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Salt Reduction Using a Smartphone Application Based on an Artificial Intelligence System for Dietary Assessment in Patients with Chronic Kidney Disease: A Single-Center Retrospective Cohort Study

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Abstract: This study evaluated the clinical usefulness of an artificial intelligence-powered smartphone application in reducing the daily salt intake of patients with chronic kidney disease (CKD). This study included 35 patients with CKD who were classified into app users (i.e., 13 outpatients who used the app for 3 months and whose salt intake was evaluated before and after using the app) and app nonusers (i.e., 22 outpatients not using the application; their salt intake was similarly evaluated). The primary outcome was estimated as salt intake after 3 months of using the application and at a 6-month follow-up. Linear mixed model analysis revealed that app users had a significant decrease in estimated salt intake after 3 months (-2.12 g/day; 95% CI, -4.05 to -0.19 ; $p = 0.03$) compared with app nonusers but not after 6 months (-0.96 g/day; 95% CI, -3.13 to 1.20 ; $p = 0.38$). App users showed a significant decrease in body mass index at 3 months (-0.42 kg/m² [95% CI, -0.78 to -0.049 ; $p = 0.03$]) and 6 months (-0.65 kg/m² [95% CI, -1.06 to -0.24 ; $p = 0.002$]). The application promoted short-term reduction in salt intake. These results provide a strong rationale for future trials.

Keywords: salt reduction; chronic kidney disease; artificial intelligence; smartphone application; urinary protein



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1. Introduction

Salt restriction in patients with chronic kidney disease (CKD) is important in reducing hypertension, CKD progression, cardiovascular events, and all-cause mortality [1–3]. The Japanese Society of Nephrology recommends limiting salt intake to 3–6 g/day [4]; however, encouraging salt restriction without the patients' knowledge of their actual intake is difficult. In this regard, a questionnaire survey of Japanese hypertensive patients could show the salt intake of salt-conscious patients was only about 1 g/day lower than that of non-salt-conscious patients [5]. Likewise, another study reported that only about 10% of the population among Japanese hypertensive patients had achieved an average salt intake of less than 6 g/day [6].

Therefore, it was hypothesized that the “visualization” of salt intake would be useful to reduce it in patients, having already previously shown that feedback of estimated salt intake from spot urine at every outpatient visit in CKD patients can help them limit their salt intake [7]. The effectiveness of spot urine-guided salt reduction was also described in cardiology outpatients during a short follow-up period [8]. These interventions, however, can only be carried out on an outpatient basis, that is, once a month at most. Therefore, we focused on the artificial intelligence (AI)-based function for meal image analysis using

deep learning with neural networks (<https://dl.sony.com> accessed on 6 September 2022), which calculates the calories and nutrients of a dish via a picture alone, ideally promoting patient awareness regarding their daily salt intake. Moreover, the number of patients using their smartphones, in addition to the smartphone applications targeting patients, has been on the rise, and the use of AI complements/enhances smartphone applications.

This retrospective cohort study aimed to verify the usefulness of a smartphone application, Gohan Coach, developed and brought to market by Kirin Holdings (Tokyo, Japan). The company considered the app to still be in the validation stage and that it was therefore too early to distribute widely for a fee. A test operation period with free usage of the app was provided to patients referred by a limited number of medical institutions, including our clinic. The present study was conducted during this test operation period. The app has an AI-based meal image analysis function based on a validated web application program interface (API) and was the only app that supported Japanese with similar functions to goFOOD™, which was validated for clinical use but does not support Japanese [9]. The accuracy of the analysis was further enhanced by the function that allowed manual input of the information by users, including the amounts and the kinds of food and seasonings consumed. This study evaluated the importance of these functions in reducing salt intake, urinary protein excretion, blood pressure (BP), and body weight (BW) or body mass index (BMI).

2. Materials and Methods

2.1. Study Design and Population

The present study and its protocols were reviewed and approved by the ethics committee of Kitasato University Hospital (Approved number: 20075) and are in accordance with the principles of the Declaration of Helsinki. This was a single-center, retrospective cohort study in which longitudinal changes in clinical parameters, including estimated salt intake, were compared between two groups: patients who used the app and those who did not.

We assessed the eligibility of all stable patients with CKD who were not receiving renal replacement therapy at our clinic during the trial period of the app, i.e., August 2019 to December 2019 ($n = 314$; Figure 1a). In the present study, we defined CKD as an eGFR (<60 mL/min/1.73 m²) and/or markers of kidney damage, including proteinuria, urine sediment abnormalities (including hematuria), and structural abnormalities. In the clinic, CKD outpatients are essentially followed every 3 months, and we strongly asked patients to perform periodical 24 h urine collection to estimate their salt intake. During this period, the patients in the clinic could use the app for free for 3 months. We recruited patients who wanted to use the smartphone application on a clinical basis in August 2019 (not all patients were necessarily recommended the use of the application directly by their doctors), the first month of the trial period of the app. These patients were also asked to perform 24 h urine collection for biochemical tests as much as possible immediately before and after app use to evaluate the clinical usefulness of the app. As such, all the patients in the app user group started using the app in August or September 2019 and stopped using the app in November or December 2019. Additionally, salt intake in the app user group was assessed immediately before and after the 3-month use of the app ($n = 13$; Figure 1b). Conversely, the app nonuser group included patients who did not use the smartphone application and those whose salt intake was estimated at the two outpatient visits conducted during the study period ($n = 22$). It was likely that only a small percentage of the patients, who did not use the app, performed 24 h urine collection during daily clinical practice, given the constraints associated with the collection as well as the additional charges at our clinic (around ¥3000). We assumed that the patients would be able to follow the 24 h urine collection method when using the app as described above, which might have led to the small number of patients choosing to use the app.

Due to the retrospective design of this study, written informed consent to use the application was not obtained. The use of the app by patients was optional. Patients aged

<20 years (n = 7) and who did not visit a doctor (e.g., those who sought vaccination) between August 2019 and December 2019 (n = 15) were excluded as the minimum required clinical data could not be obtained.

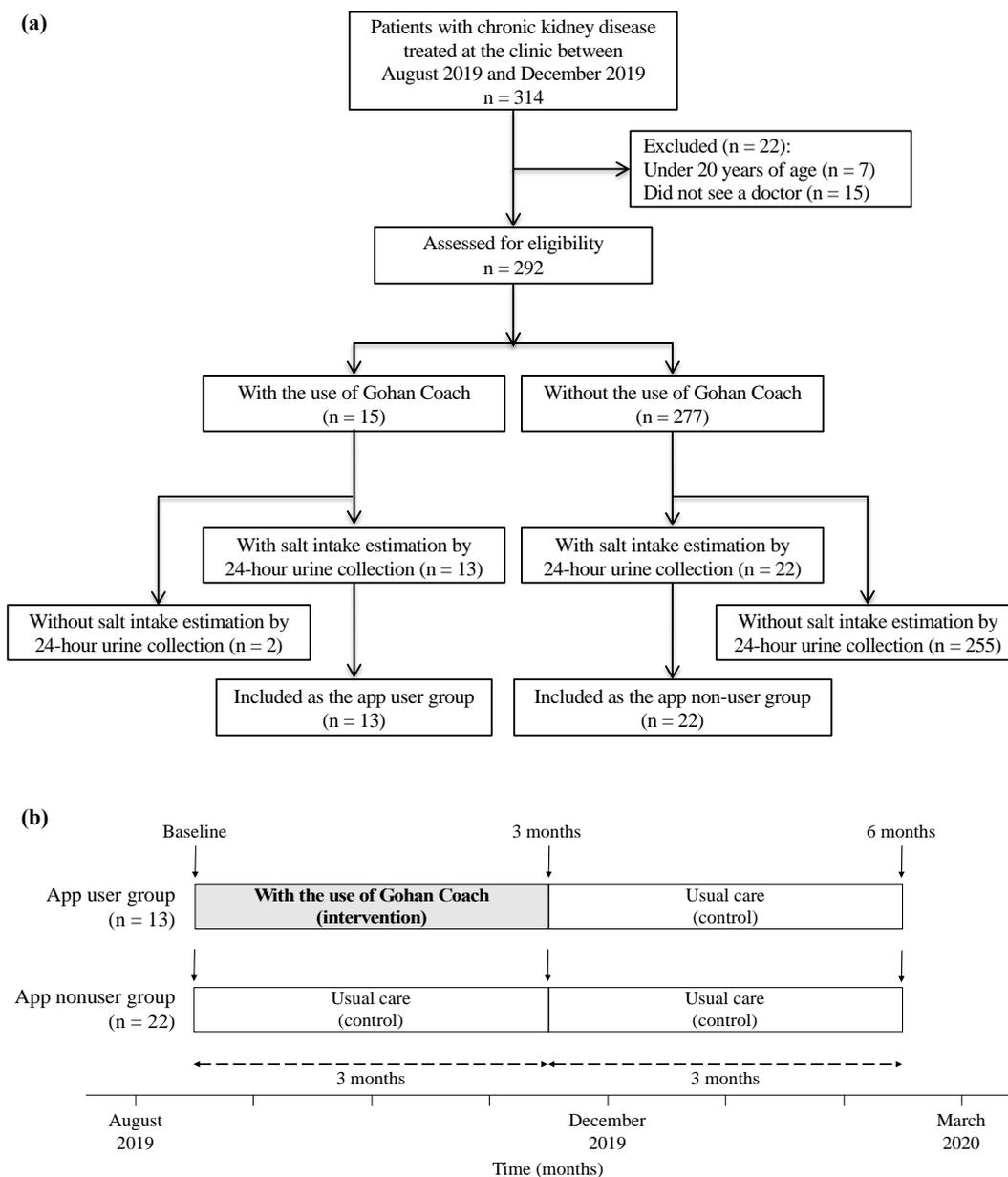


Figure 1. The flowchart of (a) the recruitment process and (b) the study process.

2.2. Outcome Measures and Data Collection

The primary study outcome was change in estimated salt intake assessed with 24 h urine collection. Secondary outcomes were urinary protein excretion, BP, BW, BMI, and estimated glomerular filtration rate (eGFR).

Although 24 h urine collection has been the gold standard for evaluating salt intake, it has limitations including its complexity, difficulty in performing repeated assessments, and the need for assessment of 24 h creatinine excretion to ensure the validity of urine collection, as described in the Scientific Statement of the Japanese Society Hypertension [10]. The Society also describes two methods for 24 h urine collection: (1) whole-urine collection; and (2) collection using a partition cup (Urinemate P, Sumitomo Bakelite Co., Ltd., Tokyo, Japan). The latter requires a rather complex procedure, whereas the collecting container allows

collection outside the home. In this retrospective study, we performed urine collection using a partition cup, with all recruited patients receiving a detailed explanation of the method, and performed 24 h urine collection using the method at least once prior to the commencement of the study. Although we were unable to strictly and prospectively ensure the accuracy of 24 h urinary collection, the accuracy of 24 hr urine collection was assessed by each physician. First, the start and end time points of urine collection were determined to confirm that the duration of urine collection was 24 h and that patients did not miss collecting any urine samples. Second, each physician ensured that the variation in 24 h urinary creatinine excretion and its deviation from the estimated 24 h creatinine excretion was limited to 0.2 g/day [11,12].

In addition, the following demographic data were collected at the time of the first estimation of salt intake (baseline) from medical records according to age, sex, the primary disease for CKD, CKD stage, comorbidities, and the use of antihypertensive drugs. BP was measured twice in a relaxed seated position using an automated device, and the mean BP for each participant was thus used for the analysis. Additionally, BW (kg), height (m), and BMI (kg/m^2) were collected as anthropometric data.

As biochemical data, serum total protein (g/dL), albumin (g/dL), hemoglobin (mg/dL), sodium (mEq/L), potassium (mEq/L), urea nitrogen (mg/dL), creatinine (mg/dL), uric acid (mg/dL), low-density lipoprotein cholesterol (mg/dL), high-density lipoprotein cholesterol (mg/dL), and triglyceride (mg/dL) levels were measured from blood samples. eGFRs were calculated using three-variable Japanese equations, which used serum creatinine levels [13]. The salt intake (g/day) and protein excretion (g/day) estimates were obtained from 24 h urine samples.

2.3. Intervention and Follow-Up

Gohan Coach was developed to provide services tailored to the individual circumstances of the patients, with the patients' goal to more easily and naturally perform their dietary management, which plays a key role in disease management. Patients in the app user group recorded the contents of each meal on the app and were critiqued weekly, through automatically generated feedback from the application, on their estimated salt, protein, and total energy intake, the target intakes of which were based on guidelines for CKD stage and the presence of diabetes [4,14] (Figure 2). Patients first took a photo of their dishes, which the AI automatically analyzes for the nutrient content. This AI-based meal image analysis function was based on the web API "Calorie Check API" (<https://iot.sonymnetwork.co.jp/service/caloriecheck/> accessed on 6 September 2022, in Japanese). Calorie Check API was developed by Sony Network Communications Inc. (Tokyo, Japan), which has been conducting research and development on machine learning since before 2000 and has created its own unique meal image analysis technology. The meal content is analyzed for nutrient information derived from a food composition database of about 110,000 items (<https://www.eatsmart.co.jp/service/> accessed on 6 September 2022, in Japanese) provided by Eat Smart, Inc. (Tokyo, Japan). Subsequently, the menu, ingredients, and amount are displayed on the Gohan Coach app. Considering that it is impossible (1) to grasp the amount of food and (2) determine the differences in seasoning from meal images alone, a function that enables patients to modify the information manually if necessary was added to Gohan Coach. Therefore, the accuracy of the output data mostly depends on the accuracy of the patients' inputs. Theoretically, the nutrients and calories, including salt content, in the meals should be accurate, provided that the meal information is properly entered in the app. Based on the results of each registration (numerical values), an algorithm-based critique and feedback report, specifically on the salt, energy, and protein content, is provided. This algorithm itself is not AI-based but generates a feedback report in response to changes from the previous week in the parameters determined from the data entered by the patients, such as salt intake, calories, BP, and BW, or based on a comparison with individual target values of the parameters. This feedback was sent to the patients on a weekly basis (e.g., the salt intake was lower than that of last week, but did not reach the

target value of 6 g/day) (Figure 2). Instructions on how to use the application were given only during the outpatient visit when the patients started using the app, according to the manufacturer's instructions.

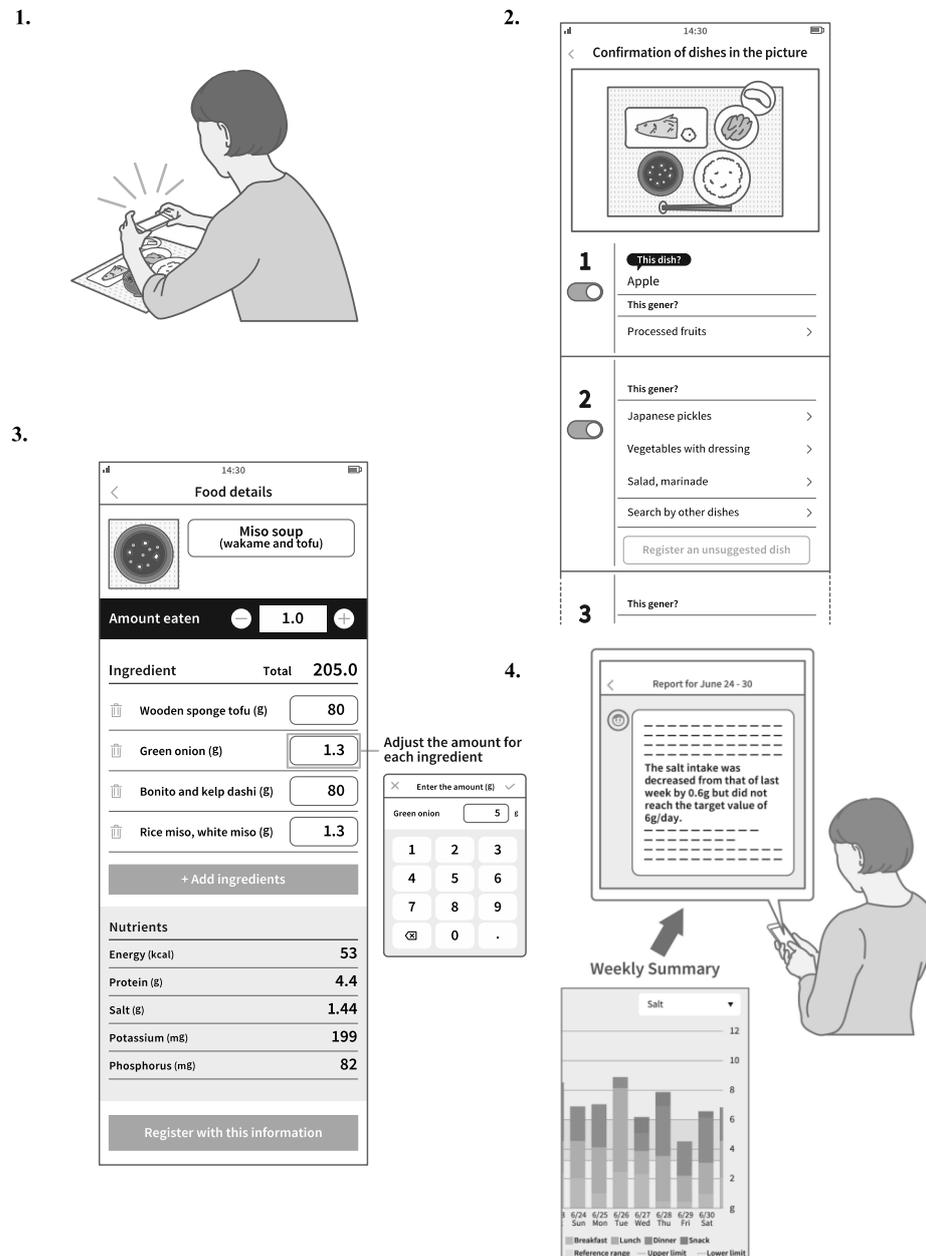


Figure 2. The flow of how to use the artificial intelligence-powered smartphone application, Gohan Coach. (1) The patients take a picture of their dishes. (2) Artificial intelligence automatically analyzes the meal from the photo. The meal content can be manually modified by the patients themselves as necessary and recorded. (3) The meal content is then linked to the amount of nutrients indicated in a food composition database. Then, the amount and ingredients are manually changed as necessary by the patients and recorded. Therefore, the accuracy of the output data mostly depends on the accuracy of patients' inputs. (4) Based on the information registered for each meal (numerical values), algorithm-based feedback specifically reports on the salt, energy, and protein intakes; blood pressure; and body weight. This algorithm generates a feedback report in response to certain changes in those parameters recorded in the previous week as determined from the data input by the patients or as compared with the individual target values of the parameters. A weekly report is created and sent to the patients.

Only the patients in the app user group used the application for the 3 months between the first (0 month/baseline) and second (3 months/intervention phase) salt intake assessments performed at the corresponding outpatient visit. The patients in the app user group did not receive any interventions such as seeing a nutritionist outside the service of the application. The patients in the app nonuser group received the usual care from nephrologists with instructions on salt reduction (as did the case group) but did not receive intervention from nutritionists (Figure 1b). Furthermore, patients in both the app user and nonuser groups were followed up until the next outpatient visit (6 months from the baseline/maintenance phase). Measurements of BP and anthropometric and biochemical data were repeated at the 3-month and 6-month milestones.

2.4. Statistical Analyses

As this study was a retrospective study rather than a prospective study, a definitive sample size calculation was not performed. Instead, an a priori power analysis was performed as follows: the effect size was 1.05, which was calculated from the difference in salt intake between groups in a randomized controlled trial assessing the effectiveness of sodium restriction in patients with CKD [15] and from the standard deviation (SD) of the estimated salt intake determined according to the results of the control and intervention groups in a Japanese cohort [7]. In the present study, 13 and 22 patients were enrolled in the app user and app nonuser groups, respectively. We determined that the a priori statistical power of the study was 0.83, which was calculated using G*Power for Mac (ver. 3.1.9.4) [16] with a two-tailed significance value of 0.05 and an effect size of 1.05.

All continuous variables are expressed as means \pm SD after confirming their normality by using the Shapiro–Wilk test, and binary variables are expressed as numbers with percentages. The unpaired Student's *t*-test (continuous variables) and Fisher's exact test (binary variables) were used to compare the parameters between the groups. Additionally, the paired *t*-test was performed to compare continuous variables within each group.

For the pivotal analysis of this study, we primarily analyzed the effect of the study group over time using linear mixed models to assess the association of the use of Gohan Coach with the primary and secondary outcomes [15,17] considering the potential differences in the characteristics between the app user and app nonuser groups and missing data at 6 months. These models included the following fixed effects: group, time (baseline and 3 and 6 months), age, sex, and baseline eGFR, given the well-accepted and reported notion that age, sex, and eGFR affect sodium intake [18,19]. Models were additionally adjusted for the baseline value of each dependent variable so that the estimates presented would be more precise. An interaction term was also included as a fixed effect, time \times group, which indicated the effect of the study group over time, and the models included the number of participants as a random effect.

The SPSS software for Mac (ver. 26; IBM Corp., New York, NY, USA) was used to perform all statistical analyses, and $p < 0.05$ indicated statistical significance.

3. Results

3.1. Baseline Characteristics

Table 1 summarizes the baseline clinical characteristics of the study participants and the comparison between the app user and the nonuser groups according to their respective interventions of the Gohan Coach application (Table 1). There were no statistically significant differences in demographic, anthropometric, and biochemical data between the groups.

Among the patients who used the application, age, sex, BW, eGFR, and BP did not significantly vary between patients who did not perform urine collection ($n = 2$, 1 male, 50.0 ± 8.5 years) and those who did (app user group). Patients who did not perform the 24 h urinary collection were excluded from the analysis, regardless of whether they were app users or nonusers.

Table 1. Baseline characteristics of the study population and a comparison between the app user and app nonuser groups.

Variables	Total (n = 35)	App Nonuser Group (n = 22)	App User Group (n = 13)	p Value	t Value
Age (years)	60.5 ± 15.0	63.3 ± 15.9	55.8 ± 12.7	0.15	1.47
Male/female	21/14 (60/40%)	13/9 (59/41%)	8/5 (62/38%)	1	–
Body weight (kg)	65.6 ± 15.0	64.2 ± 15.7	68.1 ± 13.9	0.46	–0.75
Body mass index (kg/m ²)	24.0 ± 3.8	23.6 ± 3.8	24.8 ± 3.8	0.35	–0.95
CKD stages					
2	11 (31%)	8 (36%)	3 (23%)	0.43	–
3a	11 (31%)	6 (27%)	5 (38%)	0.71	–
3b	3 (9%)	1 (5%)	2 (15%)	0.54	–
4	10 (29%)	7 (32%)	3 (23%)	0.71	–
Comorbidity					
Hypertension	26 (74%)	16 (73%)	10 (77%)	1	–
Diabetes	13 (37%)	9 (41%)	4 (31%)	0.72	–
Cardiovascular disease	3 (9%)	2 (9%)	1 (8%)	1	–
Arrhythmia	5 (14%)	4 (18%)	1 (8%)	0.63	–
Cerebrovascular disease	0 (0%)	0 (0%)	0 (0%)	1	–
Malignancy	0 (0%)	0 (0%)	0 (0%)	1	–
Use of antihypertensive drugs					
Calcium channel blocker	13 (37%)	7 (32%)	6 (46%)	0.48	–
RAS inhibitor	18 (51%)	11 (50%)	7 (54%)	1	–
Diuretics	2 (6%)	0 (0%)	2 (15%)	0.13	–
Number of prescribed antihypertensive drugs					
0	15 (42%)	10 (45%)	5 (38%)	0.74	–
1	8 (23%)	6 (27%)	2 (13%)	0.68	–
2	11 (31%)	6 (27%)	5 (38%)	0.71	–
3	1 (3%)	0 (0%)	1 (7%)	0.37	–
Systolic blood pressure (mmHg)	132.0 ± 14.6	132.4 ± 12.6	131.4 ± 18.1	0.85	0.19
Diastolic blood pressure (mmHg)	76.9 ± 12.0	75.7 ± 9.5	78.8 ± 15.6	0.47	–0.74
Mean blood pressure (mmHg)	95.3 ± 11.0	94.6 ± 8.2	96.4 ± 15.0	0.66	–0.45
Total protein (g/L)	7.2 ± 0.4	7.1 ± 0.4	7.3 ± 0.4	0.08	–1.81
Albumin (g/dL)	4.3 ± 0.3	4.2 ± 0.3	4.4 ± 0.2	0.07	–1.90
Hemoglobin (g/dL)	13.2 ± 1.7	13.2 ± 1.9	13.2 ± 1.4	1	0.0027
Sodium (mEq/L)	141.3 ± 1.9	141.6 ± 1.6	140.8 ± 2.3	0.26	1.14
Potassium (mEq/L)	4.1 ± 0.5	4.0 ± 0.5	4.2 ± 0.4	0.46	–0.74
Urea nitrogen (mg/dL)	22.0 ± 13.8	22.2 ± 13.2	21.7 ± 15.2	0.92	0.10
Creatinine (mg/dL)	1.36 ± 0.75	1.35 ± 0.76	1.38 ± 0.76	0.91	–0.12
eGFR (mL/min/1.73 m ²)	50.9 ± 23.4	52.3 ± 24.4	48.7 ± 22.3	0.67	0.43
Low-density lipoprotein cholesterol (mg/dL)	99.5 ± 29.4	98.9 ± 26.8	100.5 ± 34.6	0.88	–0.16
High-density lipoprotein cholesterol (mg/dL)	62.9 ± 20.3	64.9 ± 22.5	60.8 ± 18.5	0.62	0.50
Triglyceride (mg/dL)	131.7 ± 56.6	128.9 ± 59.3	136.5 ± 53.8	0.71	–0.38
Estimated salt intake (g/day)	7.86 ± 2.70	7.26 ± 2.57	8.87 ± 2.71	0.09	–1.76
Urinary protein (g/day)	0.54 ± 0.83	0.48 ± 0.67	0.63 ± 1.06	0.61	–0.52

Continuous variables are expressed as mean ± standard deviation and binary variables as numbers (percentage). Abbreviations: CKD, chronic kidney disease; RAS, renin-angiotensin system; eGFR, estimated glomerular filtration rate.

As indicated in the inclusion criteria, all participants were followed up at 3 months with a 24 h urine collection. However, several patients refused to perform 24 h urine collection ($n = 6$) and/or to visit the clinic partly because of the coronavirus disease 2019 pandemic ($n = 2$) at 6 months. Eventually, 12 patients in the app user group and 17 patients in the nonuser group were followed up until 6 months. No patients died, were transferred to other clinics, or changed their antihypertensive agents during the follow-up period.

Based on the login records of the 11 patients, 7 used the app for the entire 3 months, 2 used it for 2–3 months, and 2 used it for only ≤ 2 months. Additionally, among the eight patients who set behavioral goals as a purpose for using the application, seven achieved them using the app. Analyses were performed for all patients, comparing the app user group with the app nonuser group, without considering adherence and achievement of goals. There were no questions or complaints regarding the usability of the app from study participants, although we did not quantitatively assess the usability of the app with scientifically validated tools.

3.2. Within-Group Comparison on Salt Reduction

The results of the intra-group comparisons on the primary outcome are shown in Table 2 (baseline and 3 months) and Table S1 (baseline and 6 months). Estimated salt intake tended to decrease from baseline to 3 months in the app user group ($p = 0.09$), but no difference was observed between baseline and 6 months. Three-month changes in estimated salt intake were -1.17 ± 2.31 g/day and 0.96 ± 2.57 g/day in the app user group and nonuser group, respectively, and the effect size was calculated as 0.87. Using this effect size, an error of 0.05, and the sample size of the present study, the post hoc power of the unpaired t -test was calculated as 0.68.

Linear mixed models confirmed that the estimated salt intake with the estimated marginal mean in the app user group changed from 8.29 ± 0.56 g/day at baseline to 7.12 ± 0.56 g/day at 3 months and 7.95 ± 0.63 g/day at 6 months, whereas 7.70 ± 0.43 , 8.65 ± 0.43 , and 8.32 ± 0.57 g/day were registered in the nonuser group, respectively (Figure 3). Furthermore, although the app user group demonstrated a mean change of -2.12 g/day (95% confidence interval [CI], -4.05 to -0.19 ; $p = 0.03$) in estimated salt intake at 3 months as compared with the app nonuser group, the significant difference diminished at 6 months, which is the maintenance phase (-0.96 g/day [95% CI, -3.13 to 1.20 ; $p = 0.38$]).

Table 2. Within-group comparisons of parameters obtained at baseline and after 3 months.

	App User Group			App Nonuser Group		
	Baseline (0 Months)	3 Months	p Value	0 Months	3 Months	p Value
Estimated salt intake (g/day)	8.87 ± 2.71	7.71 ± 2.81	0.09	7.26 ± 2.57	8.21 ± 3.21	0.1
Urinary protein (g/day)	0.63 ± 1.06	0.41 ± 0.81	0.07	0.47 ± 0.67	0.49 ± 0.65	0.83
Systolic blood pressure (mmHg)	131.9 ± 18.1	127.2 ± 14.8	0.23	132.4 ± 12.6	135.6 ± 9.2	0.18
Diastolic blood pressure (mmHg)	78.8 ± 15.6	73.9 ± 14.4	0.03	75.7 ± 9.5	78.4 ± 10.5	0.23
Mean blood pressure (mmHg)	96.4 ± 15.0	91.7 ± 13.5	0.07	94.6 ± 8.2	97.5 ± 7.8	0.18
Body weight (kg)	68.1 ± 13.9	67.3 ± 14.4	0.08	64.2 ± 15.7	64.4 ± 15.2	0.51
Body mass index (kg/m^2)	24.8 ± 3.8	24.5 ± 4.0	0.07	23.6 ± 3.8	23.7 ± 3.7	0.4
eGFR ($\text{mL}/\text{min}/1.73 \text{ m}^2$)	48.7 ± 22.2	48.1 ± 22.2	0.71	52.3 ± 24.4	52.2 ± 24.7	0.43

Data are expressed as mean \pm standard deviation. eGFR, estimated glomerular filtration rate.

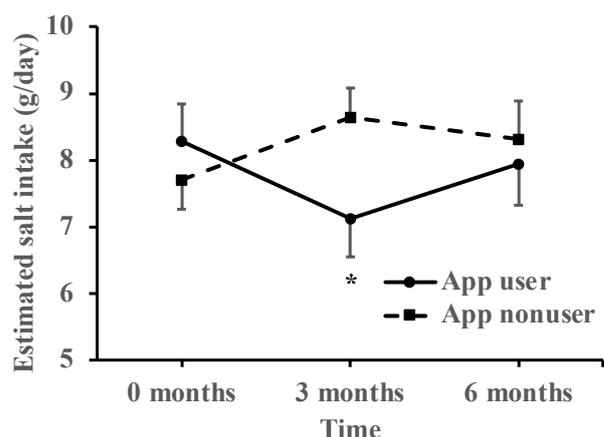


Figure 3. Salt intake estimated by 24 h urine collection at baseline after the use of the Gohan Coach application (3 months) and during the maintenance phase (6 months). * p value = 0.03 versus control group. Error bars represent standard error of mean.

3.3. Within-Group Comparisons on Secondary Outcomes

From baseline to 3 months in the app user group, urinary protein, MBP, BW, and BMI tended to decrease ($p = 0.07, 0.07, 0.08,$ and $0.07,$ respectively), whereas diastolic BP (DBP) significantly decreased ($p = 0.03$) (Table 2). However, BW and BMI significantly increased ($p = 0.02$ for both), whereas eGFR significantly decreased ($p = 0.01$), from baseline to 6 months in the app nonuser group (Table S1).

The app user group showed a trend to decrease in the mean change in the urinary protein of -0.23 g/day (95% CI, -0.46 to 0.0026 ; $p = 0.05$) at 3 months, which persisted at 6 months (-0.27 g/day; 95% CI, -0.55 to 0.0052 ; $p = 0.05$) (Table 3). Diastolic and mean BP also tended to decrease with the intervention at 3 months [-7.60 mmHg (95% CI, -15.62 to 0.41 ; $p = 0.06$) and -7.57 mmHg (95% CI, -15.32 to 0.18 ; $p = 0.06$), respectively], but the impact of these changes decreased at 6 months [-5.98 mmHg (95% CI, -15.35 to 3.38 ; $p = 0.21$) and -4.50 mmHg (95% CI, -13.61 to 4.61 ; $p = 0.33$), respectively]. BW (-0.42 kg/ m^2 ; 95% CI, -0.78 to -0.049 ; $p = 0.03$) and BMI (-1.06 kg; 95% CI, -2.05 to -0.059 ; $p = 0.04$) significantly decreased in the app user group at 3 months, which persisted at 6 months (BW: -0.65 kg/ m^2) (95% CI, -1.06 to -0.24 ; $p = 0.002$) and BMI: -1.75 kg (95% CI, -2.89 to -0.61 ; $p = 0.003$).

Table 3. Linear Mixed-Effects Model for the use of the Gohan Coach Smartphone Application.

	App User Group *			App Nonuser Group *			Effect of Intervention †			
	0 Months	3 Months	6 Months	0 Months	3 Months	6 Months	$\Delta 0-3$ mo	P Value	$\Delta 0-6$ mo	P Value
Estimated salt intake (g/day)	8.29 ± 0.56	7.12 ± 0.56	7.95 ± 0.63	7.70 ± 0.43	8.65 ± 0.43	8.32 ± 0.57	-2.12 ± 0.96	0.03	-0.96 ± 1.08	0.38
Urinary protein (g/day)	0.56 ± 0.08	0.34 ± 0.08	0.26 ± 0.09	0.57 ± 0.06	0.58 ± 0.06	0.55 ± 0.08	-0.23 ± 0.12	0.05	-0.27 ± 0.14	0.05
Systolic blood pressure (mmHg)	132.0 ± 3.2	127.7 ± 3.2	131.1 ± 4.1	132.0 ± 2.5	135.3 ± 2.5	132.7 ± 3.3	-7.5 ± 5.4	0.17	-1.6 ± 6.3	0.8
Diastolic blood pressure (mmHg)	78.1 ± 2.3	73.2 ± 2.3	76.8 ± 2.9	76.5 ± 1.8	79.2 ± 1.8	81.2 ± 2.4	-7.6 ± 4.0	0.06	-6.0 ± 4.7	0.21
Mean blood pressure (mmHg)	96.1 ± 2.3	91.4 ± 2.3	94.9 ± 2.9	95.0 ± 1.8	97.8 ± 1.8	98.3 ± 2.4	-7.6 ± 3.9	0.06	-4.5 ± 4.6	0.33
Body weight (kg)	63.9 ± 1.4	63.0 ± 1.4	63.3 ± 1.4	64.9 ± 1.1	65.1 ± 1.1	66.0 ± 1.2	-1.1 ± 0.5	0.04	-1.8 ± 0.6	0.003
Body mass index (kg/ m^2)	24.1 ± 0.1	23.8 ± 0.1	23.9 ± 0.1	24.1 ± 0.1	24.2 ± 0.1	24.5 ± 0.1	-0.4 ± 0.2	0.03	-0.7 ± 0.2	0.002
eGFR (mL/min/1.73 m^2)	49.4 ± 0.9	48.8 ± 0.9	47.6 ± 0.9	49.5 ± 0.7	49.0 ± 0.7	46.8 ± 0.9	-0.1 ± 1.6	0.96	0.8 ± 1.4	0.56

* Estimated marginal mean and standard error. † Effect of interaction term time \times group with standard error. Abbreviations: eGFR, estimated glomerular filtration rate; $\Delta 0-3$ mo, change between 0 and 3 months; $\Delta 0-6$ mo, change between 0 and 6 months.

4. Discussion

Apart from the importance of salt restriction in patients with CKD [1–3], the evaluation of their salt intake and the patients' education in salt restriction is left to each medical facility, requiring continuous efforts and the precious time of medical staff and facilities. Even though several trials evaluating various interventions to reduce patients' salt intake were able to demonstrate that these interventions were effective in reducing the patient's salt intake by approximately 2 g/day in a relatively short period [15,17,20–22], these salt-reducing effects are proved to diminish after long-term tracking, even in highly motivated patients who are willing to participate in clinical trials [15,17,20], making it easy to understand how difficult it is to instruct patients how to reduce their salt intake in a daily clinical practice context. Meanwhile, our groups and other groups have raised the relevance of visualizing salt intake by providing frequent feedback on salt intake estimates during outpatient visits [7,8]. It is therefore desirable to create and use a uniform salt restriction tool that includes the visualization of salt intake so as to improve the efficiency and the quality of daily clinical practices.

In the present study, we focused on Gohan Coach, a smartphone application with AI-based image recognition systems that estimates the amount of nutrients such as salt in each meal and that provides an algorithm that provides weekly critiques of meals based on the estimated nutrient content. As many Japanese foods are seasoned with salt, soy sauce, or soybean paste, we believe that dietary sodium restriction is particularly challenging for Japanese people who are not aware of their actual salt intake. A previous Japanese study reported that awareness of the need for salt restriction led to only approximately a 1 g/day reduction in urinary salt excretion [5]. A separate Japanese study reported that only around 10% of patients achieved an average urinary salt excretion of less than 6 g/day [6]. Based on these findings, we previously posited that "visualization" of salt intake has utility in reducing salt intake in patients with CKD [7], and such an application allows patients to be aware of their daily estimated salt intake in a timely manner and to receive feedback on their diet on a weekly basis, which is more frequent than can be provided on an outpatient basis. In contrast, the impact of app use on salt reduction was not sustained at the 6-month follow-up visit after the end of the 3-month period of app use, as described in previous trials [15,17]. Further studies are warranted to examine whether continued use of the app or transition to other interventions at the end of the period of app use lead to sustained salt intake reductions.

In contrast to the app user group, salt intake, urinary protein, BP, and BW with BMI in the app nonuser group were maintained or slightly increased from baseline to 3 and 6 months after, which occurred during the transition from the warm (baseline) to cold (3 and 6 months) season in Japan. A similar seasonal pattern, especially an increase in the intake or urinary excretion of salt, from warm to cold seasons, had been well documented in CKD patients and in healthy individuals [23–25]. Simultaneously, a slight increase in salt intake from baseline to 3 months in the app nonuser group suggested that the instruction related to salt reduction, provided during daily clinical practice was extremely inadequate, which is the reason why several trials with various interventions have aimed to reduce the patients' salt intake [15,17,20–22]. The decrease in urinary protein and BW with BMI persisted during the maintenance period after the patients had finished using the application, and the extent of reduction in estimated salt intake and BP were attenuated as they were in previous trials [15,17,20], indicating that the app or other interventions to reduce salt intake were effective in the short term but might prove insufficient for promoting behavioral change in the long term. Although a BP drop of approximately -7.50 mmHg at 3 months in this study was relatively high, the BP variation among patients and the small sample size contributed to the lack of statistically significant changes between the groups. While similar discrepancies were admitted in the previous trial, it is difficult to determine for certain the reason for this discrepancy, in which decreases in urinary protein excretion and BW persisted after the intervention in spite of a disappearance of the salt reduction effect [15]. Given that our application automatically estimates the amount of salt and

calories in every meal and sends feedback on the data to the patients, the patients using the application likely consequently reduced both their calorie and salt intakes, which would have contributed to the decreases in BW and BMI [26]. From these results regarding dietary habit modifications, salt reduction is expected to be more difficult to sustain than calorie restriction. In addition to salt intake, being overweight is closely associated with proteinuria and CKD progression [27,28], so the maintenance of the reduction in urinary protein admitted in our study and in the previous trial might be due to the sustained decrease in BW and BMI. The decreases in BW in the app user group at 3 and 6 months are comparable to that of a previous trial on salt reduction [15]; however, the clinical significance of such decreases in BW with BMI observed in this study, which did not necessarily include obese patients, remains uncertain and should be investigated in future studies.

Nowadays, the number of patients using their smartphones is on the rise, and we can expect a corresponding increase in the number of smartphone applications targeting patients with CKD [29]. Two small observational studies suggested the feasibility, acceptability, and clinical usefulness of a smartphone-based self-management system in patients with advanced CKD [30] and remote dietary counseling by means of smartphone applications in patients with mild CKD [31], respectively. Although the patients included in these studies were relatively young with a mean age of approximately 60 years, the findings of the present study corroborate the results of these studies. However, the “digital divide” is an issue that cannot be ignored in healthcare, and it is important to take human factors into account when assessing the utility of smartphone applications [32]. Accordingly, the usefulness and feasibility of smartphone applications, particularly among elderly patients, remain unclear. Further studies should aim to include more diverse patient populations that include a greater proportion of elderly patients.

This study has several limitations. First, this was a retrospective study. Although adjustments were made for several baseline parameters in clarifying the usefulness of Gohan Coach, the presence of various biases was unavoidable. Although no significant differences in background characteristics were observed between the two groups, this perceived balance may have been due to the small sample size. At the same time, all selected patients in both the app user and nonuser groups, who performed troublesome 24 h urine collection during daily clinical practice throughout the study period, had undergone 24 h urine collection at least once prior to the start of the study. Therefore, potential confounders, including treatment adherence, might also be similar between the two groups. Moreover, the patients’ satisfaction with the app, trust, and implementation of the app’s recommendations are important aspects for analyzing the effects of the app. Unfortunately, we did not obtain the data systematically. Second, this pilot study was conducted in a single center with a small sample size, which might lead to the lack of significant changes in some of the parameters, such as urinary protein and BPs. Actually, a post hoc power analysis for the unpaired *t*-test to compare the 3-month change in estimated salt intake (the primary outcome) between the groups was calculated as 0.68, which indicated insufficient power (<0.80) to overcome the risk of type II error. In addition, the number of subjects was too small to represent CKD patients. Third, long-term follow-up is necessary to demonstrate the impact of the application on cardiovascular events or mortality, but not on the surrogate markers that include estimates of salt intake. Finally, due to the nature of this retrospective study, the frequency of using the application as well as the amount of protein intake that can be estimated from 24 h urine collection was evidently unavailable. Furthermore, at this time, the AI-based meal image analysis function of the application is unable to estimate the amount of food consumed or the amount of seasoning used. Therefore, the accuracy of the estimated salt intake and other data mostly depended on the accuracy of patients’ inputs. Although this manual modification function would improve the accuracy of those estimations, it could simultaneously make the analysis and the results of this study more subjective. Despite these limitations on the use of the application, we found significant differences in the analyses of the parameters of interest.

5. Conclusions

We demonstrated the potential utility of the smartphone application with an AI-based image recognition system Gohan Coach in the short-term reduction of estimated salt intake, urinary protein excretion, diastolic and mean BP, and BW with BMI. These results provide a strong rationale for a randomized controlled trial in the future.

Supplementary Materials: The following supporting information can be downloaded at <https://www.mdpi.com/article/10.3390/kidneydial3010012/s1>, Table S1: Within-Group Comparisons of Parameters Between Baseline and at 6 Months.

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Informed Consent Statement: Informed consent for participation in this study was obtained in the form of an opt-out method on the website, given the retrospective design of the study.

Data Availability Statement: All data generated or analyzed during this study have been included in this article and its supplementary file.

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