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ORIGINAL RESEARCH

# Effectiveness of Sodium-Glucose Transporter 2 Inhibitors and Semaglutide on Body Composition in Type 2 Diabetes Mellitus and Chronic Kidney Disease: A Real-World Cohort Study with Bioelectrical Impedance Analysis

Qing Yang[1,2], Chunmei Qin[1,2], Yanlin Lang[1,2], Wenjie Yang[3], Fenghao Yang[4], Jia Yang[1,2], Ke Liu[1,2], Jiamin Yuan[1,2], Yutong Zou[1,2], Fang Liu[1,2,5]

[1]Department of Nephrology, West China Hospital of Sichuan University, Chengdu, People's Republic of China; [2]Laboratory of Diabetic Kidney Disease, Centre of Diabetes and Metabolism Research, West China Hospital of Sichuan University, Chengdu, People's Republic of China; [3]Department of Project Design and Statistics, West China Hospital of Sichuan University, Chengdu, People's Republic of China; [4]Department of Clinical Medicine, Southwest Medical University, Luzhou, People's Republic of China; [5]Department of Clinical Research Management, West China Hospital of Sichuan University, Chengdu, People's Republic of China

Correspondence: Fang Liu, Department of Nephrology, West China Hospital of Sichuan University, No. 37, Guoxue Alley, Chengdu, Sichuan, 610041, People's Republic of China, Tel +86-18980601214, Fax +86-28-85422335, Email liufangfh@163.com



**Background:** Sodium-glucose transporter 2 inhibitors (SGLT-2Is) and Semaglutide may increase the risk of sarcopenia and bone fragility in vulnerable populations, yet their effects on body composition in patients with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) remain unclear. This study evaluated changes in body composition by SGLT-2Is alone or combined with Semaglutide.

**Methods:** This retrospective cohort included T2DM-CKD patients treated with SGLT-2Is ± Semaglutide for ≥6 months. Body composition (fat, muscle, water, bone mineral content [BMC]) was measured via bioelectrical impedance analysis pre- and post-treatment.

**Results:** Among 73 participants (SGLT-2Is: n = 61; combination: n = 12), both groups showed reductions in total fat mass, total muscle mass, total body water, and BMC. Combination therapy exhibited greater fat mass loss (−0.9 kg [IQR: −3.7,0.4] vs −0.6 kg [−1.7,0.7]; $P = 0.011$) and muscle mass decline (−1.1 ± 1.2 kg vs −0.4 ± 0.8 kg; $P = 0.015$) versus monotherapy. Fat mass index (FMI: −1.3 ± 2.4 kg/m² vs −0.2 ± 0.8 kg/m²; $P = 0.008$) and skeletal muscle index (SMI: −0.4 ± 0.3 kg/m² vs −0.2 ± 0.2 kg/m²; $P = 0.002$) reduction were also larger with combination therapy. However, muscle mass-to-body weight percentage was increased more in the combination group (1.2 ± 2.4% vs 0.2 ± 1.2%; $P = 0.041$). No differences between to groups in BMC, fat percentage, or fat-to-muscle ratio ($P>0.05$). Within the SGLT-2Is group, higher baseline SMI correlated with greater muscle loss, while higher baseline FMI was associated with attenuated BMC decline.

**Conclusion:** SGLT-2Is with/without Semaglutide reduced body composition parameters of fat, muscle, water, and BMC in T2DM-CKD. Combination therapy exacerbated absolute muscle loss but increased the muscle mass-to-body weight percentage, without significantly altering fat-to-muscle ratio. Baseline muscle and fat mass may influence treatment-related changes. Long-term studies in high-risk populations are needed.

**Keywords:** sodium-glucose transporter 2 inhibitors, semaglutide, type 2 diabetes mellitus, chronic kidney disease, body composition, skeletal muscle index

## Introduction

People with diabetes mellitus (DM) and chronic kidney disease (CKD) have increased in proportion to the growing incidence of DM itself, facing high risk of kidney failure, heart failure, and premature mortality.[1] Sarcopenia is age-related skeletal

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muscle loss coupled with loss of muscle strength and/or decreased physical performance.[2] Research indicates that the incidence of sarcopenia spans from 7% to 29.3% in type 2 DM (T2DM),[3] with a 2-fold increased risk of sarcopenia relative to the general population.[4] Individuals with CKD are also twice more likely to experience sarcopenia compared to those without CKD,[5] with the prevalence of sarcopenia ranging from 4% to 49%.[6] Moreover, sarcopenia has been linked to an increased risk of mortality in patients with T2DM[7] and the danger of progression to end-stage kidney disease (ESKD) in CKD population.[5] A rising incidence of fragility fractures is also observed in T2DM.[8] With the progressive decline of renal function in T2DM, a complication of CKD-mineral bone disorder (CKD-MBD) occurs, resulting in bone fragility.[9] Therefore, enhancing muscle quality (both muscle mass and function) and lowering the risk of bone fragility is of the utmost significance for the clinical management of T2DM-CKD.

Most people with T2DM and CKD require lifelong anti-hyperglycemia medication treatment, and sarcopenia and osteoporosis are age-related diseases.[10] Thus, the effect of drugs on muscle quality and bone mineral content (BMC) is a crucial factor to take into account. Sodium-glucose transporter 2 inhibitors (SGLT-2Is), as the first-line therapeutic agent, are recommended by major guidelines in T2DM concurrent CKD.[1,11] To achieve personal glycemic goal or gain additional kidney and heart protection, glucagon-like peptide-1 receptor agonists (GLP-1RAs) are also suggested.[12,13] Semaglutide is a long-acting GLP-1RA approved for the subcutaneous administration on a once-weekly basis for the treatment of T2DM or/and obesity.[14] The available evidence indicates that Semaglutide is the best drug in the GLP-1RAs class for weight loss.[15] Weight loss is expected to result in changes of body composition, and it is essential to evaluate the impact of weight loss on muscle mass and BMC in T2DM and CKD. However, current research on body composition has predominantly focused on individuals with T2DM or obesity, with significant heterogeneity observed across studies.[16–19] This differentiation probably arises from the effects of population, comorbidity, and drug-specific property.[18] Therefore, the potential negative impact of SGLT-2Is and GLP-1ARs on muscle mass have raised concerns.[20,21] To date, there is a lack of research investigating the effects of SGLT-2Is and Semaglutide on body composition in the more susceptible population of T2DM patients with CKD. The resolution of this research gap will provide more precise therapeutic guidance for this high-risk population.

Bioelectrical impedance analysis (BIA) is a straightforward and non-invasive method that is widely utilized for the evaluation of body composition.[22] BIA uses a low-level electrical current flowing through the whole body to measure the varying impedance of different tissues, such as muscle (low impedance) and fat (high impedance), thereby estimating the mass of body composition.[22] This study retrospectively analyzed BIA-measured body composition data to assess the effects of SGLT-2Is and Semaglutide on muscle mass and bone minerals in T2DM patients with CKD.

# Methods

## Study Design

This investigation was a retrospective cohort study conducted at a single center, aimed at assessing alterations in body composition and metabolic profiles among people with T2DM concurrent CKD using SGLT-2Is or/and Semaglutide. The study received approval from the ethics committee of West China Hospital and adhered to the principles outlined in the Declaration of Helsinki (Ethical Number: 20231196). Given the retrospective design, informed consent was waived. All data were fully de-identified before analysis to ensure patient privacy.

## Patients

The research was performed on individuals diagnosed with T2DM-CKD who received SGLT-2Is or/and Semaglutide treatment in West China Hospital of Sichuan University from November 2021 to June 2022. The diagnostic criteria for T2DM were based on the 2018 American Diabetes Association (ADA) diagnostic criteria.[23] The definition of CKD was estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m2 or albumin to creatinine ratio (ACR) ≥30 mg/g for lasting 3 months.

Individuals who underwent body composition measurements via BIA both prior to and following 6 months treatment were considered for inclusion. We excluded people if they were (1) undergoing dialysis; (2) with malignant tumors, hepatic cirrhosis, or severe infections; (3) in pregnancy; (4) treated with glucocorticoids; (5) without follow-up data over 6 months.

## Data Collection

Patient information was obtained from the hospital information system and supplemented by telephone follow-up, involving demographic, medical and medication history, laboratory, and body composition data. Metabolic indicators, including glycosylated hemoglobin, fasting blood sugar (FBS), serum albumin, hemoglobin, ACR, uric acid, triglycerides, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol etc, were all measured using standard laboratory methods. The eGFR was computed utilizing the formula established by Chronic Kidney Disease Epidemiology Collaboration.[24] Body composition was evaluated using the direct segmental multi-frequency bioelectrical impedance analysis technique (Inbody770, Biospace, Korea). Patients removed their shoes and wore only close-fitting clothes, and a professional technician performed the measurement procedure. The BIA equipment estimated the total muscle mass, total fat mass, total body water, BMC, etc. The calculation methods of the derivative indicators are as follows. Skeletal muscle index (SMI) was determined by dividing the appendicular lean mass by the square of individual's height. Fat mass index (FMI) was calculated by dividing the total fat mass by the square of the height. Fat-to-muscle ratio (FMR) was total fat mass divided by total muscle mass.

## Outcomes

The main outcome of the study was the change in body composition parameters relative to baseline after 6 months. The secondary outcome was the change in metabolic indicators relative to baseline after 6 months.

## Statistical Analysis

Statistical analysis was performed by R language 4.4.0. Categorical variables were expressed as absolute and relative frequency (n, %). Quantitative variables were reported as the mean ± standard deviation (SD) when normally distributed, and as medians with interquartile ranges (IQR) in cases of skewed distribution. Means were compared using a matched *t*-test for within-patient pre-to-post treatment, and a two-sample *t*-test for two groups. Medians were compared using a Wilcoxon signed-rank test for within-patient pre-to-post treatment, and a Wilcoxon rank sum test for two groups. Chi-squared test or Fisher's Exact was used to compare the categorical variables. ANCOVA model was used to analyze the differences between two groups with adjustment for age and CKD stages for clinical variables, and age and BMI for body composition variables. We further conducted a subgroup analysis among people using SGLT-2Is only. The differences within subgroups were explored by one-way ANCOVA analysis. A two-tailed *P*-value <0.05 was deemed statistically significant.

# Results

## Baseline Features of Patients

Seventy-three people were included as the overall population, with 61 people only using SGLT-2Is and 12 people using SGLT-2Is and Semaglutide (Figure 1). Regarding the use of SGLT-2Is, most people were on dapagliflozin and 3 (4.9%) people were on empagliflozin. People initiated Semaglutide almost for obesity at least after 3 months of SGLT-2Is use. The maintenance dose of Semaglutide was 0.5–1.0 mg per week. Among 73 patients with T2DM and CKD, 4 (5.5%) people were biopsy-confirmed IgA nephropathy, and 1 (1.4%) were biopsy-confirmed membranous nephropathy.

The baseline clinical characteristics are summarized in Table 1. The average age of included patients was 51.3 ± 9.6 (SD) years, with 82.2% male. The median DM duration was 7.7 ± 5.5 (SD) years. A total of 78.1% of the patients had hypertension. The mean of eGFR was 67.3 ± 24.9 (SD) mL/min/1.73 m2. The median of ACR was 267 (IQR, 98.3–623.2) mg/g. Among them, 20.5% of the subjects were prescribed insulin. The body composition metrics for all the patients were detailed in Table 2. The mean of BMI was 25.9 ± 3.5 (SD) kg/m2. The mean of SMI was 7.6 ± 0.9 (SD) kg/m2.

Compared people in the SGLT-2Is group, people in the SGLT-2Is plus Semaglutide group were generally younger, demonstrated elevated levels of ACR and triglyceride, and exhibited a significantly higher level of BMI, SMI, FMI, BMC, total body water, visceral fat area, and upper limb muscle circumference.

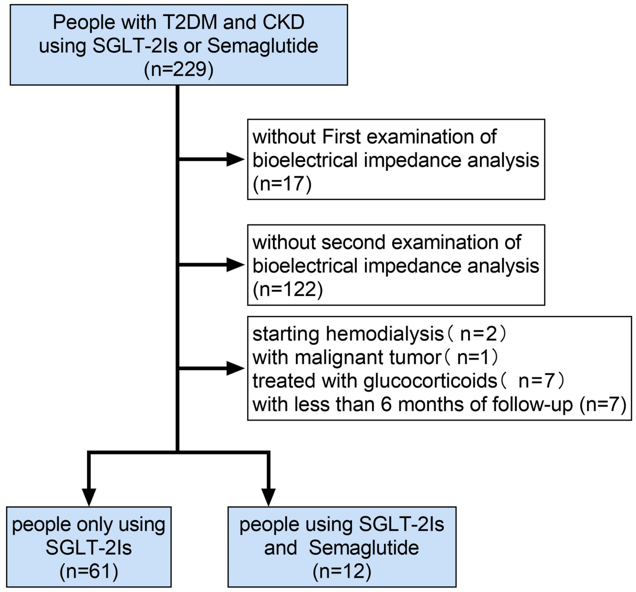


**Figure 1** Flowchart of included patients in this study.
**Abbreviations**: T2DM, type 2 diabetes mellitus; CKD, chronic kidney disease; SGLT-2Is, sodium-glucose co-transporter inhibitors.

## Change of Metabolic Indicators After 6 Months Compared to the Baseline

The changes of metabolic indicators after 6 months were summarized in Table 3. For SGLT-2Is group, serum albumin showed a subtle rise ($P$ = 0.025). For SGLT-2Is plus Semaglutide group, serum albumin was also increased ($P$ = 0.016).

**Table 1** Baseline Clinical Characteristics of Patients with T2DM and CKD Using SGLT-2Is or Using SGLT-2Is Plus Semaglutide

| Variables | Overall (n=73) | SGLT-2Is (n=61) | SGLT-2Is plus Semaglutide (n=12) | *P* |
|---|---|---|---|---|
| Age (mean (SD)), years | 51.3 (9.6) | 52.4 (9.2) | 45.8 (10.2) | **0.028** |
| Sex (male, %) | 60 (82.2) | 51 (83.6) | 9 (75.0) | 0.764 |
| Duration of diabetes (mean (SD)), years | 7.7 (5.5) | 7.1 (4.4) | 10.3 (9.1) | 0.086 |
| Hypertension (%) | 57 (78.1) | 46 (75.4) | 11 (91.7) | 0.388 |
| HbA1c (median [IQR]), % | 6.5 [6.0, 7.0] | 6.5 [6.0, 7.0] | 6.5 [6.1, 7.0] | 0.97 |
| FBS (mean (SD)), mmol/L | 7.2 (1.8) | 7.2 (1.8) | 7.4 (1.5) | 0.67 |
| eGFR (mean (SD)), mL/min/1.73 m2 | 67.3 (24.9) | 65.9 (24.2) | 74.2 (28.4) | 0.296 |
| ACR (median [IQR]), mg/g | 267.0 [98.3, 623.2] | 236.8 [72.7, 468.0] | 623.0 [258.5, 876.8] | 0.06 |
| Triglyceride (median [IQR]), mmol/L | 1.9 [1.3, 2.9] | 1.8 [1.3, 2.6] | 2.8 [1.7, 3.3] | 0.057 |
| Total cholesterol (median [IQR]), mmol/L | 4.3 [3.7, 5.1] | 4.3 [3.7, 5.0] | 4.3 [3.9, 5.7] | 0.512 |
| HDL-C (median [IQR]), mmol/L | 1.2 [1.0, 1.4] | 1.2 [1.0, 1.5] | 1.1 [0.9, 1.3] | 0.448 |
| LDL-C (median [IQR]), mmol/L | 2.3 [1.8, 2.9] | 2.3 [1.9, 2.8] | 2.3 [1.8, 3.2] | 0.699 |
| Serum albumin (median [IQR]), g/L | 47.0 [44.3, 48.4] | 47.1 [44.4, 48.6] | 44.7 [43.9, 47.0] | 0.143 |
| Uric acid (mean (SD)), umol/L | 359.4 (80.5) | 365.8 (74.8) | 327.2 (102.8) | 0.13 |
| Hemoglobin (mean (SD)), g/L | 146.6 (16.6) | 146.3 (16.7) | 148.0 (16.4) | 0.754 |
| Insulin (%) | 15 (20.5) | 13 (21.3) | 2 (16.7) | 1 |
| DDP-4Is (%) | 21 (28.8) | 18 (29.5) | 3 (25.0) | 1 |
| RASIs (%) | 37 (50.7) | 27 (44.3) | 10 (83.3) | **0.031** |
| Lipid-lowering therapy (%) | 32 (43.8) | 26 (42.6) | 6 (50.0) | 0.879 |

**Note**: Bold represents statistical significance.
**Abbreviations**: T2DM, type 2 diabetes mellitus; CKD, chronic kidney disease; SGLT-2Is, sodium-glucose co-transporter inhibitors; HbA1c, glycosylated hemoglobin; eGFR, estimated glomerular filtration rate; ACR, albumin-to-creatinine ratio; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FBS, fasting blood sugar; DDP-4, dipeptidyl peptidase-4; RASIs, renin–angiotensin system inhibitors.

**Table 2** Baseline Body Composition Characteristics of Patients with T2DM and CKD Using SGLT-2Is or Using SGLT-2Is Plus Semaglutide

| Variables | Overall (n=73) | SGLT-2Is (n=61) | SGLT-2Is Plus Semaglutide (n=12) | P |
|---|---|---|---|---|
| Weight (mean (SD)), kg | 70.4 (12.6) | 67.3 (8.9) | 86.5 (16.3) | **<0.001** |
| BMI (mean (SD)), kg/m2 | 25.9 (3.5) | 25.0 (2.8) | 30.5 (3.4) | **<0.001** |
| Total fat mass (median [IQR]), kg | 20.6 [15.1, 24.4] | 19.1 [15.1, 23.2] | 30.9 [23.6, 34.6] | **<0.001** |
| Total muscle mass (mean (SD)), kg | 27.3 (4.6) | 26.5 (3.7) | 31.1 (6.8) | **0.001** |
| Total body water (mean (SD)), L | 36.5 (5.7) | 35.6 (4.5) | 41.4 (8.3) | **0.001** |
| Intracellular water (mean (SD)), L | 22.5 (3.5) | 21.9 (2.8) | 25.4 (5.2) | **0.001** |
| Extracellular water (mean (SD)), L | 14.0 (2.2) | 13.7 (1.7) | 16.0 (3.1) | **<0.001** |
| Extracellular water rate (mean (SD)) | 0.4 (0.0) | 0.4 (0.0) | 0.4 (0.0) | 0.404 |
| Bone mineral content (mean (SD)), kg | 2.8 (0.4) | 2.7 (0.3) | 3.2 (0.7) | **<0.001** |
| SMI (mean (SD)), kg/m2 | 7.6 (0.9) | 7.4 (0.8) | 8.4 (1.0) | **<0.001** |
| FMI (mean (SD)), kg/m2 | 7.6 (2.4) | 7.0 (1.9) | 10.8 (2.4) | **<0.001** |
| Total muscle mass/weight (mean (SD)), % | 38.9 (3.5) | 39.5 (3.3) | 35.8 (3.2) | **0.001** |
| Total fat mass/weight (mean (SD)), % | 29.2 (6.1) | 28.1 (5.7) | 35.1 (5.0) | **<0.001** |
| Fat-to-muscle ratio (mean (SD)) | 0.8 (0.2) | 0.7 (0.2) | 1.0 (0.2) | **<0.001** |
| Waist hip rate (mean (SD)) | 0.9 (0.1) | 0.9 (0.1) | 0.9 (0.1) | **0.007** |
| Visceral fat area (median [IQR]), cm2 | 85.4 [66.4, 106.5] | 81.2 [64.4, 102.3] | 148.6 [108.0, 155.2] | **<0.001** |
| Upper limb muscle circumference (mean (SD)), cm | 27.0 (2.0) | 26.7 (1.8) | 28.9 (2.4) | **<0.001** |

**Note**: Bold represents statistical significance.
**Abbreviations**: T2DM, type 2 diabetes mellitus; CKD, chronic kidney disease; SGLT-2Is, sodium-glucose co-transporter inhibitors; BMI, body mass index; SMI, skeletal muscle index; FMI, fat mass index.

The levels of FBS (−0.88 ± 1.23 (SD) mmol/L, $P$=0.03) and triglyceride (−0.98, (IQR, −1.63–0) mmol/L, $P$ = 0.042) were significantly declined. ACR showed a declining tendency (−200 (IQR, −515– −33) mg/g, $P$ = 0.06). After the adjustment of covariates by ANCOVA models, the increase of serum albumin and uric acid and the reduction of total cholesterol were significant in SGLT-2Is plus Semaglutide group compared with SGLT-2Is groups.

## Change of Body Composition After 6 Months Compared to the Baseline

The changes of body composition after 6 months were presented in Table 3. There was a notable decrease for SGLT-2Is group in total fat mass by −0.6 kg (IQR, 1.7–0.7), total body water by −0.6 kg ± 1.2 (SD) (with a subsequent reduction in extracellular water), total muscle mass by −0.4 kg ± 0.8 (SD), and BMC by −0.03 kg ± 0.1 (SD). SMI, FMI, visceral fat area, and upper limb muscle circumference also decreased ($P$<0.05). FMR showed no significant change.

For SGLT-2Is plus Semaglutide group, a significant reduction was observed in total fat mass (−0.9, IQR (−3.7–0.4) kg), total body water (−1.5 ±1.4 (SD) kg), total muscle mass (−1.1 ±1.2 (SD) kg), and BMC (−0.1 ±0.11 (SD) kg). Additionally, SMI showed significant declines ($P$=0.001), and FMR remained stable.

In both the *t*-test and the ANCOVA test to correct for confounding factors, the SGLT-2Is plus Semaglutide group had more reductions in BMI, FMI and SMI than the SGLT-2Is group (Table 3, Figure 2A–C, Figure S1A and S1C). There was no significant difference in the proportion of total fat mass to weight between the two groups, but the proportion of total muscle mass to weight was increased and higher in SGLT-2Is plus Semaglutide group (Table 3, Figure 2B and D, Figure S1B and S1D). FMR indicated no statistically significant difference between the two groups, with approximately 50% of patients experiencing an increase and 50% experiencing a decrease (Table 3, Figure 2E and F and Figure S1E).

## Subgroup Analysis of Body Composition Changes Within People Only Using SGLT-2Is

Given the significant changes in body composition observed after 6 months of SGLT-2Is treatment, we further explored whether these changes differed across subgroups stratified by age, sex and other covariates (of tertiles). The changes in BMI and FMI were consistent across all subgroups (Figure 3A and B). Although not statistically significant, a greater reduction in SMI was observed in the subgroup with higher baseline SMI (Figure 3C). BMC appeared to decrease less in

**Table 3** Change From Baseline to Over 6 months in Clinical and Body Composition Parameters

| Variable | SGLT-2Is (n=61) | $P^a$ | SGLT-2Is Plus Semaglutide (n=12) | $P^a$ | $P^b$ | $P^c$(ANCOVA) |
|---|---|---|---|---|---|---|
| Δ HbA1c (median [IQR]), % | 0.300 [−0.300, 0.500] | 0.102 | −0.450 [−1.125, −0.150] | 0.056 | **0.011** | 0.092 |
| Δ FBS (mean (SD)), mmol/L | −0.051 (1.749) | 0.821 | −0.881 (1.231) | **0.031** | 0.122 | 0.119 |
| Δ Serum albumin (median [IQR]), g/L | 0.700 [−1.000, 2.100] | **0.025** | 2.450 [0.675, 4.625] | **0.016** | **0.041** | **0.021** |
| Δ Hemoglobin (mean (SD)), g/L | 2.098 (12.506) | 0.195 | 1.667 (10.526) | 0.594 | 0.911 | 0.91 |
| Δ eGFR (mean (SD)), mL/min/1.73 m2 | −1.840 (7.949) | 0.076 | −5.919 (13.716) | 0.163 | 0.159 | 0.163 |
| Δ ACR (median [IQR]), mg/g | −6.400 [−139.100, 89.200] | 0.752 | −200.800 [−514.650, −33.000] | 0.064 | **0.021** | 0.14 |
| Δ Uric acid (mean (SD)), umol/L | 0.197 (69.302) | 0.982 | 66.500 (180.681) | 0.229 | **0.031** | **0.035** |
| Δ Triglyceride (median [IQR]), mmol/L | −0.060 [−0.640, 0.350] | 0.464 | −0.980 [−1.628, 0.000] | **0.042** | 0.065 | 0.474 |
| Δ Total cholesterol (median [IQR]), mmol/L | 0.050 [−0.390, 0.370] | 0.946 | −0.370 [−1.467, 0.072] | 0.092 | 0.066 | **0.039** |
| Δ HDL-C (median [IQR]), mmol/L | 0.050 [−0.070, 0.110] | 0.155 | 0.165 [−0.112, 0.242] | 0.213 | 0.239 | 0.28 |
| Δ LDL-C (median [IQR]), mmol/L | −0.130 [−0.340, 0.220] | 0.221 | −0.290 [−0.907, 0.182] | 0.11 | 0.258 | 0.256 |
| Δ Weight (mean (SD)), kg | −1.333 (1.888) | **<0.001** | −5.700 (8.052) | **0.032** | **<0.001** | **<0.001** |
| Δ BMI (mean (SD)), kg/m2 | −0.720 (1.852) | **0.004** | −2.042 (2.684) | **0.023** | **0.04** | **0.026** |
| Δ Total fat mass (median [IQR]), kg | −0.600 [−1.700, 0.700] | **0.021** | −0.900 [−3.725, 0.400] | **<0.001** | 0.404 | **0.011** |
| Δ Total muscle mass (mean (SD)), kg | −0.390 (0.809) | **<0.001** | −1.067 (1.190) | **0.01** | **0.017** | **0.015** |
| Δ Total body water (mean (SD)), kg | −0.603 (1.176) | **<0.001** | −1.492 (1.415) | **0.004** | **0.024** | **0.023** |
| Δ Extracellular water rates (mean (SD)) | −0.002 (0.004) | **0.003** | −0.002 (0.003) | 0.126 | 0.996 | 0.996 |
| Δ Bone mineral content (mean (SD)), kg | −0.030 (0.112) | **0.045** | −0.095 (0.112) | **0.014** | 0.069 | 0.073 |
| Δ SMI (mean (SD)), kg/m2 | −0.159 (0.238) | **<0.001** | −0.408 (0.320) | **0.001** | **0.003** | **0.002** |
| Δ FMI (mean (SD)), kg/m2 | −0.231 (0.837) | **0.035** | −1.192 (2.310) | 0.102 | **0.013** | **0.012** |
| Δ total muscle mass/weight (mean (SD)), % | 0.242 (1.196) | 0.1193 | 1.197 (2.353) | 0.106 | **0.039** | **0.041** |
| Δ total fat mass/weight (mean (SD)), % | −0.504 (3.345) | 0.2439 | −1.601 (4.421) | 0.236 | 0.329 | 0.331 |
| Δ Fat-to-muscle ratio (mean (SD)) | −0.013 (0.104) | 0.318 | −0.074 (0.174) | 0.168 | 0.107 | 0.11 |
| Δ Waist hip rate (mean (SD)) | 0.002 (0.032) | 0.691 | 0.003 (0.054) | 0.875 | 0.94 | 0.941 |
| Δ Visceral fat area (median [IQR]), cm2 | −1.500 [−8.100, 1.000] | **0.007** | −2.750 [−19.925, 5.875] | 0.38 | 0.899 | 0.077 |
| Δ Upper limb muscle circumference (mean (SD)), cm | −0.302 (0.592) | **<0.001** | −0.450 (1.393) | 0.287 | 0.545 | 0.529 |

**Notes**: [a]comparison between baseline and 6 months later; [b]Comparison of changes between SGLT-2Is group and SGLT-2Is plus Semaglutide group; [c]Comparison of changes between two groups using ANCOVA model adjusted for age and CKD stages for clinical variables, and age and BMI for body composition variables. Bold represents statistical significance.

**Abbreviations**: HbA1c, glycosylated hemoglobin; eGFR, estimated glomerular filtration rate; ACR, albumin-to-creatinine ratio; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FBS, fasting blood sugar; BMI, body mass index; SMI, skeletal muscle index; FMI, fat mass index.


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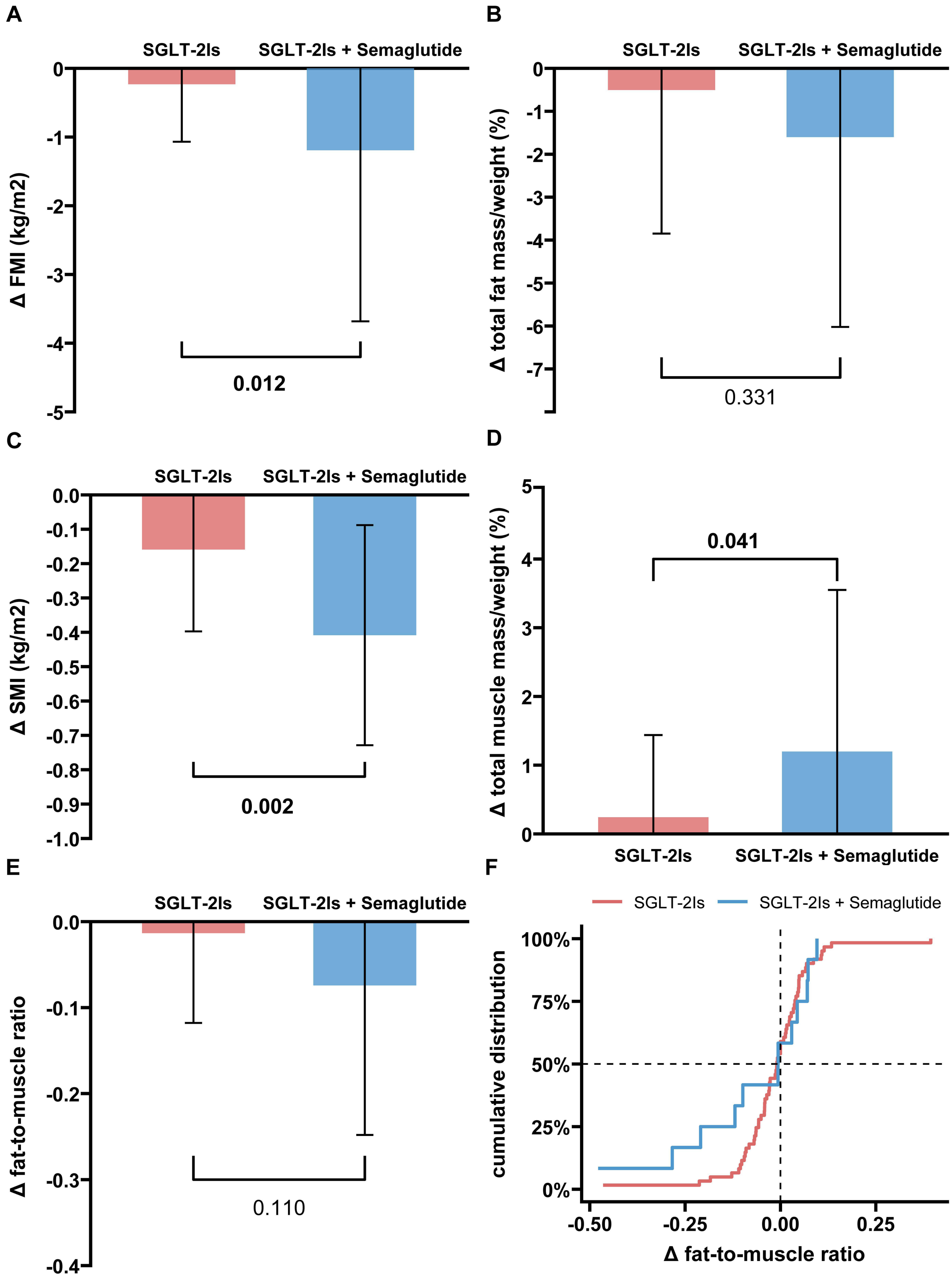


**Figure 2** Changes in fat and muscle parameters after 6 months of SGLT-2Is or SGLT-2Is plus Semaglutide treatment in T2DM and CKD.

**Notes**: average change of (**A**) FMI; (**B**) total fat mass/weight; (**C**) SMI; (**D**) total muscle mass/weight; (**E**) fat-to-muscle ratio; (**F**) cumulative change of fat-to-muscle ratio. *P*-value was using ANCOVA model adjusted for age and body mass index. Bold represents statistical significance.

**Abbreviations**: SGLT-2Is, sodium-glucose co-transporter inhibitors; T2DM, type 2 diabetes mellitus; CKD, chronic kidney disease; FMI, fat mass index; SMI, skeletal muscle index.

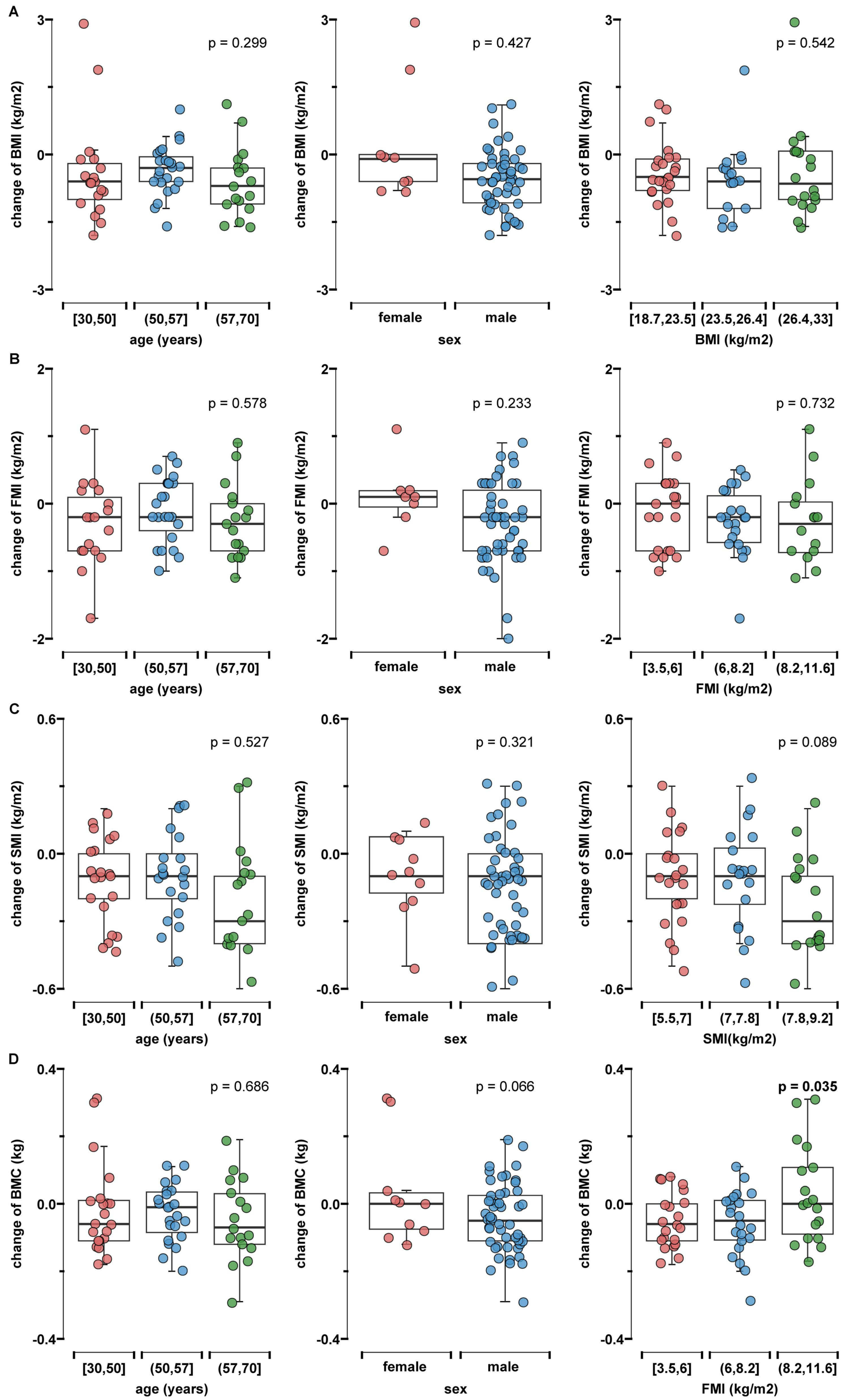


**Figure 3** Continued.

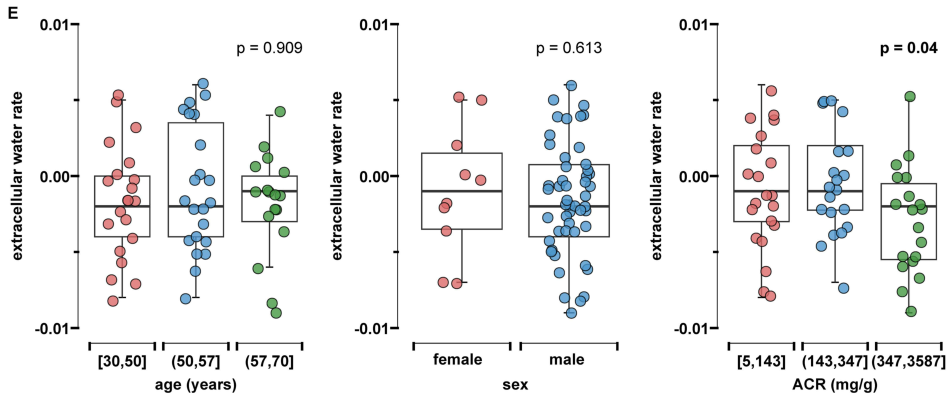


**Figure 3** Change in body compositions after 6 months by different subgroups in patient with T2DM and CKD only using SGLT-2Is.
**Notes**: (**A**) subgroup analysis of BMI; (**B**) subgroup analysis of FMI; (**C**) subgroup analysis of SMI; (**D**) subgroup analysis of BMC; (**E**) subgroup analysis of extracellular water rate. The differences within subgroups were explored by one-way ANCOVA analysis. Bold represents statistical significance.
**Abbreviations**: SGLT-2Is, sodium-glucose co-transporter inhibitors; BMI, body mass index; FMI, fat mass index; SMI, skeletal muscle index; BMC, bone mineral content.

the subgroup with higher FMI (Figure 3D). The extracellular water ratio showed a greater reduction in the group with higher ACR (Figure 3E). Detailed numerical data can be found in Table S1-7.

## Discussion

Age-related clinical manifestations such as wasting and sarcopenia have been recognized as important risk factors in patients with T2DM and CKD.[25,26] Novel antidiabetic agents exhibit varying efficacy in weight reduction, but their impact on sarcopenia remains debated. Potential drug effects on the human body composition cannot be overlooked. To address this issue, we firstly employed BIA to investigate alterations in body composition before and after treatment of SGLT-2Is and Semaglutide in people with T2DM and CKD.

Our study demonstrated that after 6 months treatment with either SGLT-2Is alone or SGLT-2Is combined with Semaglutide, patients with T2DM and CKD exhibited reduction in total fat mass, total muscle mass, total body water, and BMC, without significance of FMR. When comparing treatments, the combination therapy group showed significantly greater reductions in both total fat mass and total muscle mass than the SGLT-2Is alone group. The combination group also led to a greater decrease in the SMI, a key indicator of sarcopenia. However, the combination group achieved a more significant increase in the proportion of muscle relative to total body weight. The results may suggest a preferential loss of fat than muscle with SGLT-2Is-Semaglutide combination therapy.

Our findings are partially consistent with previous reports of Semaglutide in patients with T2DM or obesity. Semaglutide significantly reduces muscle mass but increases the proportion of muscle mass relative to total body weight, with ambiguous changes in bone. In a substudy of SUSTAIN8 (n = 178), weekly injections of 1 mg Semaglutide for 1 year reduced absolute lean body mass but increased the proportion of lean body mass relative to total body weight in T2DM patients.[27] Additionally, a study of 43 obese Chinese patients found no significant changes in SMI or grip strength after 6 weeks of Semaglutide treatment.[28] A systematic review of six studies further confirmed that while Semaglutide reduced absolute lean body mass in overweight or obese patients, the percentage of lean to body weight mass significantly increased, suggesting an overall beneficial effect.[29] Nevertheless, a study of T2DM patients treated with GLP-1RAs (n = 24 with Semaglutide) for 1 year found a significant reduction in femoral and lumbar bone mineral density (BMD) as measured by dual-energy X-ray absorptiometry (DXA), while radiofrequency echo ultrasound (REMS) and bone turnover markers showed neutral results.[30] Moreover, in population at increased risk of fractures (n = 64), 1 year of Semaglutide treatment revealed no significant changes in the bone formative marker, but increase in the bone resorptive marker and inconsistent changes in BMD by sites.[31]

Notably, the present study indicated that 19% of the weight loss induced by Semaglutide is attributed to a reduction in muscle mass. Other studies have suggested that GLP-1RAs can make decline in lean body mass from 20% to 40% weight loss.[32] However, patients with T2DM and CKD often exhibit chronic low-grade inflammation and elevated oxidative


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stress,[33,34] which promote protein breakdown and inhibit muscle synthesis.[35,36] Abnormalities of uremic toxins, vitamin D, and parathyroid hormone in advanced CKD exacerbate muscle loss and bone metabolism disorders.[37–40] A loss of 10% or more of muscle mass is equivalent to the muscle loss associated with 10 or more years of aging.[41] Significant reductions in muscles may adversely affect metabolic health and elevate the likelihood of sarcopenic obesity after discontinuation of treatment.[42] Therefore, when evaluating the fat-reducing benefits of Semaglutide, the negative impact of muscle and BMC loss in specific populations cannot be overlooked.

Current studies indicate that the weight loss effect of Semaglutide reaches a plateau after 6 to 12 months treatment, with most research on body composition changes limited to this timeframe or shorter.[16–19] However, with the long-term use of antidiabetic drugs, aging, and the progression of CKD, these patients may face a higher risk of muscle loss and bone fragility. Whether the trends in muscle mass and BMC stabilize, improve, or worsen after weight stabilization in T2DM and CKD remains unclear and requires further long-term studies. Additionally, research focusing on different high-risk populations will provide more comprehensive evidence for clinical practice.

GLP-1RAs induce weight loss primarily by modulating appetite centers to reduce food intake. However, maintenance of muscle quality during calorie restriction-induced weight loss largely depends on two critical factors: nutritional intake and physical exercise.[43] Adequate intake of high-quality protein and micronutrients should be ensured. Clinical studies have shown that compared to exercise intervention alone, the addition of liraglutide not only enhances weight loss but also improves muscle preservation and attenuates BMD reduction.[44,45] Furthermore, some combination drug therapies exhibit potential muscle reserve function. For instance, Bimagrumab, an antibody blockade of activin type II receptor, promote fat loss while preventing muscle wasting during Semaglutide therapy in obese mice.[46] Safety and efficacy of Bimagrumab and Semaglutide in the overweight is under Phase 2 RCT to examine (NCT05616013). Based on current evidence, it is recommended that patients with T2DM and CKD receiving Semaglutide therapy regularly monitor their body weight. For patients experiencing significant weight reduction, a structured exercise regimen (mainly resistance training) should be emphasized, and protein and micronutrient supplementation should be considered for.

Previous studies on body composition changes associated with SGLT-2Is have primarily focused on individuals with T2DM, mainly showing a reduction in body water or a trend toward fat and muscle loss that lacked statistical significance.[16,17,47,48] Given the larger cohort in our SGLT-2Is group, we conducted an internal subgroup analysis and identified several findings. Among patients treated with SGLT-2Is, those with higher baseline SMI tended to show a greater reduction in SMI after 6 months, while no significant differences were observed across age subgroups. However, a study has reported that patients with T1DM using SGLT-2Is, particularly those with a lower BMI (<23kg/m2) and males over 60 years, experienced more pronounced muscle loss.[49] The possible explanation of our results may be due to the fact that individuals with greater baseline muscle mass tend to lose a higher proportion of muscle during weight loss for an adaptive metabolic response to reduce energy expenditure.[20] In our study, older patients exhibited greater heterogeneity in SMI changes, potentially due to the clinical practice of recommending resistance training to older individuals to preserve sarcopenia, thus resulting in significant interindividual variability in this subgroup. Notably, a case reports an elderly T2DM patient who experienced rapid and severe muscle loss and functional decline while using an SGLT-2Is,[50] underscoring the need for careful monitoring of muscle loss risks in older individuals receiving SGLT-2Is. In subgroups with higher FMI, the reduction in BMC appeared to be less. Traditionally, obesity has been considered protective against fractures, with an inverse relationship between BMI and fracture risk, although excessively high BMI may attenuate this effect.[51] Adipokines such as adiponectin, secreted by adipose tissue, may contribute to bone protection.[52] Furthermore, the extracellular water ratio decreased more significantly in subgroups with higher ACR. Because patients with severer proteinuria often exhibit greater sodium and water retention and interstitial edema.[53] Consequently, the inhibition of sodium reabsorption by SGLT-2Is may lead to more in extracellular water.

Several limitations exist in this study. First, as a retrospective study based on a small cohort, it only assessed short-term outcomes. The SGLT-2Is plus Semaglutide group had a smaller sample size and higher body weight. However, after adjustment using an ANOVA model, statistically significant results were still observed, offering insights for future research. Additionally, since the use of SGLT-2Is is strongly recommended in patients with T2DM-CKD, this study did not include a control group without SGLT-2Is treatment. Second, the study primarily evaluated muscle mass through body composition analysis without multi-scale indicators such as muscle function and pathology. However, by employing multiple metrics, including SMI, percentage changes in muscle mass relative to body weight, and FMR, this study provided relatively robust evidence to support the findings. Third, although older patients and those with low muscle mass probably received additional recommendations for resistance exercise and food, this study did not collect information on exercise or diets that can influence muscle mass. Future research could further investigate the impact of dietary or exercise on body composition in patients with T2DM-CKD using Semaglutide and evaluate their long-term outcomes.

## Conclusion

After 6-month administration of SGLT-2Is or a combination of SGLT-2Is with Semaglutide, patients with T2DM and CKD exhibited reduction in total fat mass, total muscle mass, total body water, and BMC. Compared to the SGLT-2Is group, the combination therapy group showed a greater absolute reduction in muscle mass, but a more increase in muscle mass-to-body weight percent, while the relative ratio of fat to muscle remained unchanged. In the SGLT-2Is group, patients with higher baseline muscle mass experienced greater muscle loss, whereas those with higher fat mass had less bone mineral loss. Further studies with longer treatment periods and a focus on more vulnerable populations are needed.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare that they have no competing interests.

## References

1. de Boer IH, Khunti K, Sadusky T. et al. Diabetes management in chronic kidney disease: a consensus report by the American diabetes association (ADA) and kidney disease: improving global outcomes (KDIGO). *Kidney Int*. 2022;102(5):974–989. doi:10.1016/j.kint.2022.08.012
2. Chen LK, Woo J, Assantachai P, et al. Asian working group for sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Directors Assoc*. 2020;21(3):300–307.e2. doi:10.1016/j.jamda.2019.12.012
3. Izzo A, Massimino E, Riccardi G, Della Pepa G. A narrative review on sarcopenia in type 2 diabetes mellitus: prevalence and associated factors. *Nutrients*. 2021;13(1):183. doi:10.3390/nu13010183
4. Park SW, Goodpaster BH, Lee JS, et al. Excessive loss of skeletal muscle mass in older adults with type 2 diabetes. *Diabetes Care*. 2009;32(11):1993–1997. doi:10.2337/dc09-0264
5. Wilkinson TJ, Miksza J, Yates T, et al. Association of sarcopenia with mortality and end-stage renal disease in those with chronic kidney disease: a UK Biobank study. *J Cachexia Sarcopenia Muscle*. 2021;12(3):586–598. doi:10.1002/jcsm.12705
6. Ribeiro HS, Neri SGR, Oliveira JS, Bennett PN, Viana JL, Lima RM. Association between sarcopenia and clinical outcomes in chronic kidney disease patients: a systematic review and meta-analysis. *Clin Nutr*. 2022;41(5):1131–1140. doi:10.1016/j.clnu.2022.03.025
7. Takahashi F, Hashimoto Y, Kaji A, et al. Sarcopenia is associated with a risk of mortality in people with type 2 diabetes mellitus. *Front Endocrinol*. 2021;12:783363. doi:10.3389/fendo.2021.783363
8. Wolverton D, Blair MM. Fracture risk associated with common medications used in treating type 2 diabetes mellitus. *Am J Health Syst Pharm*. 2017;74(15):1143–1151. doi:10.2146/ajhp160319
9. Isakova T, Nickolas TL, Denburg M, et al. KDOQI US commentary on the 2017 KDIGO clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease–mineral and bone disorder (CKD-MBD). *Am J Kidney Dis*. 2017;70(6):737–751. doi:10.1053/j.ajkd.2017.07.019
10. He C, He W, Hou J, et al. Bone and muscle crosstalk in aging. *Front Cell Dev Biol*. 2020;8:585644. doi:10.3389/fcell.2020.585644
11. American Diabetes Association Professional Practice Committee. 11. chronic kidney disease and risk management: *standards of medical care in diabetes—2022*. *Diabetes Care*. 2022;45(Supplement_1):S175–S184. doi:10.2337/dc22-S011
12. ElSayed NA, McCoy RG, Aleppo G, American Diabetes Association Professional Practice Committee. 11. chronic kidney disease and risk management: standards of care in Diabetes—2025. *Diabetes Care*. 2025;48(Supplement_1):S239–S251. doi:10.2337/dc25-S011
13. Navaneethan SD, Zoungas S, Caramori ML, et al. Diabetes management in chronic kidney disease: synopsis of the KDIGO 2022 clinical practice guideline update. *Ann Intern Med*. 2023;176(3):381–387. doi:10.7326/M22-2904

14. Milluzzo A, Manuella L, Sciacca L. Semaglutide: a game changer for metabolic diseases? *Explor Med*. 2022;3(2):173–180. doi:10.37349/emed.2022.00083
15. Stretton B, Kovoor J, Bacchi S, et al. Weight loss with subcutaneous semaglutide versus other glucagon-like peptide 1 receptor agonists in type 2 diabetes: a systematic review. *Intern Med J*. 2023;53(8):1311–1320. doi:10.1111/imj.16126
16. Koshizaka M, Ishikawa K, Ishibashi R, et al. Effects of ipragliflozin versus metformin in combination with sitagliptin on bone and muscle in Japanese patients with type 2 diabetes mellitus: subanalysis of a prospective, randomized, controlled study (PRIME-V study). *J Diabetes Investig*. 2021;12(2):200–206. doi:10.1111/jdi.13340
17. Matsuba I, Takihata M, Takai M, et al. Effects of 1-year treatment with canagliflozin on body composition and total body water in patients with type 2 diabetes. *Diabetes Obes Metab*. 2021;23(12):2614–2622. doi:10.1111/dom.14508
18. Neeland IJ, Linge J, Birkenfeld AL. Changes in lean body mass with glucagon-like peptide-1-based therapies and mitigation strategies. *Diabetes Obes Metab*. 2024;26(Suppl 4):16–27. doi:10.1111/dom.15728
19. Afsar B, Afsar RE. Sodium-glucose co-transporter 2 inhibitors and sarcopenia: a controversy that must be solved. *Clin Nutr*. 2023;42(12):2338–2352. doi:10.1016/j.clnu.2023.10.004
20. Linge J, Birkenfeld AL, Neeland IJ. Muscle mass and glucagon-like peptide-1 receptor agonists: adaptive or maladaptive response to weight loss? *Circulation*. 2024;150(16):1288–1298. doi:10.1161/CIRCULATIONAHA.124.067676
21. Zhang S, Qi Z, Wang Y, Song D, Zhu D. Effect of sodium-glucose transporter 2 inhibitors on sarcopenia in patients with type 2 diabetes mellitus: a systematic review and meta-analysis. *Front Endocrinol*. 2023;14:1203666. doi:10.3389/fendo.2023.1203666
22. Holmes CJ, Racette SB. The utility of body composition assessment in nutrition and clinical practice: an overview of current methodology. *Nutrients*. 2021;13(8):2493. doi:10.3390/nu13082493
23. American Diabetes Association. 2. classification and diagnosis of diabetes: standards of medical care in diabetes-2018. *Diabetes Care*. 2018;41 (Suppl 1):S13–S27. doi:10.2337/dc18-S002
24. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604–612.
25. Duarte MP, Almeida LS, Neri SGR, et al. Prevalence of sarcopenia in patients with chronic kidney disease: a global systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle*. 2024;15(2):501–512. doi:10.1002/jcsm.13425
26. Mesinovic J, Fyfe JJ, Talevski J, et al. Type 2 diabetes mellitus and sarcopenia as comorbid chronic diseases in older adults: established and emerging treatments and therapies. *Diabetes Metab J*. 2023;47(6):719–742. doi:10.4093/dmj.2023.0112
27. McCrimmon RJ, Catarig AM, Frias JP, et al. Effects of once-weekly semaglutide vs once-daily canagliflozin on body composition in type 2 diabetes: a substudy of the SUSTAIN 8 randomised controlled clinical trial. *Diabetologia*. 2020;63(3):473–485. doi:10.1007/s00125-019-05065-8
28. Xiang J, Ding XY, Zhang W, et al. Clinical effectiveness of semaglutide on weight loss, body composition, and muscle strength in Chinese adults. *Eur Rev Med Pharmacol Sci*. 2023;27(20):9908–9915. doi:10.26355/eurrev_202310_34169
29. Bikou A, Dermiki-Gkana F, Penteris M, Constantinides TK, Kontogiorgis C. A systematic review of the effect of semaglutide on lean mass: insights from clinical trials. *Expert Opin Pharmacother*. 2024;25(5):611–619. doi:10.1080/14656566.2024.2343092
30. Al Refaie A, Baldassini L, Mondillo C, et al. Glucagon-like peptide-1 receptor agonists and diabetic osteopathy: another positive effect of incretines? A 12 months longitudinal study. *Calcif Tissue Int*. 2024;115(2):160–168. doi:10.1007/s00223-024-01240-1
31. Hansen MS, Wölfel EM, Jeromdesella S, et al. Once-weekly semaglutide versus placebo in adults with increased fracture risk: a randomised, double-blinded, two-centre, phase 2 trial. *EClinicalMedicine*. 2024;72:102624. doi:10.1016/j.eclinm.2024.102624
32. Dubin RL, Heymsfield SB, Ravussin E, Greenway FL. Glucagon-like peptide-1 receptor agonist-based agents and weight loss composition: filling the gaps. *Diabetes Obesity Metab*. 2024;26(12):5503–5518. doi:10.1111/dom.15913
33. Vassalle C, Gaggini M. Type 2 diabetes and oxidative stress and inflammation: pathophysiological mechanisms and possible therapeutic options. *Antioxidants*. 2022;11(5):953. doi:10.3390/antiox11050953
34. Ebert T, Neytchev O, Witasp A, Kublickiene K, Stenvinkel P, Shiels PG. Inflammation and oxidative stress in chronic kidney disease and dialysis patients. *Antioxid Redox Signal*. 2021;35(17):1426–1448. doi:10.1089/ars.2020.8184
35. Zhang H, Qi G, Wang K, et al. Oxidative stress: roles in skeletal muscle atrophy. *Biochem Pharmacol*. 2023;214:115664. doi:10.1016/j.bcp.2023.115664
36. Zhang L, Chen Q, Chen Z, et al. Mechanisms regulating muscle protein synthesis in CKD. *J Am Soc Nephrol*. 2020;31(11):2573–2587. doi:10.1681/ASN.2019121277
37. Chang MC, Choo YJ. Effects of whey protein, leucine, and vitamin D supplementation in patients with sarcopenia: a systematic review and meta-analysis. *Nutrients*. 2023;15(3):521. doi:10.3390/nu15030521
38. Romagnoli C, Brandi ML. Muscle physiopathology in parathyroid hormone disorders. *Front Med*. 2021;8:764346. doi:10.3389/fmed.2021.764346
39. Hung KC, Yao WC, Liu YL, et al. The potential influence of uremic toxins on the homeostasis of bones and muscles in chronic kidney disease. *Biomedicines*. 2023;11(7):2076. doi:10.3390/biomedicines11072076
40. Chen H, Lips P, Vervloet MG, van Schoor NM, de Jongh RT. Association of renal function with bone mineral density and fracture risk in the longitudinal aging study Amsterdam. *Osteoporos Int*. 2018;29(9):2129–2138. doi:10.1007/s00198-018-4592-8
41. Locatelli JC, Costa JG, Haynes A, et al. Incretin-based weight loss pharmacotherapy: can resistance exercise optimize changes in body composition? *Diabetes Care*. 2024;47(10):1718–1730. doi:10.2337/dci23-0100
42. Stefanakis K, Kokkorakis M, Mantzoros CS. The impact of weight loss on fat-free mass, muscle, bone and hematopoiesis health: implications for emerging pharmacotherapies aiming at fat reduction and lean mass preservation. *Metabolism*. 2024;161:156057. doi:10.1016/j.metabol.2024.156057
43. Mechanick JI, Butsch WS, Christensen SM, et al. Strategies for minimizing muscle loss during use of incretin-mimetic drugs for treatment of obesity. *Obes Rev*. 2025;26(1):e13841. doi:10.1111/obr.13841
44. Grannell A, Martin WP, Dehestani B, Al-Najim W, Murphy JC, le Roux CW. Liraglutide does not adversely impact fat-free mass loss. *Obesity*. 2021;29(3):529–534. doi:10.1002/oby.23098
45. Jensen SBK, Sørensen V, Sandsdal RM, et al. Bone health after exercise alone, GLP-1 receptor agonist treatment, or combination treatment: a secondary analysis of a randomized clinical trial. *JAMA Network Open*. 2024;7(6):e2416775. doi:10.1001/jamanetworkopen.2024.16775
46. Nunn E, Jaiswal N, Gavin M, et al. Antibody blockade of activin type II receptors preserves skeletal muscle mass and enhances fat loss during GLP-1 receptor agonism. *Mol Metab*. 2024;80:101880. doi:10.1016/j.molmet.2024.101880

47. Zeng YH, Liu SC, Lee CC, Sun FJ, Liu JJ. Effect of empagliflozin versus linagliptin on body composition in Asian patients with type 2 diabetes treated with premixed insulin. *Sci Rep*. 2022;12(1):17065. doi:10.1038/s41598-022-21486-9
48. Sasaki T, Sugawara M, Fukuda M. Sodium-glucose cotransporter 2 inhibitor-induced changes in body composition and simultaneous changes in metabolic profile: 52-week prospective LIGHT (luseogliflozin: the components of weight loss in Japanese patients with type 2 diabetes mellitus) study. *J Diabetes Investig*. 2019;10(1):108–117. doi:10.1111/jdi.12851
49. Yoshimura Y, Hashimoto Y, Okada H, et al. Changes in glycemic control and skeletal muscle mass indices after dapagliflozin treatment in individuals with type 1 diabetes mellitus. *J Diabetes Investig*. 2023;14(10):1175–1182. doi:10.1111/jdi.14054
50. Czarnecka P, Czarnecka K, Tronina O. Unexpectedly rapid onset of severe sarcopenia in an elderly diabetic man following SGLT2i administration: a case report. *J Clin Med*. 2024;13(10):2828. doi:10.3390/jcm13102828
51. Paccou J, Compston JE. Bone health in adults with obesity before and after interventions to promote weight loss. *Lancet Diabetes Endocrinol*. 2024;12(10):748–760. doi:10.1016/S2213-8587(24)00163-3
52. Neumann E, Junker S, Schett G, Frommer K, Müller-Ladner U. Adipokines in bone disease. *Nat Rev Rheumatol*. 2016;12(5):296–302. doi:10.1038/nrrheum.2016.49
53. Doucet A, Favre G, Deschênes G. Molecular mechanism of edema formation in nephrotic syndrome: therapeutic implications. *Pediatr Nephrol*. 2007;22(12):1983–1990. doi:10.1007/s00467-007-0521-3