Korean Circ J. 2026 Jan;56(1):100-102
https://doi.org/10.4070/kcj.2025.0348
pISSN 1738-5520·eISSN 1738-5555

kcj
Korean Circulation Journal

Research Letter

Check for updates

Sodium-glucose Co-transporter 2 Inhibitors on Body Composition in Lean Heart Failure With Preserved Ejection Fraction

Yuki Shimoya, RD[1,2], Kazuki Kagami, MD, PhD[1], Naoki Yuasa, MD[1], Yuta Tani, MSc[1,3], Tomonari Harada, MD, PhD[1], Tsukasa Murakami, MD, PhD[1], Eijiro Yamada, MD, PhD[4], Naoki Wada, MD, PhD[5], Hideki Ishii, MD, PhD[1], and Masaru Obokata, MD, PhD[1]

[1]Department of Cardiovascular Medicine, Gunma University Graduate School of Medicine, Maebashi, Japan
[2]Division of Nutrition Management, Department of Medical Support, Gunma University Hospital, Maebashi, Japan
[3]Department of Rehabilitation Sciences, Gunma University Graduate School of Health Sciences, Maebashi, Japan
[4]Division of Endocrinology and Metabolism, Department of Internal Medicine, Gunma University Graduate School of Medicine, Maebashi, Japan
[5]Department of Rehabilitation Medicine, Gunma University Graduate School of Medicine, Maebashi, Japan

OPEN ACCESS

Received: Aug 12, 2025
Revised: Oct 11, 2025
Accepted: Nov 19, 2025
Published online: Jan 5, 2026

Correspondence to
Masaru Obokata, MD, PhD
Department of Cardiovascular Medicine, Gunma University Graduate School of Medicine, 3-39-22 Showa-machi, Maebashi, Gunma 371-8511, Japan.
Email: obokata.masaru@gunma-u.ac.jp

ORCID iDs
Kazuki Kagami
https://orcid.org/0000-0002-1743-4409
Naoki Yuasa
https://orcid.org/0000-0002-2090-1530
Yuta Tani
https://orcid.org/0009-0002-8942-6448
Tomonari Harada
https://orcid.org/0000-0003-4662-2991
Tsukasa Murakami
https://orcid.org/0009-0004-8583-9303
Eijiro Yamada
https://orcid.org/0000-0002-0332-8605
Naoki Wada
https://orcid.org/0000-0002-3816-6247

Sodium-glucose cotransporter-2 (SGLT2) inhibitors have changed heart failure with a preserved ejection fraction (HFpEF) into a treatable disease.[1] They cause modest weight loss by promoting urinary calorie loss and reducing fat mass.[2] Although their benefits on clinical outcomes are consistent across baseline body mass index (BMI) categories in HFpEF,[1] concerns about muscle loss or worsening sarcopenia may limit use in some populations, especially elderly, lean patients.[2-4] The EMPA-ELDERLY (efficacy and safety of the sodium-glucose co-transporter-2 inhibitor empagliflozin in elderly Japanese adults (≥65 years) with type 2 diabetes) trial reported that 52-week empagliflozin treatment did not reduce muscle mass versus placebo in elderly patients with type II diabetes (mean age 74 years; mean BMI 25.6 kg/m^2).[2] However, this trial included only individuals with a BMI ≥22 kg/m^2, and evidence remains limited regarding the effects of SGLT2 inhibitors on muscle mass in elderly, lean HFpEF patients. Accordingly, this preliminary study aimed to report longitudinal body-composition changes after SGLT2 inhibitor initiation in lean HFpEF and to compare findings with those of the EMPA-ELDERLY trial.

Consecutive HFpEF patients and a BMI <22 kg/m^2 who were started on SGLT2 inhibitors (empagliflozin 10 mg or dapagliflozin 10 mg) for heart failure (HF) treatment after body composition analysis were retrospectively screened. The BMI cutoff was based on the exclusion criteria used in the EMPA-ELDERLY trial.[2] From this cohort, we selected patients who underwent repeated body composition analyses 3–6 months after the initial assessment. This timeframe was based on findings from the EMPEROR-Preserved trial, where body weight reduction plateaued at first 3 months after SGLT2 inhibitor initiation in HFpEF with a BMI <25 kg/m^2.[1] Body composition was measured at baseline and follow-up by bioelectrical impedance analysis (BIA) (MC-780A-N; Tanita, Tokyo, Japan).[2] The definition of HFpEF was defined by the universal definition and classification of HF. The study was approved by the Gunma University Hospital, Clinical Research Review Board with the waiver of consent due to its retrospective design (HS2025-131). Data are reported as mean ± standard deviation,

kcj
Korean Circulation Journal

Hideki Ishii
https://orcid.org/0000-0003-4348-0123
Masaru Obokata
https://orcid.org/0000-0002-5473-0688

Funding

Dr. Obokata received research grants from the Japanese College of Cardiology, AMI Inc., Nippon Boehringer-Ingelheim, Janssen Pharmaceutical K.K., JSPS KAKENHI (21K16078, 25K11404), and AMED (JP25jm0210104, JP256f0137008). Dr. Ishii received scholarship funds or Donations from Abbott Medical Japan, Boehringer Ingelheim Japan, Bristol-Myers Squibb Inc. and Pfizer Japan Inc.

Conflict of Interest

Dr. Obokata received speaker honoraria from Novartis, Otsuka Pharmaceutical, AstraZeneca, Eli Lilly, and Nippon Boehringer-Ingelheim. Dr. Ishii received speaker honoraria from AstraZeneca Inc., Bayer Pharmaceutical Co., Ltd., Boehringer Ingelheim Japan, Bristol-Myers Squibb Inc., Daiichi-Sankyo Pharma Inc., MSD K. K., Mitsubishi Tanabe Pharma Co., Ltd., Mochida Pharmaceutical Co., Ltd., Novartis Japan, and Pfizer Japan Inc. Dr. Wada received lecture fees from GlaxoSmithKline plc, Teijin Pharma, and Daiichi-Sankyo Pharma Inc. The remaining authors have nothing to disclose.

Data Sharing Statement

The data generated in this study is not available from the corresponding author upon reasonable request.

mean (95% confidence intervals), median (interquartile range), or number (%). Differences within groups were compared using paired t-test for normally distributed variables or Wilcoxon signed-rank test for non-normally distributed variables. No adjustment was applied due to the exploratory nature of the analysis. All tests were 2-sided, with statistical significance set at $p<0.05$.

After excluding 11 patients with BMI ≥22 kg/m^2 and 2 patients with ejection fraction <50%, 21 individuals with repeated body composition analyses were identified. Among them, SGLT2 inhibitors were discontinued in 2 patients due to rash (n=1) or worsening peripheral edema (n=1), leaving 19 patients with HFpEF. Before initiation of SGLT2 inhibitors, 16 of 19 patients underwent nutritional assessment by a registered dietitian, and 5 started receiving oral nutritional supplements (200–300 kcal/day). There were no clear adverse events associated with SGLT2 inhibitors, including genital or urinary tract infections, hypoglycemia, or ketoacidosis.

Patients with HFpEF were elderly (74±8 years), predominantly female (74%), and presented with typical comorbidities (hypertension 84%, diabetes 21%, dyslipidemia 32%, and atrial fibrillation 27%). By definition, patients had a relatively low BMI. The median time between baseline and follow-up assessments was 112 days (91–133). No cardiovascular drugs changed during this period, except that one patient began an angiotensin receptor blocker for hypertension. Body weight modestly decreased from 46.9±7.7 to 46.6±7.4 kg after the initiation of SGLT2 inhibitors (**Table 1**). The mean reduction in body weight (−0.4 [−1.5, 0.7] kg) was only 12% of that observed in the EMPA-ELDERLY cohort (−3.3±0.3 kg). No significant relationship was observed between body weight reduction after SGLT2 inhibitor initiation and age, baseline body weight, or BMI (all $p>0.2$). There was no significant decrease in muscle mass or total body water during the study period. Skeletal muscle mass index decreased with SGLT2 inhibitor treatment, but the magnitude of reduction was modest compared to that in the EMPA-ELDERLY cohort. Most of the weight loss (−0.4 kg) was likely due to a decrease in body fat mass (−0.4 kg), with a strong correlation observed between the two ($r=0.80$, $p<0.0001$). However, fat mass loss was relatively minor compared to that in the EMPA-ELDERLY cohort.

Table 1. Serum markers and body composition parameters at baseline and follow-up in heart failure with preserved ejection fraction

Variables	Baseline	Follow-up	p value*	Absolute change	Absolute change in the EMPA-ELDERLY cohort
Serum and nutritional markers					
NT-proBNP (pg/mL, n=14/15)	398 (172, 935)	258 (198, 509)	0.54	-	-
Albumin (g/dL, n=18/18)	3.9±0.4	3.9±0.5	0.59	-	-
eGFR (n=17/18)	53.0±23.0	49.0±20.0	0.24	-	-
GNRI (n=18/18)	93.6±7.7	94.1±9.2	0.76	-	-
Body composition analysis					
Body weight (kg)	46.9±7.7	46.6±7.4	0.50	−0.4 (−1.5, 0.7)	−3.3±0.3
Body fat mass (kg)	9.9±2.8	9.5±3.3	0.40	−0.4 (−1.4, 0.6)	−1.8±0.3
Lean body mass (kg)	37.0±7.4	37.3±7.0	0.66	0.1 (−0.5, 0.8)	−1.6±0.3
Muscle mass (kg)	35.0±7.0	35.0±6.6	0.97	0.01 (−0.6, 0.6)	−1.6±0.4
Total body water (kg)	26.4±5.6	26.4±4.9	0.87	0.1 (−0.8, 0.9)	−1.4±0.2
Skeletal muscle index (kg/m^2)	6.2±1.0	6.1±0.8	0.58	−0.1 (−0.3, 0.2)	−0.3±0.1

Data are mean ± standard deviation, mean (95% confidence intervals), or median (interquartile range).
eGFR = estimated glomerular filtration rate; EMPA-ELDERLY = efficacy and safety of the sodium-glucose co-transporter-2 inhibitor empagliflozin in elderly Japanese adults (≥65 years) with type 2 diabetes; GNRI = geriatric nutritional risk index; NT-pro BNP = N-terminal pro B-type natriuretic peptide.
*The p values for comparisons between baseline and follow-up assessments.

https://doi.org/10.4070/kcj.2025.0348

Author Contributions

Conceptualization: Obokata M; Data curation: Shimoya Y; Formal analysis: Kagami K, Yuasa N, Tani Y; Investigation: Tani Y, Harada T, Murakami T, Obokata M; Supervision: Obokata M; Writing - original draft: Shimoya Y; Writing - review & editing: Kagami K, Yuasa N, Tani Y, Harada T, Murakami T, Yamada E, Wada N, Ishii H, Obokata M.

Despite their proven efficacy, SGLT2 inhibitors are sometimes avoided in elderly, lean HFpEF due to concerns about muscle loss and worsening sarcopenia.[2)3)] Although direct comparison was not possible in this exploratory study, weight loss was modest in our cohort compared with the EMPA-ELDERLY cohort. Most weight loss reflected a reduction in fat mass rather than muscle mass. This finding is consistent with a previous observation that individuals with lower baseline BMI experienced less weight loss with SGLT2 inhibitors,[1)] possibly due to reduced caloric loss in underweight populations. Nutritional assessments and the use of oral nutritional supplements may also have contributed. Recent studies showed SGLT2 inhibitors reduced mortality and HF hospitalization without increasing adverse events in HF patients over 80 years.[4)5)] Given the small sample size, retrospective observational design, short follow-up, and use of BIA instead of dual-energy X-ray absorptiometry, our findings should be considered hypothesis-generating and require confirmation in larger, longer-term cohorts.

REFERENCES

1. Sattar N, Butler J, Lee MMY, et al. Body mass index and cardiorenal outcomes in the EMPEROR-Preserved trial: principal findings and meta-analysis with the DELIVER trial. *Eur J Heart Fail* 2024;26:900-9. PUBMED | CROSSREF
2. Yabe D, Shiki K, Homma G, et al. Efficacy and safety of the sodium-glucose co-transporter-2 inhibitor empagliflozin in elderly Japanese adults (≥65 years) with type 2 diabetes: a randomized, double-blind, placebo-controlled, 52-week clinical trial (EMPA-ELDERLY). *Diabetes Obes Metab* 2023;25:3538-48. PUBMED | CROSSREF
3. Obokata M, Sorimachi H, Harada T, Kagami K, Saito Y, Ishii H. Epidemiology, pathophysiology, diagnosis, and therapy of heart failure with preserved ejection fraction in Japan. *J Card Fail* 2023;29:375-88. PUBMED | CROSSREF
4. Nakano K, Kanenawa K, Isotani A, et al. The efficacy and safety of sodium-glucose cotransporter 2 inhibitors in patients aged over 80 years with heart failure. *ESC Heart Fail* 2025;12:2087-97. PUBMED | CROSSREF
5. Noiri JI, Tanaka H, Odajima S, et al. Efficacy of sodium-glucose cotransporter 2 inhibitors for super-aged heart failure population. *Int J Cardiol* 2025;439:133647. PUBMED | CROSSREF