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【 ORIGINAL ARTICLE 】

Elevated Crude Mortality in Obese Chronic Kidney Disease Patients with Loss of Exercise Habit: A Cohort Study of the Japanese General Population

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Abstract:

Objective The relationship between obesity and risk of death in chronic kidney disease (CKD) patients remains controversial. In addition, no clear evidence has been accumulated regarding whether or not exercise improves mortality in CKD patients.

Methods The original cohort was based on a Japanese general population of 685,889 people from 40 to 74 years old who had undergone annual specific health checkups. The number of all-cause deaths during follow-up (mean, 4.7 years) in this study was 1,490. Information on walking and exercise habits was obtained by questionnaires. The study population was divided into 4 categories by the combination of CKD and obesity [body mass index (BMI) ≥25.0 kg/m^2]. Changes in the BMI and walking and exercise habits were determined by results for the first year and following year.

Results Obese CKD patients with weight gain (BMI increase by more than +1.0 kg/m^2/year) showed a higher crude mortality (1.32%) than those with a stable BMI (within ±1.0 kg/m^2/year; 0.69%). In the obese CKD population, mortality was higher with loss of exercise habits (0.96%) than in those continuously maintaining exercise habits (0.52%). The age- and sex-adjusted hazard ratio for all-cause death was 2.23 in the group with weight gain compared to the group with stable weight ($p<0.01$) and 2.08 in the group with loss of exercise habits compared to those who maintained exercise habits ($p<0.01$).

Conclusion This observational cohort study suggested that loss of exercise habits as well as weight gain of more than 1 kg/m^2/year might worsen all-cause mortality in the obese CKD population.

Key words: mortality, chronic kidney disease, body mass index, obesity, exercise

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Introduction

Obesity is considered to increase the risk of developing major risk factors for chronic kidney disease (CKD), such as diabetes and hypertension, and is also involved in the development of CKD and end-stage kidney disease (1). Awareness of the risk of obesity and education regarding a healthy lifestyle, including proper nutrition and exercise, are considered to help prevent obesity and the CKD onset (1).

CKD is a definitive risk factor for both cardiovascular disease mortality and end-stage kidney disease (2). Although many observational studies have examined the relationship between obesity and risk of death in CKD patients, whether or not obesity is associated with an increased risk of death in CKD patients remains controversial (3-9). A few studies

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have failed to detect obesity as a risk factor for death (4-7). Conversely, other reports have found obesity to be associated with a reduced risk of mortality (3, 8). The complexity of this situation is aggravated by sourcing of data from Western countries, making health promotion difficult to adapt to the Japanese population, as the ethnicity and background of CKD patients has varied among studies. An examination of how body weight affects mortality is therefore needed in order to accumulate relevant evidence regarding the beneficial effects of body weight reduction for obese Japanese CKD patients.

Cohort studies and meta-analyses examining the effects of weight change on mortality in the general population, regardless of CKD, have reported that weight changes (i.e. not only weight gain but also weight loss) increase the risk of death in the elderly (10, 11). However, the results should be interpreted with consideration of individual conditions, including the presence of comorbidities such CKD, and whether or not weight loss was achieved by interventions aimed at improving obesity, such as diet, exercise, appetite-suppressing medications, and weight loss surgery. A meta-analysis to investigate the benefits of weight loss interventions in obese CKD patients failed to achieve clarity regarding whether or not weight loss interventions can help reduce cardiovascular outcomes or the risk of death, so further research is needed (12).

Since weight loss at its most basic includes the loss of muscle mass, which then leads to more sedentary behavior, sarcopenia, and frailty, "keeping weight unchanged" through exercise habits may actually improve one's life prognosis. In renal rehabilitation guidelines (13), moderate exercise therapy is recommended for patients with non-dialysis-dependent CKD in consideration of the age and physical function, as the exercise may improve or maintain exercise tolerance and the quality of life related to the physical functions. However, the guideline also stated that clear evidence that exercise improves the life prognosis of patients with CKD is lacking. We were also unable to find any reports clarifying the effects of changes in exercise habits on mortality in obese CKD patients. However, we hypothesized that improving lifestyles, particularly in terms of acquiring exercise habits and not gaining excessive weight, would improve the life prognosis in obese CKD patients.

The present study analyzed the effects of changes in body weight and exercise habits on mortality among obese CKD patients in a cohort of patients undergoing specific health checkups in Japan.

Materials and Methods

The study cohort was based on a general population of 685,889 individuals who had participated in annual specific health checkups since 2008 according to "the Specific Health Check and Guidance in Japan." Thus, most study participants were relatively healthy, community-dwelling residents between 40 and 74 years old. Since this investigation required sequential information to determine changes in the body mass index (BMI) and exercise habits, participants with results available from fewer than three examinations were omitted from analyses. The subjects included in the final analysis were thus 300,052 individuals (59.1% women) for whom all data necessary for this study were available (namely, information on the age, sex, height, weight, systolic blood pressure, diastolic blood pressure, habitual smoking and alcohol intake, use of antihypertensive drugs, lipid-lowering drugs, and hypoglycemic drugs, as well as relevant laboratory data).

The database was used and managed solely by the statistician, and the principal analyses to identify those screened subjects who had died were completed by December 2018. The total number of all-cause deaths among study subjects was 1,490. Data from the study cohort were obtained only after concluding memoranda with the municipal heads, and all data were anonymized. Information transfer was coordinated through local government officials, and the standard analytical file (SAF) version 3.5 was developed according to the approved study protocol.

The original ethics approval was obtained from Fukushima Medical University (approval nos. #1485, #2771) and the institutional review board for ethical issues at the University of Tsukuba (approval no. 999, UMIN: 000019774). Further analyses were then performed using the SAF without any personal identifiers.

Measurement of parameters and the evaluation of comorbidities

A urinalysis by the dipstick method was performed on a single-spot urine specimen. Urine dipstick results were interpreted by the medical staff at each local medical institution and recorded as (-), (+/-), (+), (2+), or (3+). In Japan, the Japanese Committee for Clinical Laboratory Standards (http://jccls.org/) proposes that all urine dipstick results of (+) be considered correspond to a urinary protein level of 30 mg/dL. Proteinuria was thus defined in samples with a result of (+) or more. Blood samples were assayed within 24 hour using an automatic clinical chemical analyzer after collection. The serum creatinine level was measured using the enzymatic method. The annual change in the BMI (ΔBMI) was determined using primary and secondary measurement data and divided by the interval between measurements in years.

Statistical analyses

CKD was defined as a reduced estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 or positive proteinuria at the baseline year. The criteria for determining obesity differ from country to country, and the World Health Organization (WHO) standard defines "obese" as a BMI ≥30 kg/m^2 (14). According to the standards set by the Japan Society for the Study of Obesity, we defined "obesity" as a BMI ≥25 kg/m^2 in this study (15). Based on our previous study, a rapid reduction or increase in the BMI was defined

Table 1. Study Population Categorized by the Baseline Body Mass Index and CKD.

		CKD (-) Obesity (-)	CKD (+) Obesity (-)	CKD (-) Obesity (+)	CKD (+) Obesity (+)
Study size	(n, %)	186,074 (62.0%)	34,150 (11.4%)	62,037 (20.7%)	17,791 (5.9%)
Sex	Women (%)	64.0	51.6	53.8	40.9
Age	(years)	62±8	65±6	62±8	65±6
Height	(cm)	157.0±8.3	158.3±8.2	157.2±9.0	155.8±8.7
Weight	(kg)	53.6±7.9	55.5±8.0	67.7±9.3	69.3±9.2
BMI	kg/m^2	21.7±2.0	22.1±2.0	27.3±2.3	27.5±2.5
Systolic blood pressure	(mmHg)	126±17	129±17	133±16	135±17
Diastolic blood pressure	(mmHg)	75±10	76±11	79±10	80±11
Use of anti-hypertensive drugs	(%)	21.7	32.9	39.2	53.0
Free blood sugar	(mg/dL)	95±17	97±20	101±21	105±25
Hemoglobin A1c	(%)	5.3±0.6	5.3±0.6	5.5±0.7	5.6±0.9
Use of hypoglycemic drugs	(%)	3.3	5.1	6.6	10.1
Triglycerides	(mg/dL)	110±73	121±78	144±96	153±98
Low-density lipoprotein	(mg/dL)	125±30	126±31	129±30	129±31
High-density lipoprotein	(mg/dL)	64.6±16.2	61.8±16.3	56.5±13.5	54.1±13.3
Use of lipid-lowering drugs	(%)	12.9	16.3	18.3	22.8
Smoking	(%)	13.0	11.8	13.1	12.6
Alcohol intake habit	Yes (%)	47.1	46.3	46.5	47.1
ΔBMI	(kg/m^2/year)	0.0±0.8	0.0±0.8	-0.2±1.1	-0.2±1.1
Time to endpoint	(days)	1,726±393	1,680±393	1,683±385	1,633±387
eGFR	(mL/min/1.73 m^2)	79.2±15.1	57.8±12.8	78.7±14.5	59.2±14.6
Proteinuria	Yes (%)	0	23.7	0	34.7
Low eGFR,<60 mL/min/1.73 m^2	Yes (%)	0	82.6	0	75.3
Exercise habit	Yes (%)	46.6	51.1	40.6	46.6
Walking habit	Yes (%)	51.3	54.1	48.6	50.5

CKD: chronic kidney disease, BMI: body mass index, eGFR: estimated glomerular filtration rate

as a change exceeding -1.0 kg/m^2/year or +1.0 kg/m^2/year, respectively (16). The Specific Health Check includes questionnaires regarding walking and exercise habits, assessed by binary items such as, "At least 1 hour per day of walking or equivalent physical activity in daily life" and "Light sweaty exercise for at least 30 minutes at least 2 days a week for at least 1 year," respectively. We utilized baseline and subsequent information to define "loss of habit" for change from "yes" to "no" in each participant's answer and "gain of habit" for change from "no" to "yes." Follow-up health checks were conducted through April 2015, as previously reported (17, 18).

The outcomes for the analysis were all-cause deaths during follow-up among subpopulations divided by the annual ΔBMI between the primary and secondary surveys, with a mean interval of 1.2 years. The outcome was also assessed among the subpopulation by change in walking habit and any exercise habit.

Categorical variables are presented as numbers and percentages, and continuous variables are presented as means and standard deviation (Table 1). Time to the outcome was assessed using the unadjusted log-rank test and Cox proportional hazards model with adjustment for age and sex. Analyses stratifying categories by CKD and obesity and subdivided by changes in the BMI or exercise habits were able to be performed, but multivariate analyses for adjusting co-factors could not be performed due to limitations in the number of outcomes. A value of $p<0.05$ was considered significant.

Statistical analyses and graphical presentations were performed using the SPSS software program, version 27 (IBM, Armonk, USA).

Results

Among the 685,889 individuals who underwent specific health checkups, 332,741 who participated in ≥3 checkups were identified. We ultimately examined 300,052 subjects who remained after excluding those without sufficient data on the BMI, proteinuria, or serum creatinine level for the diagnosis of obesity and CKD. The number of subjects with CKD and obesity combined was not large (5.9%), and the presence of obese CKD tended to be more common in men than in women, with hypertension, abnormalities of lipid metabolism, and abnormal glucose tolerance more prevalent than non-CKD or non-obese population (Table 1).

Table 2 shows crude all-cause mortality in each category by CKD and obesity. Mortality among non-CKD, non-obese individuals was the lowest among any of the CKD-obesity categories when the BMI was reduced by more than 1.0 kg/m^2/year (0.53%), stayed within ±1.0 kg/m^2/year (0.44%), or increased by more than 1.0 kg/m^2/year (0.63%). Mortality

Table 2. Crude All-cause Mortality of Study Population Stratified by the BMI and Exercise Habit Changes.

		CKD (-) Obesity (-)	CKD (+) Obesity (-)	CKD (-) Obesity (+)	CKD (+) Obesity (+)
Change in the BMI	Reduced BMI, >-1	70/13,307 (0.53%)	19/2,378 (0.80%)	49/8,783 (0.56%)	20/2,510 (0.80%)
	Stable BMI, -1 to +1	683/156,895 (0.44%)	158/28,757 (0.55%)	205/47,103 (0.44%)	94/13,569 (0.69%)
	Gained BMI, >+1	80/12,771 (0.63%)	19/2,506 (0.64%)	36/4,931 (0.73%)	19/1,444 (1.32%)
	Missing data	3,101	509	1,220	268
Change in walking habit	Yes-Yes	228/57,862 (0.39%)	50/11,248 (0.44%)	74/16,732 (0.44%)	26/4,953 (0.52%)
	Yes-No (loss of habit)	126/23,745 (0.53%)	32/4,144 (0.77%)	47/7,303 (0.64%)	16/1,943 (0.82%)
	No-Yes (gain of habit)	125/24,612 (0.51%)	20/4,099 (0.49%)	42/7,896 (0.53%)	16/2,130 (0.75%)
	No-No	218/53,304 (0.41%)	48/9,106 (0.53%)	74/17,701 (0.42%)	43/4,662 (0.94%)
	Missing data	26,551	5,553	12,405	4,103
Change in any exercise	Yes-Yes	219/52,487 (0.42%)	49/11,671 (0.42%)	68/14,860 (0.46%)	26/4,990 (0.52%)
	Yes-No (loss of habit)	81/15,349 (0.53%)	17/2,951 (0.58%)	30/5,338 (0.56%)	14/1,455 (0.96%)
	No-Yes (gain of habit)	94/18,331 (0.51%)	14/3,278 (0.43%)	31/6,263 (0.49%)	12/1,687 (0.71%)
	No-No	302/73,362 (0.41%)	71/10,724 (0.66%)	108/23,196 (0.47%)	51/5,591 (0.91%)
	Missing data	26,545	5,526	12,380	4,068

BMI: body mass index, CKD: chronic kidney disease

increased with concomitant CKD in both non-obese and obese patients. In addition, mortality was lowest in the stable BMI group (within ±1.0 kg/m^2/year) when focusing on every CKD-obesity category: 0.44% in the non-CKD, non-obese category; 0.55% in the non-obese CKD category; 0.44% in the non-CKD obese category; and 0.69% in the obese CKD category. Notably, weight gain in the obese CKD category showed the highest mortality (1.32%), clearly indicating that exacerbation of obesity leads to a poor prognosis. In obese CKD patients, mortality was lowest in those with a continuous walking habit (0.52%) and highest in those with a never-walking habit (0.94%). Mortality rates for loss (0.82%) and gain (0.75%) of walking habits were found to be intermediate between these 2 categories. In any CKD-obesity categories, groups with loss of a walking habit showed a higher mortality rate than groups with gain of a habit: 0.53% vs. 0.51% in the non-CKD non-obese category; 0.77% vs. 0.49% in the non-obese CKD category; 0.64% vs. 0.53% in the non-CKD obese category; and 0.82% vs. 0.75% in the obese CKD category. Regarding any exercise habit, in the obese CKD population, mortality was higher for those with loss of an exercise habit (0.96%) than in those with a continuous exercise habit (0.52%). Furthermore, in any CKD-obesity categories, the group with loss of any exercise habit showed a higher mortality rate than the group with gain of a habit: 0.53% vs. 0.51% in the non-CKD non-obese category; 0.58% vs. 0.43% in the non-obese CKD category; 0.56% vs. 0.49% in the non-CKD obese category; and 0.96% vs. 0.71% in the obese CKD category.

The time to all-cause death was also assessed among the BMI change groups in each CKD-obesity category by the log-rank test (Fig. 1). Subjects with a stable BMI (±1 kg/m^2/year) showed the best prognosis in any CKD-obesity categories. Subjects whose BMI increased by >1.0 kg/m^2/year showed a worse survival in the obese CKD (p<0.01) and obese non-CKD populations (p<0.01) than subjects with stable BMI. Those with a reduced BMI did not seem to experience an increased risk of substantial mortality in the obese CKD population compared to those with a stable BMI (p=0.54). Regarding walking habits (Fig. 2), changes in the habit had relatively little effect on the prognosis of the non-CKD non-obese population during the observation period (mean, 1,726 days). The presence of CKD or obesity highlighted prognostic differences due to changes in walking habits. Particularly in the obese CKD population, subjects without a walking habit exhibited a significantly higher mortality than those with a continuous walking habit (p=0.02). Furthermore, a higher mortality tended to be seen in subjects with loss of a walking habit than those with a continuous walking habit (p=0.19). A generally similar trend to the data on walking habits was revealed in the analysis of all-cause mortality by differences in exercise habits (Fig. 3). In obese CKD, mortality with loss of an exercise habit tended to be higher than with a continuous exercise habit (p= 0.051).

While the number of outcomes was too small to perform a comprehensive multivariate analysis, we confirmed these results using an age- and sex-adjusted Cox proportional hazards model (Fig. 4). The hazard ratio (HR) [95% confidence interval (CI)] of all cause death in subjects with a BMI gain >1.0 kg/m^2/year was 2.23 (1.36-3.65) in obese CKD and 2.07 (1.45-2.95) in obese non-CKD populations (p<0.01). Regarding walking habit, in the obese CKD population, the HR of subjects without a walking habit was considerably high at 1.92 (1.18-3.14). Furthermore, the HR of subjects with loss of an exercise habit was high at 2.08 (1.09-3.99), with similar results seen in subjects without any exercise habit [2.10 (1.30-3.39)] compared to those with a continuous exercise habit.

Discussion

The worldwide prevalence of overweight and obesity are

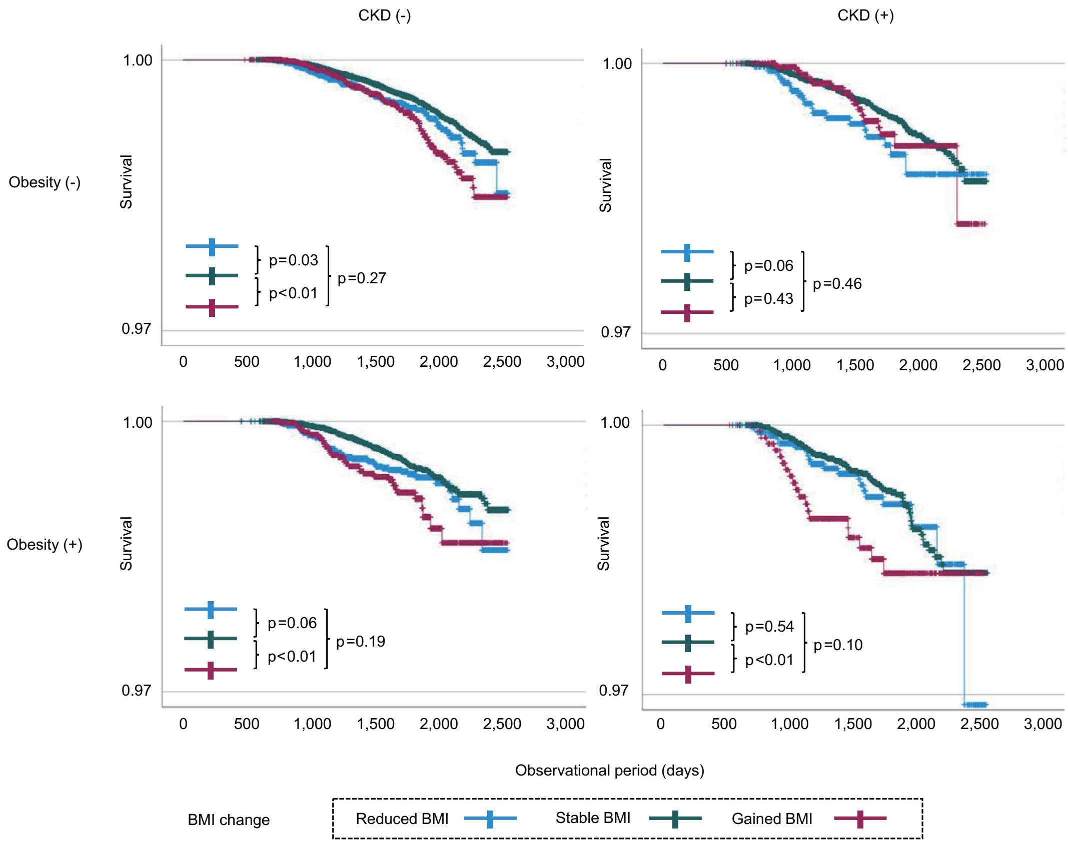

Figure 1. A comparison of all-cause mortality among groups with body mass index changes. The cohort study population is divided by chronic kidney disease (CKD) and obesity. CKD is diagnosed by a reduced eGFR (<60 mL/min/1.73 m^2) or positive dipstick proteinuria (1+ or more) at baseline. Obesity is defined as a body mass index (BMI) ≥25 kg/m^2 at baseline. Decreases and increases in the BMI are defined as a more than 1.0-kg/m^2/year decrease and a more than +1.0-kg/m^2/year increase, respectively. The survival curve for all-cause mortality is shown comparing groups with stable, gained, and reduced BMI values, respectively. The time to the outcome was assessed by the log-rank test. Values of p<0.05 were considered significant.

both high and increasing (19, 20). Furthermore, the associations of both overweight and obesity with increased all-cause mortality appear broadly consistent across Asia, Australia and New Zealand, Europe, and North America, with all-cause mortality minimal at 20.0-25.0 kg/m^2 and increasing significantly throughout the overweight range (HR 1.07, 95% CI 1.07-1.08 for BMI 25.0-27.5 kg/m^2; HR 1.20, 95% CI 1.18-1.22 for BMI 27.5-30.0 kg/m^2) (21).

Obesity is a well-known independent risk factor for CKD (22), and interventions for weight management in obese patients may have beneficial effects in preventing the development of CKD and suppressing the progression of CKD (1). Many reports, mainly based on observational studies, have discussed obesity and mortality in CKD as well as the development and progression of CKD. However, most of those studies failed to identify obesity as a risk factor for mortality (4-7), and an increased BMI is paradoxically associated with a reduced risk of death in CKD patients (3, 8). The precise reasons for the paradoxical inverse association between the BMI and mortality are unclear, but possible explanations include reverse causation as known sources of bias in observational studies (8). For instance, conditions with a high mortality rate can also induce a state of malnutrition and unnatural weight loss, thereby generating an association between a reduced BMI and increased mortality. If so, a comparison between obese CKD patients who have lost weight and those who have remained at around the same weight should theoretically identify a worse prognosis in the former population, but no previous studies have focused on such weight changes. We therefore analyzed changes in weight and exercise habits in the first year and subsequent year (mean interval, 1.2 years) by health check-ups and the consequent prognosis in obese CKD patients.

In our investigation, weight loss in non-obese CKD patients appeared to be associated with an increased mortality (HR 1.66, 95% CI 1.03-2.67), indicating a poor prognosis for non-obese CKD patients who are losing weight for some reason, intentional or otherwise, which is consistent with previous studies (3, 8). In obese CKD patients, weight loss was not necessarily associated with a poor prognosis (HR 1.24, 95% CI 0.76-2.01), but an increased mortality was seen with obesity progression exceeding 1.0 kg/m^2/year (HR 2.23, 95% CI 1.36-3.65). Based on these results, efforts to avoid exacerbating obesity may be effective for improving

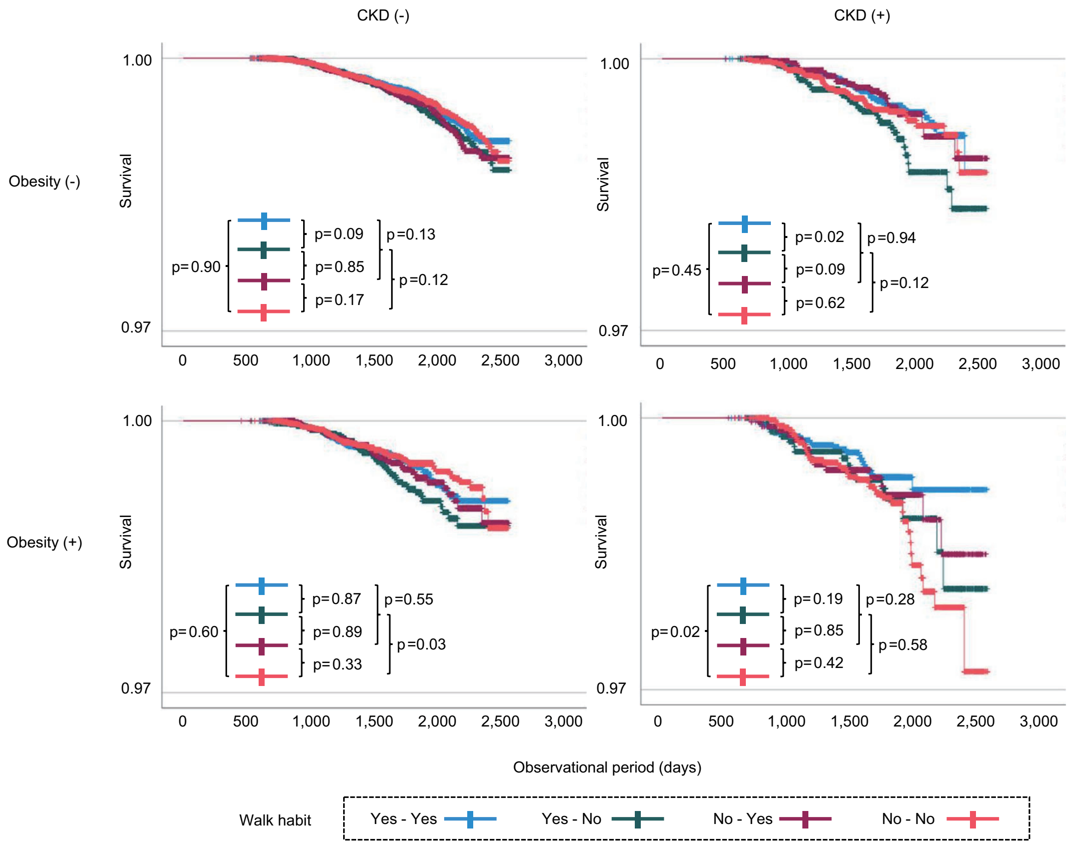

Figure 2. **A comparison of all-cause mortality among walking habit groups in obese CKD patients. The cohort study population is divided by chronic kidney disease (CKD) and obesity. CKD is diagnosed by a reduced eGFR (<60 mL/min/1.73 m^2) or positive proteinuria at baseline. Obesity is defined as body mass index (BMI) ≥25 kg/m^2 at baseline. The Specific Health Check includes questionnaires regarding walking habits using a binary question item: "At least 1 hour per day of walking or equivalent physical activity in daily life." We utilized baseline and subsequent information to define "loss of habit" as a change from "yes" to "no" in each participant's answer and "gain of habit" as a change from "no" to "yes." The survival curve for all-cause mortality is shown in continuously having a walking habit, gaining a walking habit, and losing or not having a walking habit. The time to the outcome was assessed by the log-rank test. A value of p<0.05 was considered significant.**

life expectancy, at least in patients with CKD and BMI ≥25 kg/m^2.

In Japan, obesity is defined as a BMI ≥25 kg/m^2, and the presence of health problems requiring weight loss or the accumulation of visceral fat is considered to be "obesity" (15). There are few severely obese patients with a BMI >30 kg/m^2 in Japan, but subjects receiving anti-obesity pharmacotherapy and weight-loss surgery are on the rose; however, the numbers of individuals taking such steps remain relatively low, and very few cases have been reported. Therefore, in reality, lifestyle interventions, such as diet and exercise (23, 24), are likely to remain the mainstay interventions for obese CKD patients for some time in Japan. Although improvement of obesity by behavior modification is expected to have beneficial effects on the clinical outcome in obese CKD patients, few reports have clarified whether or not these benefits reduce the actual risk of death in CKD patients (12). In this sense, the present study is significant in that it shows the impact of lifestyle modification behavior on the prognosis in obese CKD patients.

We also clarified that the subjects without walking (Fig. 2, 4) or exercise habits (Fig. 3, 4) had a significantly higher mortality than those with such habits among obese CKD patients. We also found that the prognosis was best for those with continuous walking and exercise habits in obese CKD and worse if these exercise habits were lost. Some randomized controlled studies (RCTs) have conducted interventions in terms of exercise and/or dietary restrictions in patients with CKD (24-27). Although those studies found that lifestyle interventions for obese CKD only analyzed effects on the physical activity and renal function, the impact on the life expectancy remains unknown, mainly due to the small cohort sizes and relatively short duration of follow-up. Through the present observational study, we demonstrated an association between loss of exercise habits and worsened all-cause mortality, whereas the acquisition of exercise habits seemed to improve mortality (Fig. 3, 4). This result obtained from a large, general population cohort appears very useful in practice for obese CKD patients or in providing health guidance after medical checkups in Japan, even if ob-

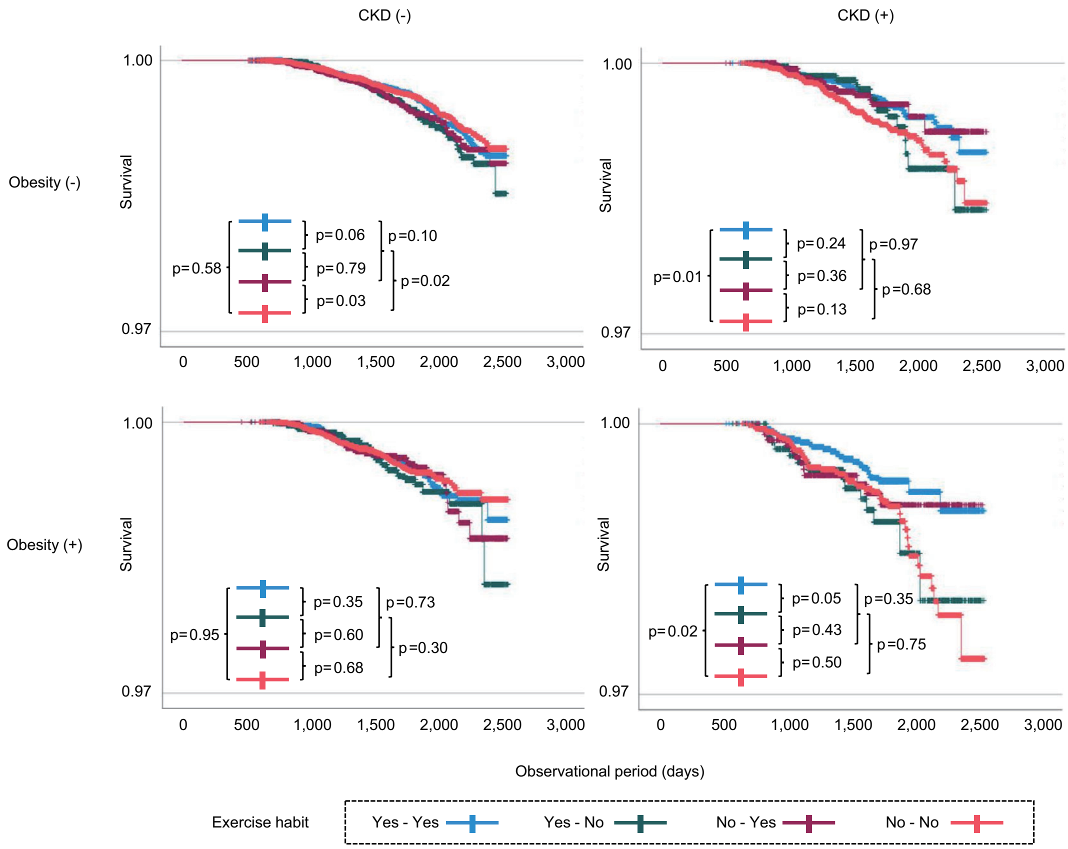

Figure 3. A comparison of all-cause mortality among groups with exercise habits in obese CKD patients. The cohort study population is divided by chronic kidney disease (CKD) and obesity. CKD is diagnosed by a reduced eGFR (<60 mL/min/1.73 m^2) or positive proteinuria at baseline. Obesity is defined as a body mass index (BMI) ≥25 kg/m^2 at baseline. The Specific Health Check includes questionnaires regarding exercise habits by a binary question item: "Light sweaty exercise for at least 30 minutes at least 2 days a week for at least 1 year." We utilized baseline and subsequent information to define "loss of habit" as a change from "yes" to "no" in each participant's answer and "gain of habit" as a change from "no" to "yes." The survival curve for all-cause mortality is shown in continuously having an exercise habit, gaining an exercise habit, and losing or not having an exercise habit. The time to the outcome was assessed by the log-rank test. A value of p<0.05 was considered significant.

servational studies offer lower levels of evidence than RCTs.

A key strength of this study is that, to our knowledge, it is the first to evaluate the prognostic impact of changes in weight and exercise habits on life expectancy in obese CKD. However, our study includes some limitations. First, the relationship between weight change and eating habits was unclear due to the high frequency of missing data for information on eating habits, and a clarification of the contribution of improved eating habits to weight change was not possible. For instance, the reduced BMI group might have included some individuals who were able to improve their lifestyles, as well as some who were unable to eat adequately due to low physical activity and poor comorbidity. Second, the number of outcomes was so small that a multivariate analysis and sub-analysis with causes of death, such as cardiovascular death, could not be performed. Similarly, we were unable to clarify whether or not weight changes and exercise habits independently affect the prognosis or instead affect the prognosis in relation to each other. It was also impossible to evaluate the X-ray findings or bioimpedance results to determine whether changes in the BMI were due to changes in actual weight or in the body fluid volume at specific health checkups, so there is some uncertainty as to whether or not reductions in the BMI were always healthy changes. In this context, we also attempted to evaluate the waist circumference as a surrogate indicator but did not obtain consistent results (data not shown).

In conclusion, this observational cohort study suggested that a loss of exercise habits, as well as a BMI gain exceeding 1 kg/m^2/year may worsen all-cause mortality among the obese CKD population.

The authors state that they have no Conflict of Interest (COI).

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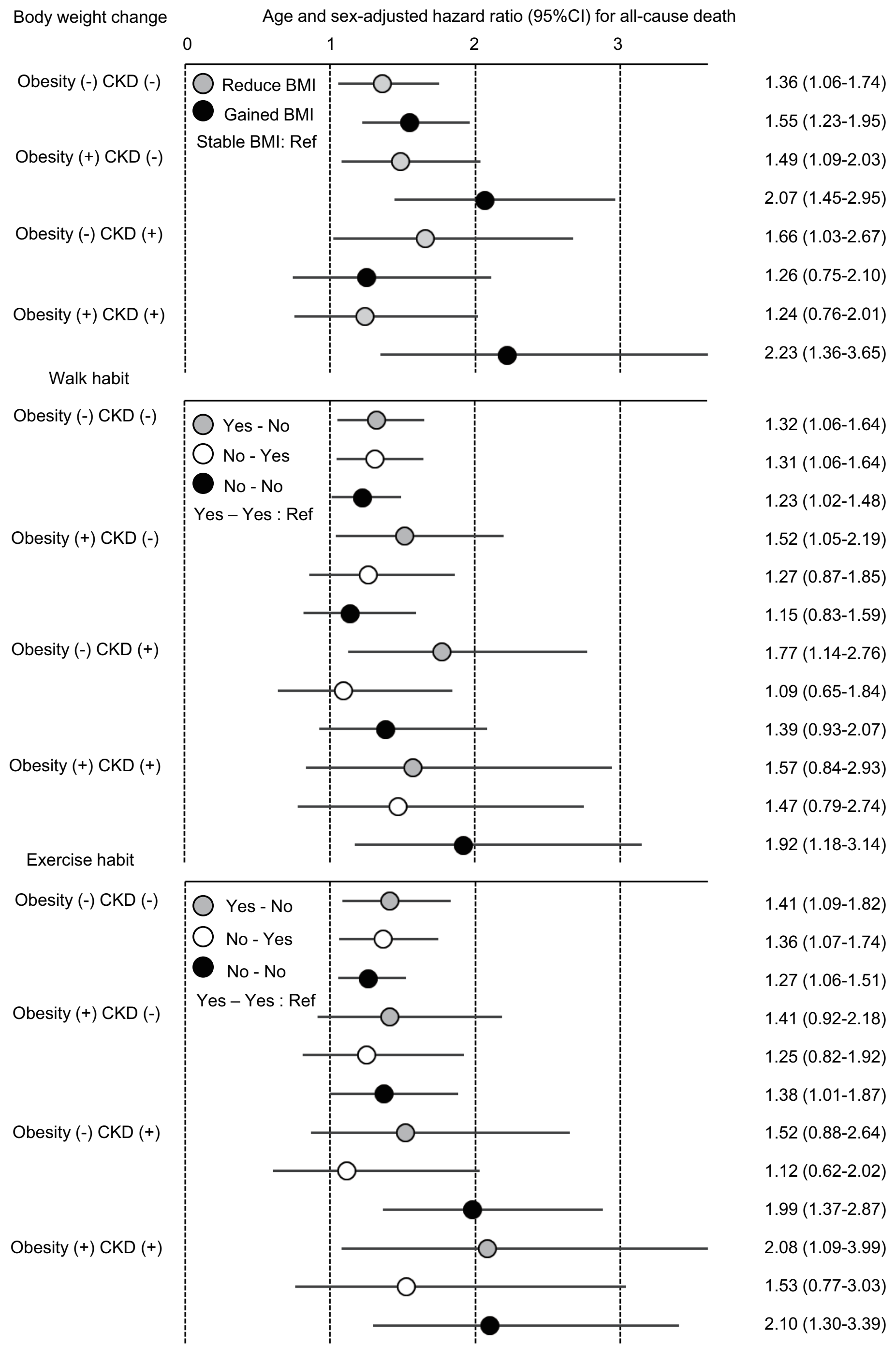

Figure 4. Age- and sex-adjusted hazard ratios of all-cause death in obese CKD with body mass index changes and with exercise habit changes. The cohort study population is divided by chronic kidney disease (CKD) and obesity. CKD is diagnosed by a reduced eGFR (<60 mL/min/1.73 m^2) or positive proteinuria at baseline. The definitions of changes in the body mass index, walking habits, and exercise habits are shown in Figs 1, 2, and 3, respectively, as well as the Methods section. The time to the outcome was assessed by Cox proportional hazards model with adjustment for age and sex. CI: confidence interval

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