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ORIGINAL ARTICLE
Heart Failure

# Efficacy and Safety of Sodium-Glucose Cotransporter 2 Inhibitors for Patients With Heart Failure and Low Body Mass Index

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***Background:*** Previous reports have shown that sodium-glucose cotransporter 2 inhibitors (SGLT2i) benefit patients with heart failure (HF), regardless of left ventricular ejection fraction. However, evidence is limited for patients who are underweight, particularly with a body mass index (BMI) <20 kg/m$^2$.

***Methods and Results:*** Between February 2022 and July 2023, 533 patients were hospitalized at the Japanese Red Cross Wakayama Medical Center for acute HF. Excluding those who died during hospitalization, we categorized 488 patients according to their BMI at discharge: <20 kg/m$^2$ (n=201), and ≥20 kg/m$^2$ (n=287). Among the BMI <20 kg/m$^2$ group, SGLT2i was prescribed to 53 patients. The cumulative incidence rates of all-cause mortality at 1 year were significantly different between BMI <20 kg/m$^2$ patients with and without SGLT2i (11.8% vs. 36.1%; log-rank P=0.004). In the multivariate Cox proportional hazard models, SGLT2i reduced the risk of all-cause mortality independent of age, frailty, walking speed, decreased albumin level, elevated C-reactive protein level, and prescriptions of renin-angiotensin-aldosterone system inhibitors and mineralocorticoid receptor antagonists. However, among patients who received SGLT2i, the SGLT2i prescription continuation rate at 1 year was not significantly different between the BMI <20 kg/m$^2$ and BMI ≥20 kg/m$^2$ groups (85.4% vs. 84.6%; log-rank P=0.869).

***Conclusions:*** SGLT2i are feasibly effective and well-tolerated drugs, even for patients with low BMI.

**Key Words:** Body mass index; Heart failure; Sodium-glucose cotransporter 2 inhibitors

Heart failure (HF) is increasingly prevalent with an increase in the aging population, and it has a major clinical and economic impact on individuals worldwide.[1] Recently, medications based on the 'quadruple therapy' paradigm have shown significant efficacy in HF with reduced ejection fraction (HFrEF).[2] In particular, several studies have shown the effectiveness of sodium-glucose cotransporter 2 inhibitors (SGLT2i) for treating not only HFrEF but also HF with preserved EF (HFpEF).[3–6] Based on these results, SGLT2i are recommended for patients with HF, regardless of EF, in the European Society of Cardiology guidelines.[7] Although the efficacy of SGLT2i is well supported, concerns regarding the increased risk of body weight loss, urinary tract infection, and diabetic ketoacidosis, among others, have not yet been resolved, particularly in older frail patients.[8] In the Japanese registry, the median age of patients hospitalized due to acute decompensated HF (ADHF) was 80 years, and the mean body mass index (BMI) was 22.8 kg/m$^2$.[9] Patients with HF in Japan were older and had a lower BMI than those in previous randomized trials.[3–6] Such elderly patients with a low BMI are at high risk of frailty. Several subanalyses have reported that the benefits of SGLT2i are consistently present across all BMI categories in patients with HF.[10–12] However, data on patients with a low BMI (particularly those with a BMI <20 kg/m$^2$) are limited.

In this study, we prospectively observed patients hospitalized with ADHF. We compared patient characteristics and evaluated the prognosis between patients with a BMI <20 kg/m$^2$ with and without an SGLT2i prescription. Furthermore, we compared the 1-year prescription continuation rate of SGLT2i between patients with a BMI <20 kg/m$^2$ and those with a BMI ≥20 kg/m$^2$. To the best of our knowledge, this is the first study to focus on the usefulness of SGLT2i in patients with a low BMI.

## Methods

### Study Population

This single-center prospective observational study enrolled consecutive patients admitted to the Japanese Red Cross Wakayama Medical Center due to ADHF for the first time

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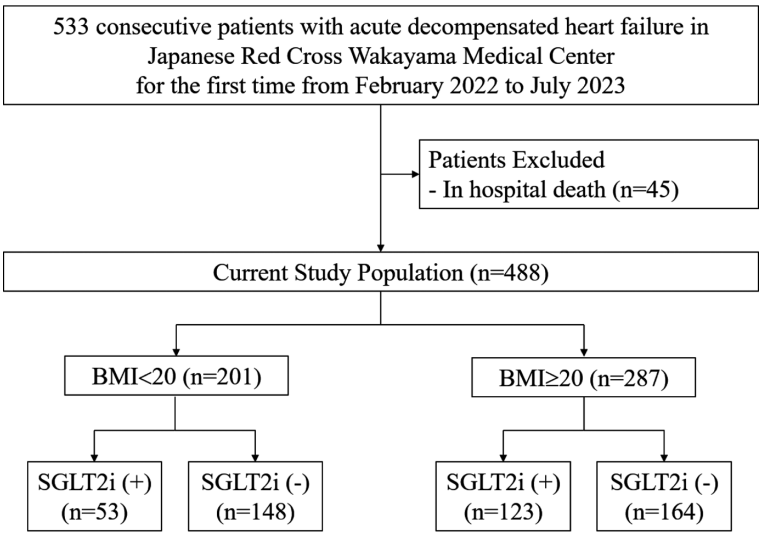



**Figure 1.** Study flowchart. BMI, body mass index; SGLT2i, sodium-glucose co-transporter 2 inhibitors.

between February 2022 and July 2023. All patients were aged ≥18 years. Patients who died during admission due to any cause were excluded from the study. ADHF is defined as the sudden or gradual onset of the signs or symptoms of HF requiring hospitalization. The BMI was calculated by dividing the total body weight (kilograms) by height squared (meters). The definition of diabetes was based on the guidelines of the Japan Diabetes Society.

### Ethics

The study was conducted according to the principles outlined in the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of Japanese Red Cross Wakayama Medical Center. Informed consent was obtained via an opt-out approach on our hospital's website, because of the use of clinical information obtained during routine clinical practice. This study was registered with the University Hospital Medical Information Network (UMIN identifier UMIN000053982).

### Outcomes

The BMI and Controlling Nutritional Status (CONUT) scores of patients who visited our hospital 2 months after discharge were measured, and a 1-year follow-up survey was conducted to investigate all-cause mortality, cardiovascular death, HF rehospitalization and continued use of SGLT2i.

### Statistical Analysis

Continuous variables are expressed as means with standard deviation or medians with interquartile ranges (IQRs), and were compared using the Student's t-test or the Wilcoxon rank-sum test as appropriate. Categorial variables are presented as counts with percentages and were compared using the chi-square test or Fisher's exact test as appropriate. The means of 2 measurements taken from the same individual were compared using a paired t-test or the Wilcoxon signed-rank test as appropriate. A P value <0.05 was used to denote statistical significance. The Kaplan-Meier method was used to estimate the cumulative 1-year incidence of clinical events, and differences were assessed using the log-rank test. Univariate and multivariate Cox proportional hazard models were used to estimate the hazard ratios and their 95% confidence intervals of the percentage survival and SGLT2i prescription continuation rates. For univariate analysis, we selected values of patients' characteristics, etiology of HF, medications at discharge, and significantly different blood sample data (hemoglobin, renal function, albumin, and C-reactive protein [CRP]) and walking speed. For the risk-adjusting variables, continuous variables were dichotomized by clinically meaningful reference values or median values: age >85 years based on median values; BMI <18 kg/m$^2$ based on median values; walking speed <2.0 km/h based on median values; left ventricular ejection fraction (LVEF) <40%; estimated glomerular filtration rate <30 mL/min/1.73 m$^2$; serum albumin <3.0 g/dL based on a previous report;[13] and anemia defined by the World Health Organization criteria (hemoglobin <12 g/dL for women and <13 g/dL for men). Univariate factors with P<0.05 were fitted into the multivariate model to assess the effects of the parameters on endpoints. All statistical analyses were performed using R (version 4.3.2; R Foundation for Statistical Computing, Vienna, Austria).

## Results

### Study Population

Between February 2022 and July 2023, 533 patients were hospitalized at the Japanese Red Cross Wakayama Medical Center because of acute HF. Forty-five patients died during the index hospitalization. Excluding those who died during hospitalization, we categorized 488 patients, according to their BMI at discharge: <20 kg/m$^2$ (n=201); ≥20 kg/m$^2$ (n=287). SGLT2i were prescribed to 53 (26%) patients with a BMI <20 kg/m$^2$ and 123 (43%) patients with a BMI ≥20 kg/m$^2$ (**Figure 1**).

### Baseline Characteristics of Patients With a BMI <20 kg/m$^2$

**Table 1** and **Supplementary Table** present the baseline characteristics and blood sample data of the patients. Among patients with a BMI <20 kg/m$^2$, those who received

SGLT2i were significantly younger and had a significantly higher BMI than those who did not receive SGLT2i. The incidence rate of dementia and the level of care required are lower in patients who received SGLT2i than in those who did not receive SGLT2i; however, no significant difference in Clinical Frailty Scale score was observed between patients who received SGLT2i and those who did not receive SGLT2i. Diabetes and cardiomyopathy were more frequent in patients who received SGLT2i, whereas valvular heart disease was more frequent in patients who did not receive SGLT2i. No significant difference in the LVEF was observed between the 2 groups. The serum levels of creatinine at admission, and CRP at admission and discharge were significantly lower in those who received SGLT2i, whereas the estimated glomerular filtration rate at admission and discharge, hemoglobin at discharge, and albumin at discharge were significantly higher in those who received SGLT2i. Patients who received

**Table 1. Baseline Characteristics of Patients With a BMI <20 kg/m²**

| | SGLT2i(+) (n=53) | SGLT2i(−) (n=148) | P value |
|---|---|---|---|
| Age (years) | 78.7±9.6 | 84.7±9.2 | <0.001 |
| Sex, male | 31 (58.5) | 75 (50.7) | 0.414 |
| BMI at discharge | 18.1±1.5 | 17.3±1.8 | 0.014 |
| No. hospitalizations due to HF | 1.53±1.59 | 1.54±1.10 | 0.675 |
| **Clinical Frailty Scale score** | | | 0.124 |
| 1–4 | 21 (39.6) | 40 (27) | |
| 5–9 | 32 (60.4) | 108 (73) | |
| Dementia | 10 (18.9) | 55 (37.4) | 0.021 |
| **Care services** | | | 0.017 |
| None | 31 (58.5) | 54 (36.5) | |
| Support required | 7 (13.2) | 23 (15.5) | |
| Required nursing care | 15 (28.3) | 71 (48) | |
| **LVEF** | | | |
| Mean | 41.6±18.7 | 44.2±16.0 | 0.335 |
| Distribution | | | 0.752 |
| <40% | 27 (50.9) | 67 (45.3) | |
| 40–59% | 7 (13.2) | 24 (16.2) | |
| ≥60% | 19 (35.8) | 57 (38.5) | |
| Diabetes | 22 (41.5) | 28 (18.9) | 0.002 |
| **Etiology** | | | |
| Ischemic heart disease | 17 (32.1) | 57 (38.5) | 0.504 |
| Cardiomyopathy | 10 (18.9) | 9 (6.1) | 0.014 |
| Valvular heart disease | 7 (13.2) | 51 (34.5) | 0.006 |
| Arrythmia | 17 (32.1) | 43 (29.1) | 0.812 |
| Hypertensive heart disease | 10 (18.9) | 34 (23.0) | 0.670 |
| **Vital signs at presentation** | | | |
| Systolic blood pressure | 137.8±34.8 | 135.7±31.5 | 0.688 |
| Pulse rate | 97.8±26.9 | 94.9±27.3 | 0.511 |
| **Blood tests at admission** | | | |
| Hemoglobin | 11.7±2.2 | 10.9±3.2 | 0.117 |
| Albumin | 3.26±0.52 | 3.17±0.51 | 0.299 |
| Creatinine | 0.98 [0.70–1.25] | 1.10 [0.86–1.67] | 0.021 |
| eGFR | 52.0 [37.0–62.0] | 44.0 [24.0–55.0] | 0.003 |
| CRP | 0.33 [0.12–3.02] | 0.89 [0.29–3.90] | 0.024 |
| NT-proBNP | 6,584 [2,802–16,629] | 9,262 [4,405–23,197] | 0.051 |
| **Blood tests at discharge** | | | |
| Hemoglobin | 11.9±1.9 | 10.9±1.8 | 0.001 |
| Albumin | 3.17±0.43 | 2.98±0.48 | 0.014 |
| Creatinine | 1.06 [0.84–1.29] | 1.16 [0.86–1.53] | 0.106 |
| eGFR | 45.0 [33.0–60.0] | 38.5 [28.0–55.3] | 0.025 |
| CRP | 0.21 [0.08–0.76] | 0.52 [0.17–1.36] | 0.008 |
| NT-proBNP | 2,732 [1,072–4,319] | 3,470 [1,356–7,828] | 0.073 |
| CONUT score | 5.0 [3.75–7.0] | 6.0 [4.0–7.0] | 0.229 |
| CONUT score >5 | 28 (58.3) | 97 (69.3) | 0.226 |

(**Table 1** continued the next page.)

| | SGLT2i(+) (n=53) | SGLT2i(−) (n=148) | P value |
|---|---|---|---|
| **Rehabilitation** | | | |
| SPPB | 7 [4–11] | 6 [1–9] | 0.041 |
| Hand grip | 17.0 [13.2–21.2] | 15.1 [10.8–20.4] | 0.067 |
| Walking speed | 2.72 [2.00–3.10] | 1.75 [1.20–2.56] | <0.001 |
| 6-min walk distance | 200 [107–300] | 100 [23–200] | <0.001 |
| **Medication at discharge** | | | |
| β-blockers | 43 (81.1) | 84 (56.8) | 0.003 |
| RAS inhibitors | | | 0.053 |
| ACE inhibitors/ARBs | 9 (17.0) | 24 (16.2) | |
| ARNIs | 20 (37.7) | 32 (21.6) | |
| MRAs | 39 (73.6) | 77 (52.0) | 0.010 |
| SGLT2i | 53 (100) | 0 (0) | <0.001 |
| Tolvaptans | 18 (34.0) | 44 (29.7) | 0.691 |
| Total no. medications | 10 [8–12] | 8 [6–10] | <0.001 |
| **Discharge route** | | | 0.005 |
| Patients' home | 39 (73.6) | 71 (48.0) | |
| Nursing home | 5 (9.4) | 23 (15.5) | |
| Ot her hospital | 9 (17.0) | 54 (36.5) | |

Unless indicated otherwise, data are presented as n (%), median [IQR] or mean ± SD. ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BMI, body mass index; CONUT, Controlling Nutritional Status; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; HF, heart failure; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal pro B-type natriuretic peptide; RAS, renin-angiotensin-aldosterone system; SGLT2i, sodium-glucose cotransporter 2 inhibitors; SPPB, Short Physical Performance Battery.

SGLT2i had higher Short Physical Performance Battery and a higher walking speed, and walked longer distances in 6 min. Patients who received SGLT2i more frequently received β-blockers and mineralocorticoid receptor antagonists (MRA) at discharge than those who did not receive SGLT2i. A higher proportion of patients who received SGLT2i were discharged to their own home.

### Changes in BMI and Nutritional Status of Patients With a Low BMI After Discharge

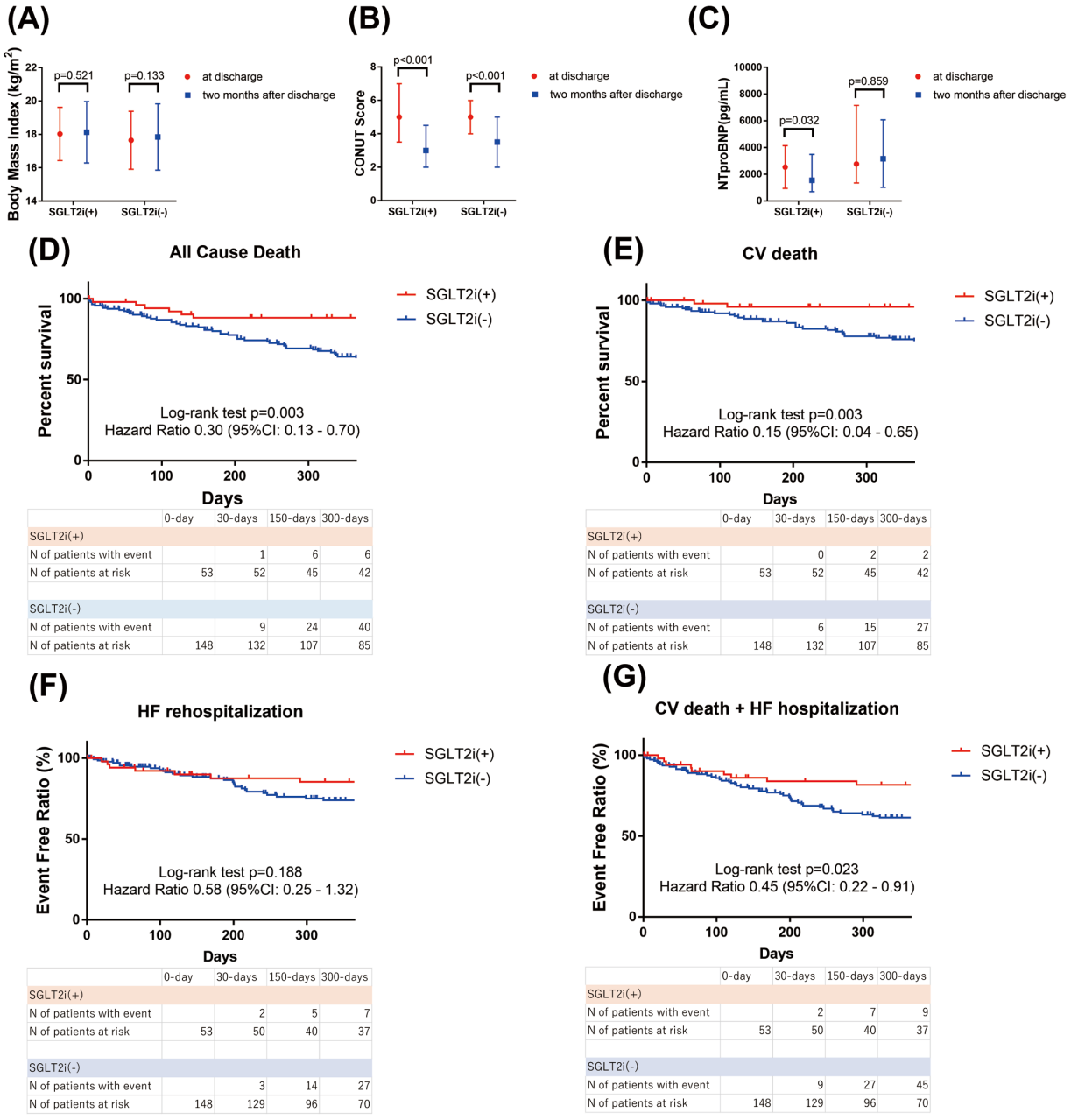
Significant concerns have been raised regarding the effects of SGLT2i on weight loss and undernutrition. Therefore, we examined changes in BMI and the CONUT score, which is an indicator of nutritional status (a score of 5–8 indicates moderate undernutrition and a score ≥9 indicates severe undernutrition),[14] 2 months after discharge in patients with a BMI <20 kg/m$^2$ who received SGLT2i. No decrease in BMI was observed (18.0±1.6 vs. 18.1±1.8 kg/m$^2$; P=0.521; **Figure 2A**) and the CONUT score decreased 2 months after discharge (5 [4–7] vs. 3 [2–4]; P<0.001; **Figure 2B**). Similar to patients who received SGLT2i, no decrease in BMI was observed (17.6±1.7 vs. 17.8±2.0 kg/m$^2$; P=0.133; **Figure 2A**) and the CONUT score decreased 2 months after discharge (5 [4–6] vs. 3.5 [2–5]; P<0.001; **Figure 2B**) in those who did not receive SGLT2i. In contrast, the serum level of N-terminal pro B-type natriuretic peptide (NT-proBNP) was significantly decreased in patients who received SGLT2i 2 months after discharge (2,539.5 [952–4,091] vs. 1,555.5 [708–3,398]; P=0.032), but no decrease was observed in those who did not receive SGLT2i (2,774 [1,361–7,142] vs. 3,164 [1,025–5,984]; P=0.859; **Figure 2C**).

### 1-Year Outcome in Patients With a BMI <20 kg/m$^2$

The cumulative incidence rates of all-cause mortality and cardiovascular death at 1 year were significantly different between patients with a BMI <20 kg/m$^2$ who received SGLT2i and those who did not receive SGLT2i (**Figure 2D**,**E**). The cumulative incidence rates of rehospitalization due to worsening HF at 1 year were not significantly different (**Figure 2F**), but the cumulative incidence rate of cardiovascular death or rehospitalization due to worsening HF was significantly higher in patients who did not receive SGLT2i than those who did receive SGLT2i. A high age (i.e., >85 years), presence of frailty (Clinical Frailty Scale score >5), decreased albumin level, elevated CRP level, and decreased walking speed (<2 km/h) were associated with an increased risk of all-cause mortality. However, prescriptions of renin-angiotensin-aldosterone system (RAS) inhibitors, MRAs, and SGLT2i at discharge were associated with a decreased risk of all-cause mortality. In the multivariable Cox proportional hazards model, the prescription of SGLT2i at discharge was significantly associated with a decreased risk of all-cause mortality independent of age, frailty, walking speed, decreased albumin level, elevated CRP level, and prescription of RAS inhibitors and MRAs (**Table 2**).

### 1-Year Outcomes in Patients Who Received SGLT2i

To investigate the safety of SGLT2i in patients with a BMI <20 kg/m$^2$, we compared the differences between patients with a BMI <20 kg/m$^2$ and those with a BMI ≥20 kg/m$^2$. **Supplementary Table** presents the baseline characteristics and blood sample data of patients with a BMI ≥20 kg/m$^2$. Among patients who received SGLT2i, the SGLT2i prescription continuation rate at 1 year was not significantly different between patients with a BMI <20 kg/m$^2$ and those with a BMI ≥20 kg/m$^2$ (86.8% vs. 84.6%; log-rank P=0.869; **Figure 3A**). No significant difference in the cumulative incidence rates of all-cause mortality at 1 year was observed




| | 0-day | 30-days | 150-days | 300-days |
|---|---|---|---|---|
| SGLT2i(+) | | | | |
| N of patients with event | | 1 | 6 | 6 |
| N of patients at risk | 53 | 52 | 45 | 42 |
| SGLT2i(-) | | | | |
| N of patients with event | | 9 | 24 | 40 |
| N of patients at risk | 148 | 132 | 107 | 85 |

| | 0-day | 30-days | 150-days | 300-days |
|---|---|---|---|---|
| SGLT2i(+) | | | | |
| N of patients with event | | 0 | 2 | 2 |
| N of patients at risk | 53 | 52 | 45 | 42 |
| SGLT2i(-) | | | | |
| N of patients with event | | 6 | 15 | 27 |
| N of patients at risk | 148 | 132 | 107 | 85 |

| | 0-day | 30-days | 150-days | 300-days |
|---|---|---|---|---|
| SGLT2i(+) | | | | |
| N of patients with event | | 2 | 5 | 7 |
| N of patients at risk | 53 | 50 | 40 | 37 |
| SGLT2i(-) | | | | |
| N of patients with event | | 3 | 14 | 27 |
| N of patients at risk | 148 | 129 | 96 | 70 |

| | 0-day | 30-days | 150-days | 300-days |
|---|---|---|---|---|
| SGLT2i(+) | | | | |
| N of patients with event | | 2 | 7 | 9 |
| N of patients at risk | 53 | 50 | 40 | 37 |
| SGLT2i(-) | | | | |
| N of patients with event | | 9 | 27 | 45 |
| N of patients at risk | 148 | 129 | 96 | 70 |

**Figure 2.** Effect of sodium-glucose co-transporter 2 inhibitors (SGLT2i) on patients with a body mass index <20 kg/m$^2$. Change in (**A**) body mass index, (**B**) Controlling Nutritional Status (CONUT) score, and (**C**) the serum level of N-terminal pro B-type natriuretic peptide (NT-proBNP) patients with a body mass index <20 kg/m$^2$ treated with SGLT2i from discharge to 2 months after discharge. Data presented as mean with standard deviation (**A**), and median with interquartile range (**B**,**C**). Kaplan-Meier curves according to SGLT2i prescription or no prescription for all-cause mortality (**D**), cardiovascular (CV) death (**E**), rehospitalization due to worsening heart failure (HF; **F**), and CV death or rehospitalization due to worsening HF (**G**). CI, confidence interval.

between the 2 groups (**Figure 3B**).

### Reasons for Discontinuation of SGLT2i

**Table 3** shows the reasons for discontinuing SGLT2i prescriptions during the 1-year follow up. The reason for discontinuing SGLT2i was loss of appetite or weight loss in 1 patient among the patients with a BMI <20 kg/m$^2$, and 2 patients among those with a BMI ≥20 kg/m$^2$. Deteriorating renal function and prescription adjustments for diabetes control were common reasons for discontinuing SGLT2i prescriptions.

## Discussion

In this study, the median age of patients was 82 years, and their mean BMI was 21.4 kg/m$^2$. Furthermore, 41.2% of

**Table 2. Hazard Ratio for Composite of All-Cause Mortality**

| | Univariate | | Multivariate model 1 | | Multivariate model 2 | |
|---|---|---|---|---|---|---|
| | Hazard ratio | P value | Hazard ratio | P value | Hazard ratio | P value |
| Age >85 years | 2.62 (1.50–4.58) | <0.001 | 1.70 (0.89–3.23) | 0.108 | | |
| Sex, male | 1.19 (0.69–2.05) | 0.526 | | | | |
| BMI at discharge <18 kg/m$^2$ | 1.33 (0.77–0.29) | 0.301 | | | | |
| Clinical Frailty Scale score >5 | 2.17 (1.11–4.21) | 0.023 | 1.34 (0.62–2.93) | 0.46 | | |
| Dementia | 1.74 (0.99–3.03) | 0.052 | | | | |
| LVEF <40% | 0.90 (0.52–1.55) | 0.704 | | | | |
| Diabetes | 0.87 (0.46–1.66) | 0.671 | | | | |
| Ischemic heart disease | 1.02 80.59–1.78) | 0.937 | | | | |
| Cardiomyopathy | 0.84 (0.33–2.11) | 0.71 | | | | |
| Valvular heart disease | 1.18 (0.66–2.10) | 0.574 | | | | |
| Arrythmia | 0.90 (0.49–1.66) | 0.74 | | | | |
| Hypertensive heart disease | 0.78 (0.38–1.61) | 0.505 | | | | |
| Anemia at discharge | 1.90 (0.90–4.04) | 0.093 | | | | |
| Albumin at discharge <3.0 g/dL | 1.84 (1.07–3.15) | 0.028 | | | 1.68 (0.96–2.96) | 0.07 |
| eGFR at discharge <30 mL/min/1.73 m$^2$ | 1.43 (0.79–2.60) | 0.242 | | | | |
| CRP >1.0 mg/dL | 2.19 (1.27–3.79) | 0.005 | | | 1.53 (0.86–2.73) | 0.15 |
| $\beta$-blockers | 0.60 (0.35–1.04) | 0.067 | | | | |
| RAS inhibitors | 0.34 (0.18–0.65) | 0.001 | | | 0.45 (0.23–0.88) | 0.019 |
| MRAs | 0.50 (0.29–0.87) | 0.013 | | | 0.66 (0.38–1.16) | 0.148 |
| SGLT2i | 0.30 (0.13–0.70) | 0.005 | 0.38 (0.15–0.99) | 0.048 | 0.41 (0.17–0.97) | 0.042 |
| Tolvaptans | 1.39 (0.79–2.43) | 0.256 | | | | |
| Walking speed <2.0 km/h | 2.83 (1.50–5.37) | 0.001 | 1.81 (0.89–3.71) | 0.104 | | |

Abbreviations as in Table 1.

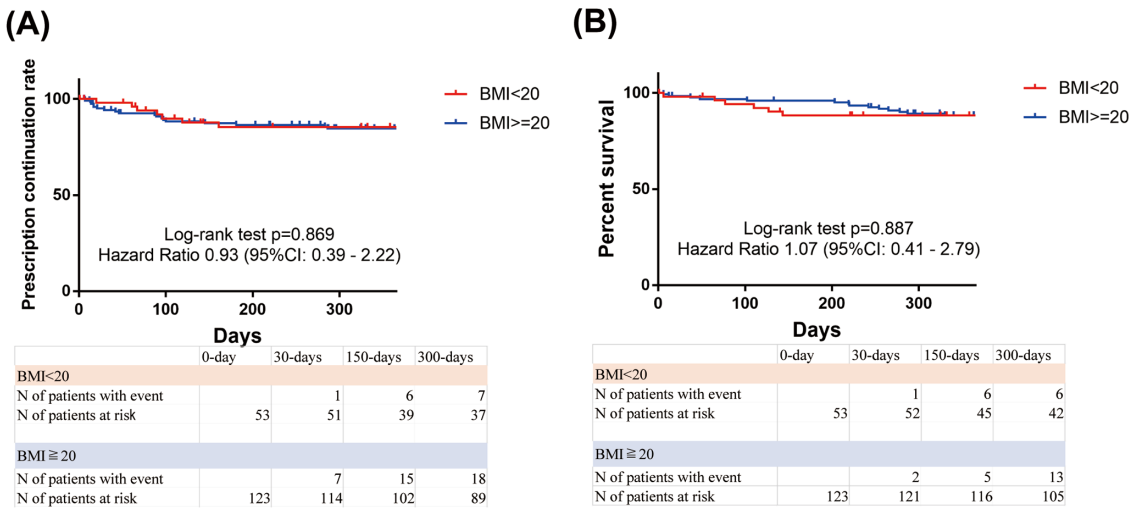



**Figure 3.** Kaplan-Meier curves according to a body mass index (BMI) <20 kg/m$^2$ or a BMI ≥20 kg/m$^2$ at discharge for sodium-glucose co-transporter 2 inhibitors prescription continuation rate (**A**), and all-cause mortality (**B**). CI, confidence interval.

patients had a BMI <20 kg/m$^2$. SGLT2i were prescribed to 36.1% of patients. Among patients with a BMI <20 kg/m$^2$, age, the presence of frailty, decreased albumin levels, elevated CRP levels, decreased walking speed, and prescription of RAS inhibitors, MRAs and SGLT2i were risk factors associated with all-cause mortality. Furthermore, SGLT2i reduced the risk of all-cause mortality even after adjusting for these factors.

SGLT2i were beneficial for HF, regardless of EF;[3–6] however, data on the patients with a low BMI (particularly those with a BMI <20 kg/m$^2$) are limited. SGLT2i have been shown to significantly reduce skeletal muscle and fat

mass.[15] Thus, significant concerns have been raised regarding the effects of SGLT2i on aggravating frailty, sarcopenia, and cachexia. Cardiac cachexia is a common complication of HF. Patients with cardiac cachexia have a poor prognosis and an increased risk of disability.[16] Cachexia and sarcopenia are predictors of adverse clinical outcomes in HF.[17] A previous report showed weight loss was associated with a higher risk of all-cause mortality in patients receiving SGLT2i, and adverse events leading to discontinuation of therapy were more likely in patients with a BMI <20 kg/m$^2$.[12] In this study, no decrease in BMI was observed 2 months after discharge in patients with a BMI <20 kg/m$^2$ who received SGLT2i. Particularly in patients with HF, body weight changes rapidly because of fluid retention. However, in this study, the serum level of NT-proBNP was significantly decreased 2 months after discharge. This result suggests that it was unlikely that fluid retention had worsened. Therefore, the fact that the BMI did not decrease may suggest there was no change in skeletal muscle mass or fat mass. Furthermore, the CONUT score, which is an indicator of nutritional status,[14] decreased 2 months after discharge. These results indicate that cachexia and sarcopenia were not aggravated and that nutritional status improved. From the perspective of adverse events, no significant difference in the 1-year SGLT2i continuation rate was observed between patients with a BMI <20 kg/m$^2$ and those with a BMI ≥20 kg/m$^2$. The SGLT2i discontinuation rate was 14.6% among patients with a BMI <20 kg/m$^2$. This rate was lower than that reported in a previous study.[18]

A low BMI was associated with a higher risk for 1-year mortality after discharge among patients with ADHF.[18] In this study, the cumulative incidence of all-cause mortality at 1 year was 29.8% among patients with a BMI <20 kg/m$^2$. This result was similar to that reported in a previous Japanese study.[19] The 1-year survival rate was better in patients who received SGLT2i (88.2% vs. 63.4%). Patients who received SGLT2i were significantly younger, had better cognitive function, and had better life activities than those who did not receive SGLT2i. However, even after multivariate analysis, SGLT2i reduced the risk of all-cause mortality. Furthermore, among patients who received SGLT2i, no significant difference in the 1-year survival rate was observed between patients with a BMI <20 kg/m$^2$ and those with a BMI ≥20 kg/m$^2$. Considering these data, SGLT2i can be considered as drugs with both safety and efficacy even in patients with a low BMI.

### Study Limitations

This study has several limitations. First, this was an observational study. The decision to prescribe SGLT2i was made by the treating physician. Therefore, the sources of bias could not be eliminated. Second, this was a single-center study. Institution-specific factors may limit the generalizability of findings, and the sample size was small; thus, the statistical power may not be enough. A large-scale multicenter study is necessary.

## Conclusions

In this 1-year observational study, patients taking SGLT2i had a better prognosis among those with a BMI <20 kg/m$^2$. No significant difference in the SGLT2i prescription continuation rate was observed between patients with a BMI <20 kg/m$^2$ and those with a BMI ≥20 kg/m$^2$.

**Table 3. Reasons for Discontinuation of SGLT2i Therapy**

| Reason | BMI <20 kg/m$^2$ | BMI ≥20 kg/m$^2$ |
|---|---|---|
| Worsening renal function | 2 | 5 |
| Patient preference | 1 | 1 |
| Lightheadedness | | 1 |
| Deterioration of general condition | 1 | 1 |
| Loss of appetite/weight loss | 1 | 2 |
| Judgment by doctors in other departments | 2 | 2 |
| Dropped out | | 1 |
| Details unknown | | 4 |
| Urinary tract infection | | 1 |

SGLT2i, sodium-glucose cotransporter 2 inhibitors.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### Disclosures

The authors declare that there are no conflicts of interest.

### IRB Information

The study protocol was approved by the Ethics Committee of Japanese Red Cross Wakayama Medical Center (approval no. 1249).

### Data Availability

Our study data will not be made available to other researchers because of our Institutional Review Board restrictions.

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## Supplementary Files

Please find supplementary file(s);
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