, we estimated the incidence rate of HF admission per 100 person-years, and HRs with 95% CIs using proportional subdistribution hazards model of Fine and Gray that treated death as a competing event (Fine and Gray 1999). Schoenfeld residual test was used to assess the proportional hazards assumptions before the survival analysis. As a sensitivity analysis, we adopted an intention-to-treat approach that did not censor follow-up at treatment interruption (switch or discontinuation). We performed subgroup analysis to investigate potential effect modification by sex, history of hospitalization for HF, chronic kidney disease, recent HF treatments. Interactions were tested using Wald test for heterogeneity. Propensity scores were re-estimated within each subgroup and the matching

was reapplied for each comparison.

All analyses were conducted using SAS Enterprise Guide version 7.1 (SAS Institute Inc., USA). This study was approved by the institutional review board of Sungkyunkwan University, with a waiver of informed consent (SKKU 2022-04-015).

Table 1. Baseline characteristics of patients initiating a SGLT2 inhibitor or an ARN inhibitor in 2020

Characteristic	Before PS* matching			After PS matching		
	SGLT2i	ARNi	SMD	SGLT2i	ARNi	SMD
Total	7,562	793		496	496	
Age, years						
Mean (SD)	67.0 (12.5)	72.0 (11.1)	–0.426	73.1 (11.3)	72.0 (11.3)	0.098
Sex, n (%)						
Male	4,129 (54.6)	483 (60.9)	–0.128	283 (57.1)	288 (58.1)	–0.020
Female	3,433 (45.4)	310 (39.1)	0.128	213 (42.9)	208 (41.9)	0.020
Comorbidities†, n (%)						
Hospitalization for heart failure	551 (7.3)	268 (33.8)	–0.695	150 (30.2)	138 (27.8)	0.053
Hypertension	4,954 (65.5)	420 (53.0)	0.257	273 (55.0)	277 (55.8)	–0.016
Dyslipidemia	2,949 (39.0)	327 (41.2)	–0.046	219 (44.2)	199 (40.1)	0.082
Atrial fibrillation or flutter	1,055 (14.0)	156 (19.7)	–0.153	112 (22.6)	102 (20.6)	0.049
Myocardial infarction	412 (5.4)	98 (12.4)	–0.244	49 (9.9)	52 (10.5)	–0.020
Coronary artery disease	1,813 (24.0)	224 (28.2)	–0.097	126 (25.4)	134 (27.0)	–0.037
Coronary revascularization	241 (3.2)	58 (7.3)	–0.186	38 (7.7)	37 (7.5)	0.008
Aortic valve surgery	7 (0.1)	3 (0.4)	–0.059	2 (0.4)	3 (0.6)	–0.028
Pacemaker or ICD	19 (0.3)	9 (1.1)	–0.107	3 (0.6)	2 (0.4)	0.028
Stroke	591 (7.8)	86 (10.8)	–0.104	51 (10.3)	52 (10.5)	–0.007
Transient ischemic attack	101 (1.3)	6 (0.8)	0.057	6 (1.2)	4 (0.8)	0.040
Peripheral arterial disease	38 (0.5)	8 (1.0)	–0.058	10 (2.0)	7 (1.4)	0.047
Cancer	491 (6.5)	79 (10.0)	–0.127	47 (9.5)	48 (9.7)	–0.007
Chronic kidney disease	396 (5.2)	136 (17.2)	–0.385	72 (14.5)	70 (14.1)	0.012
Chronic pulmonary disease	1,334 (17.6)	197 (24.8)	–0.177	128 (25.8)	125 (25.2)	0.014
Chronic liver disease	1,070 (14.1)	103 (13.0)	0.034	66 (13.3)	68 (13.7)	–0.012
Comedications†, n (%)						
Statin	5,988 (79.2)	655 (82.6)	–0.087	393 (79.2)	401 (80.8)	–0.040
Calcium-channel blocker	4,481 (59.3)	337 (42.5)	0.340	246 (49.6)	239 (48.2)	0.028
Nonsteroidal anti-inflammatory drug	5,049 (66.8)	482 (60.8)	0.125	319 (64.3)	311 (62.7)	0.034
Systemic corticosteroid	4,169 (55.1)	414 (52.2)	0.059	272 (54.8)	269 (54.2)	0.012
Antidepressants	1,540 (20.4)	154 (19.4)	0.024	104 (21.0)	99 (20.0)	0.025
Antipsychotics	1,821 (24.1)	214 (27.0)	–0.067	142 (28.6)	143 (28.8)	–0.004
Baseline diabetes treatment†, n (%)						
Metformin	6,045 (79.9)	556 (70.1)	0.228	374 (75.4)	368 (74.2)	0.028
Sulfonylurea	3,541 (46.8)	400 (50.4)	–0.072	252 (50.8)	245 (49.4)	0.028
Meglitinide	34 (0.4)	4 (0.5)	–0.008	2 (0.4)	3 (0.6)	–0.028
α-glucosidase inhibitor	147 (1.9)	21 (2.6)	–0.047	9 (1.8)	9 (1.8)	0.000
Thiazolidinedione	952 (12.6)	65 (8.2)	0.144	51 (10.3)	52 (10.5)	–0.007
Dipeptidyl peptidase-4 inhibitor	5,036 (66.6)	680 (85.8)	–0.461	417 (84.1)	411 (82.9)	0.033
GLP-1 receptor agonist	95 (1.3)	14 (1.8)	–0.042	8 (1.6)	8 (1.6)	0.000
Insulin	1,377 (18.2)	305 (38.5)	–0.461	188 (37.9)	183 (36.9)	0.021
No. of diabetes medications						
Without medications	819 (10.8)	33 (4.2)	0.255	20 (4.0)	26 (5.2)	–0.058
1 class	1,107 (14.6)	85 (10.7)	0.118	47 (9.5)	50 (10.1)	–0.020
2 class	2,018 (26.7)	237 (29.9)	–0.071	148 (29.8)	144 (29.0)	0.018
3+ class	3,618 (47.8)	438 (55.2)	–0.148	281 (56.7)	276 (55.6)	0.020

Table 1. Continued

Characteristic	Before PS* matching			After PS matching		
	SGLT2i	ARNi	SMD	SGLT2i	ARNi	SMD
Baseline heart failure treatment†, n (%)						
RAS inhibitor without neprilysin inhibitor	6,232 (82.4)	748 (94.3)	–0.378	447 (90.1)	454 (91.5)	–0.049
Beta-blocker	4,706 (62.2)	682 (86.0)	–0.564	386 (77.8)	412 (83.1)	–0.132
Mineralocorticoid antagonist	1,492 (19.7)	498 (62.8)	–0.973	290 (58.5)	270 (54.4)	0.081
Diuretic	4,199 (55.5)	700 (88.3)	–0.782	438 (88.3)	424 (85.5)	0.084
Digitalis	721 (9.5)	169 (21.3)	–0.331	113 (22.8)	100 (20.2)	0.064
No. of heart failure medications						
Without medications	175 (2.3)	5 (0.6)	0.140	9 (1.8)	5 (1.0)	0.068
1 class	1,730 (22.9)	22 (2.8)	0.630	14 (2.8)	18 (3.6)	–0.046
2 class	2,604 (34.4)	91 (11.5)	0.568	70 (14.1)	73 (14.7)	–0.017
3+ class	3,053 (40.4)	675 (85.1)	–1.044	403 (81.3)	400 (80.6)	0.015
Recent diabetes treatment‡, n (%)						
Metformin	6,466 (85.5)	363 (45.8)	0.921	277 (55.8)	273 (55.0)	0.016
Sulfonylurea	3,156 (41.7)	285 (35.9)	0.119	187 (37.7)	183 (36.9)	0.017
Meglitinide	10 (0.1)	2 (0.3)	–0.027	1 (0.2)	1 (0.2)	0.000
α-glucosidase inhibitor	55 (0.7)	7 (0.9)	–0.017	4 (0.8)	5 (1.0)	–0.021
Thiazolidinedione	391 (5.2)	23 (2.9)	0.116	18 (3.6)	20 (4.0)	–0.021
Dipeptidyl peptidase-4 inhibitor	2,312 (30.6)	547 (69.0)	–0.832	332 (66.9)	330 (66.5)	0.009
GLP-1 receptor agonist	40 (0.5)	10 (1.3)	–0.078	6 (1.2)	7 (1.4)	–0.018
Insulin	1,111 (14.7)	186 (23.5)	–0.224	132 (26.6)	128 (25.8)	0.018
No. of diabetes medications						
Without medications	570 (7.5)	164 (20.7)	–0.384	89 (17.9)	93 (18.8)	–0.021
1 class	2,675 (35.4)	136 (17.2)	0.423	78 (15.7)	78 (15.7)	0.000
2 class	2,553 (33.8)	233 (29.4)	0.094	141 (28.4)	142 (28.6)	–0.004
3+ class	1,764 (23.3)	260 (32.8)	–0.212	188 (37.9)	183 (36.9)	0.021
Recent heart failure treatment‡, n (%)						
RAS inhibitor without neprilysin inhibitor	6,253 (82.7)	364 (45.9)	0.832	310 (62.5)	305 (61.5)	0.021
Beta-blocker	4,552 (60.2)	703 (88.7)	–0.690	410 (82.7)	423 (85.3)	–0.071
Mineralocorticoid antagonist	1,490 (19.7)	483 (60.9)	–0.926	298 (60.1)	288 (58.1)	0.041
Diuretic	3,656 (48.3)	686 (86.5)	–0.891	428 (86.3)	420 (84.7)	0.046
Digitalis	649 (8.6)	125 (15.8)	–0.221	99 (20.0)	81 (16.3)	0.094
No. of heart failure medications						
1 class	2,266 (30.0)	49 (6.2)	0.650	35 (7.1)	33 (6.7)	0.016
2 class	2,675 (35.4)	206 (26.0)	0.205	104 (21.0)	117 (23.6)	–0.063
3+ class	2,621 (34.7)	538 (67.8)	–0.704	357 (72.0)	346 (69.8)	0.049
Healthcare use†, n (%)						
Hospitalizations						
0	4,611 (61.0)	263 (33.2)	0.580	155 (31.3)	174 (35.1)	–0.081
1-2	2,397 (31.7)	401 (50.6)	–0.391	247 (49.8)	238 (48.0)	0.036
3+	554 (7.3)	129 (16.3)	–0.280	94 (19.0)	84 (16.9)	0.053
Outpatient visits						
0-2	73 (1.0)	4 (0.5)	0.054	3 (0.6)	4 (0.8)	–0.024
3-5	202 (2.7)	16 (2.0)	0.043	10 (2.0)	8 (1.6)	0.030
6+	7,287 (96.4)	773 (97.5)	–0.065	483 (97.4)	484 (97.6)	–0.013

*Propensity score was estimated using a multivariable logistic regression model, which included all potential confounders shown in the Table 1 as independent variables. †Assessed during the 365-day period before cohort entry. ‡Assessed during the 30-day period before and at cohort entry. ARNi, angiotensin receptor/neprilysin inhibitor; ICD, intra-cardiac defibrillation; PS, propensity score; RAS, renin–angiotensin system; SD, standard deviation; SMD, standardized mean difference; SGLT2i, sodium-glucose cotransporter 2 inhibitor.

Results

We identified 8,355 eligible new users of SGLT2is (7,562, 90.5%) and ARNi (793, 9.5%) in our study cohort (Supplementary Fig. 1). During the follow-up period, there were 17 deaths in the SGLT2is group and 3 in the ARNi group. After propensity score matching, 496 matched pairs were included in the main analysis, with a mean age of 72.5 years and a male representation of 57.6%. Among these, there were 6 deaths in the SGLT2is group and 1 in the ARNi group during the follow-up period. All baseline covariates, except for baseline use of beta-blockers, achieved balance between groups after matching, with absolute standardized mean differences <0.1 (Table 1).

In the propensity score matched cohort, incidence rate of HF admission was 27.3 and 35.6 per 100 person-years in SGLT2is and ARNi group. When comparing the risk of HF admission associated with SGLT2is group with ARNi group, HR was 0.71 (95% CI 0.48-1.04) In the intention-to-treat analysis, HR was 0.71 (95% CI 0.49-1.02); the point estimate was nearly identical with main analysis, indicating that the effect of treatment initiation was similar to the effect of adhering to the treatment in this study.

We observed effect modification by history of hospitalization for HF (p-for-interaction = 0.002) and recent use of renin-angiotensin-system inhibitors (p-for-interaction = 0.005). Among patients with a history of hospitalization for HF, the propensity score matched HR for the risk of HF admission with SGLT2is compared to ARNi was 1.37 (95% CI 0.67-2.77), while among those without such history, it

	SGLT2i		ARNi		PS-matched HR (95% CI)	p
	Events / Patients	IR per 100 PY	Events / Patients	IR per 100 PY		
Primary analysis						
Hospitalization for HF	43 / 496	27.3	64 / 496	35.6	0.71 (0.48-1.04)	0.078
Subgroup analysis						
Age, years						
≥65	36 / 379	33.5	51 / 379	37.5	0.79 (0.52-1.21)	0.272
<65	1 / 84	3.4	8 / 84	25.0	0.13 (0.02-1.04)	0.054
Sex						
Male	20 / 270	24.0	30 / 270	29.8	0.73 (0.41-1.28)	0.266
Female	20 / 197	31.9	30 / 197	45.3	0.66 (0.38-1.17)	0.154
History of hospitalization for HF*‡						
Yes	17 / 116	46.0	13 / 116	29.1	1.37 (0.67-2.77)	0.386
No	30 / 525	18.7	56 / 525	28.8	0.58 (0.37-0.91)	0.016
History of chronic kidney disease*						
Yes	7 / 39	60.9	6 / 39	56.8	1.27 (0.44-3.71)	0.661
No	35 / 422	27.2	45 / 422	28.1	0.85 (0.54-1.32)	0.458
Current use of renin-angiotensin-system inhibitors without neprilysin inhibitors†‡						
Yes	23 / 294	23.7	42 / 294	42.4	0.55 (0.33-0.92)	0.023
No	12 / 156	29.0	17 / 156	29.6	0.77 (0.37-1.63)	0.501
Current use of beta-blockers†						
Yes	32 / 399	26.2	42 / 399	28.9	0.82 (0.52-1.30)	0.401
No	4 / 66	19.0	10 / 66	47.6	0.41 (0.13-1.30)	0.131
Current use of mineralocorticoid receptor antagonists†						
Yes	32 / 295	36.0	40 / 295	37.7	0.87 (0.54-1.39)	0.555
No	11 / 168	23.1	16 / 168	26.9	0.78 (0.37-1.65)	0.509
ITT analysis	49 / 496	23.6	70 / 496	32.8	0.71 (0.49-1.02)	0.061

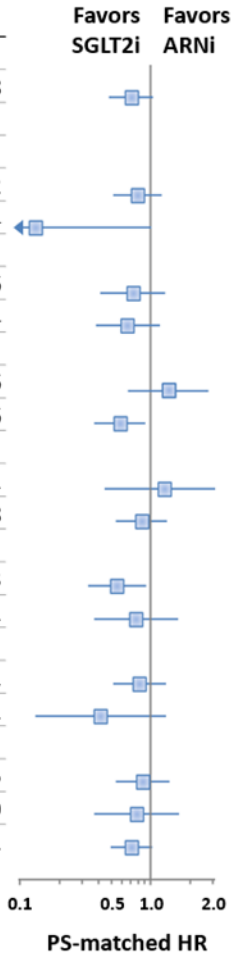

Fig 1. Risk of HF admission associated with SGLT2 inhibitor versus ARN inhibitor, using propensity score matching among subgroups population. *Assessed during 365 days before cohort entry. †Assessed during 30 days before or at cohort entry. ‡Significant interactions for history of hospitalization for HF (p = 0.002), and recent use of renin–angiotensin-system inhibitors without neprilysin inhibitors (p = 0.005). ARNi, angiotensin receptor-neprilysin inhibitor; CI, confidence interval; HF, heart failure; HR, hazard ratio; IR, incidence rate; PS, propensity score; PY, person years; SGLT2i, sodium-glucose cotransporter 2 inhibitor.

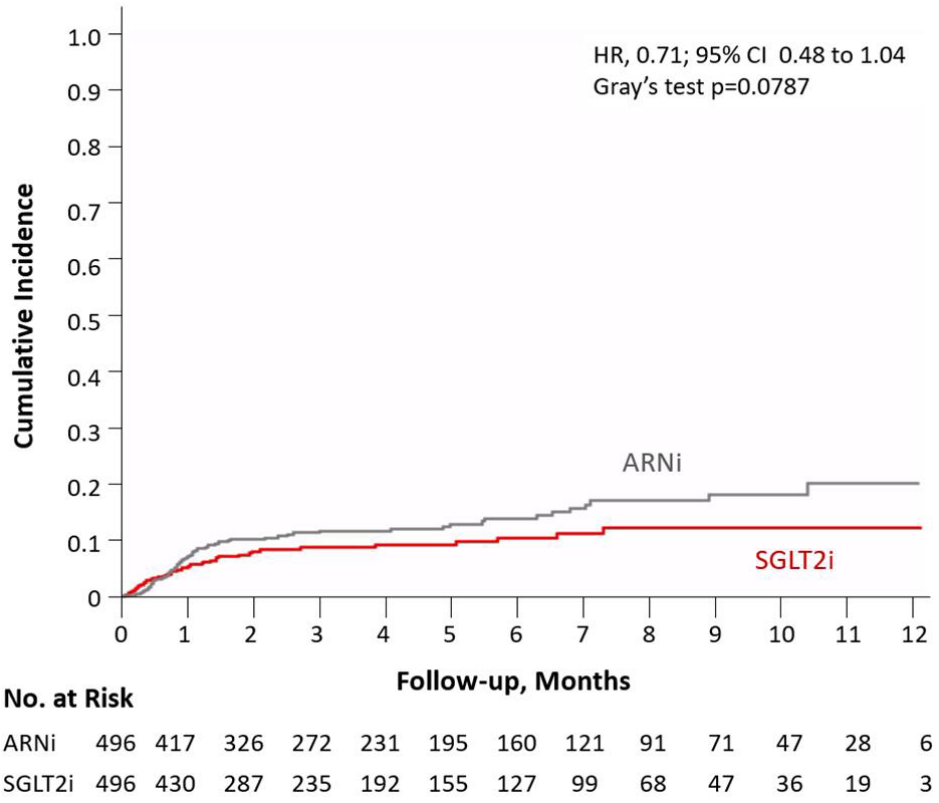

Fig 2. Cumulative incidence curve comparing risk of heart failure admission with SGLT2i versus ARNi. Propensity score was re-estimated and re-matched within each stratified subgroup. Assessed during 365 days before cohort entry. Assessed during 30 days before or at cohort entry. Significant interactions for history of hospitalization for HF (p = 0.002), and recent use of renin–angiotensin system inhibitors without neprilysin inhibitors (p = 0.005). ARNi, angiotensin receptor-neprilysin inhibitor; CI, confidence interval; HF, heart failure; HR, hazard ratio; SGLT2i, sodium-glucose cotransporter 2 inhibitor.

was 0.58 (95% CI 0.39-0.91). Regarding recent use of renin-angiotensin-system inhibitors, the propensity score matched HR for the risk of HF admission with SGLT2is compared to ARNi was 0.55 (95% CI 0.33-0.92) among users and 0.77 (95% CI 0.37-1.63) among non-users (Fig. 1 and 2).

Discussion

This is the nationwide population-based active comparator new-user cohort study that applied a target trial emulation framework to investigate the association between the risk of HF admission and the treatment with SGLT2is compared to ARNi. We have shown that there is no statistically significant difference in the risk of HF admission between SGLT2is- and ARNi-treated patients who have both type 2 diabetes and HF. Our findings from subgroup analysis suggests that the use of SGLT2is is associated with a reduced risk of HF admissions compared with ARNi, particularly in patients with a history of hospitalization for HF. Operating through mechanisms that involve the reduction of fluid accumulation and the promotion of favorable structural changes in the heart, SGLT2is may exhibit enhanced efficacy in advanced HF. Further research and clinical consideration are warranted to validate our findings.

This study has several limitations that should be considered when interpreting the findings. First, we acknowledge the substantial reduction in sample size resulting from our propensity score matching. This decision was driven by several considerations, including the relatively small comparator group of ARNi users within the larger cohort and significant differences in patient characteristics between treatment groups before matching. We applied matching to address these issues by creating a balanced cohort, enabling a more robust assessment of treatment effects while mitigating potential confounding. Second, it's important to note that our study is based on data available up to December 31, 2020. This timeframe limits our ability to extrapolate findings beyond the guideline updates made around late 2021 or early 2022. Additionally, our findings are specific to patients with HF with type 2 diabetes and may not fully reflect the land-

scape of SGLT2i and ARNi use. Third, our study could not differentiate between specific types of HF as information on ejection fraction was unavailable for assessment in the data. Fourth, the potential for differences in censoring patterns between the treatment groups should be acknowledged. Last, despite our efforts in propensity score matching, the presence of more serious health conditions among ARNi group before matching indicates that imbalances may not have been fully addressed, raising the possibility of residual unmeasured confounding.

These preliminary real-world findings align with current guidelines for HF management (McDonagh et al. 2021; Bayés-Genís et al. 2022; Heidenreich et al. 2022), and previous network meta-analyses of trials (Aimo et al. 2021; Yan et al. 2021). However, a meta-analysis of 25 RCTs, including 47,275 individuals, reported a comparable risk of hospitalization for HF between SGLT2is and ARNi. Although these differences in point estimates are not statistically significant, they could be due to unmeasured confounding factors inherent in observational studies, which lack randomization (Teo et al. 2022). Future studies should utilize more recent data and improve control over residual confounders to validate our findings.

These results indicate that SGLT2is may provide comparable benefits to ARNi in the context of routine clinical care. This can potentially inform healthcare in clinical decision-making regarding HF management.

Supplementary Materials

Supplementary materials can be found via https://doi.org/10.58502/DTT.24.0001.

Conflict of Interest

JYS received grants from the Ministry of Food and Drug Safety, the Ministry of Health and Welfare, the National Research Foundation of Korea, and pharmaceutical companies, including Pfizer, Celltrion, and SK Bioscience outside the submitted work. HEJ is employed by the Lunit Inc.

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