Original Article

Body Mass Index Modifies an Association between Self-Reported Regular Exercise and Proteinuria

A Nationwide Cross-Sectional Survey in Japan

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Aim: Regular exercise habits are well-known to exert a favorable effect on the metabolic syndrome, which may cause proteinuria and chronic kidney disease (CKD). However, it remains unknown if exercise exerts a favorable effect on proteinuria and kidney dysfunction. The aim of this study was to reveal the association between exercise and the prevalence of proteinuria and kidney dysfunction and the attenuation by obesity.

Methods: This study was a cross-sectional cohort study that included 292,013 participants who underwent the Specific Health Check and Guidance in Japan. The exercise score (range 0-3) was based on the number of positive answers to three questions regarding exercise habits. The outcome was defined as urinary protein detected by a dipstick test and kidney dysfunction [estimated glomerular filtration rate (GFR) less than 45 ml/min/1.73 m²].

Results: The exercise score was significantly associated with the prevalence of proteinuria in both males [vs. exercise score 0; exercise score 1, multivariate-adjusted odds ratio 0.86 (95% confidence interval 0.81-0.92), $P < 0.001$; exercise score 2, 0.84 (0.79-0.90), $P < 0.001$; exercise score 3, 0.77 (0.72-0.82), $P < 0.001$] and females (same as in males). After the male subjects were divided into quintiles according to body mass index (BMI) in more than three groups ($22.9 < \text{BMI} < 24.1$), there was no significant association between the exercise score and the prevalence of proteinuria. In females, a higher exercise score was associated with a lower prevalence of proteinuria, regardless of BMI. The association between the exercise score and kidney dysfunction was as similar as that between the exercise score and proteinuria, except the attenuation of BMI.

Conclusion: Exercise may associate with a lower prevalence of proteinuria and kidney dysfunction, and a high BMI may attenuate this association between exercise and proteinuria in male subjects.

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Introduction

The concept of chronic kidney disease (CKD) was developed because CKD has a strong relationship with cardiovascular diseases (CVDs) as well as with

end-stage renal diseases (ESRDs)¹⁻³). Originally, CKD was defined by proteinuria and glomerular filtration rates (GFRs)⁴). In the original definition of CKD, CKD stages 2-5 were defined only by GFR, while proteinuria was used only for the diagnosis of CKD stage 1. Recently, proteinuria has become a more important factor in the definition of CKD⁵) because several reports have indicated that proteinuria is one of the most important risk factors for CVD and ESRD, regardless of the GFR^{3, 6}). These reports showed that subjects with positive proteinuria had a higher incidence of CVD or ESRD than those with no proteinuria whose GFRs were similar.

Exercise had been reported to improve endothelial function⁷) and metabolic factors⁸⁻¹⁰), resulting in the prevention of atherosclerotic lesions^{11, 12}). Therefore, regular exercise was recommended for the patients with atherosclerotic diseases^{13, 14}). Indeed, exercise has been reported to ameliorate the incidence of CVD events in general cohorts¹⁵). Several prospective studies have evaluated the joint effects of exercise and obesity on total mortality¹⁶⁻¹⁸). These reports suggested that exercise suppressed the incidence of CVD and that this suppression is attenuated by obesity. Similar to CVD, modifiable lifestyle factors such as smoking^{19, 20}) and sleeping²¹) contribute to CKD; however, there is no evidence that has suggested that exercise could suppress the incidence of CKD. Moreover, there is a possibility that the suppression of CKD by exercise is attenuated by obesity.

Aim

The aim of the present cross-sectional survey of 292,013 individuals who were undergoing the Specific Health Check and Guidance in Japan was to compare associations between various exercise habits and proteinuria (defined as $\geq 1+$ of urinary protein by dipstick test) and kidney dysfunction [defined as an estimated glomerular filtration rate (eGFR) less than 45 ml/min/1.73 m²]. In addition, a further aim of this study was to evaluate the joint effects of exercise and obesity on the prevalence of proteinuria.

Subjects and Methods

Study Population

The present nationwide cross-sectional survey included members of the general Japanese population who underwent the Specific Health Check and Guidance in Japan between April 2008 and March 2009. Because a recent survey indicated that the prevalence of diabetes, hypertension, dyslipidemia, obesity, and

the metabolic syndrome has been increasing in Japan, the Ministry of Health, Labor and Welfare of Japan has therefore developed a systematic healthcare strategy that involves the specific health checkups and that targets members of the insured population who are aged 40 years or older. This strategy aims to detect and manage the metabolic syndrome at an earlier stage. We analyzed the data of individuals who were undergoing the Specific Health Check and Guidance in Japan in eight prefectures (Miyagi, Fukushima, Ibaraki, Tokyo, Niigata, Osaka, Fukuoka, and Okinawa). Of the 506,807 participants aged 40 years or older (Miyagi 16,640, Fukushima 50,304, Ibaraki 39,775, Tokyo 40,278, Niigata 58,882, Osaka 25,615, Fukuoka 149,785, and Okinawa 125,528), 292,013 (57.6%) were included in the present analysis; 214,794 participants (42.4%) were excluded because of missing data (primarily a lack of answers to the questions related to exercise habits). The study protocol was approved by the ethics committee at Fukushima Medical University (No.715) and Osaka University Hospital (No 13085).

Measurements

Demographic, physical, and laboratory data included age; sex; body mass index [BMI; weight (kg)/height² (m²)]; mean arterial pressure [MAP; diastolic blood pressure + (systolic blood pressure – diastolic blood pressure)/3]; serum concentration of creatinine (enzymatic method); and levels of hemoglobin A1c, triglycerides, high-density lipoprotein (HDL) cholesterol, and urinary protein as detected by a dipstick test. Proteinuria was defined as 1+ or more of urinary protein. The eGFR was calculated using the following equation: $\text{eGFR (mL/min/1.73 m}^2\text{)} = 194 \times \text{age [years]}^{-0.287} \times \text{serum creatinine [mg/dL]}^{-1.094} (\times 0.739, \text{ if female})^{22}$.

Information regarding lifestyle, current medication for comorbidities, and past medical histories was based on self-reported standard questionnaires that all participants were required to complete at the time of their health check-up. The exercise score (range 0-3) was based on the number of positive answers to three questions regarding exercise habits: “Do you have ≥ 30 minutes of a sweat-inducing workout more than once a week?”, “Do you walk or exercise for more than one hour per day?”, and “Do you think that you walk faster compared with others of the same age?” Smoking status was evaluated based on positive answers to the question “Do you smoke now?” Drinking status was evaluated by asking the question “How often do you drink alcoholic beverages?” The possible answers were as follows: (i) everyday, (ii) occasionally, or (iii) rarely. The past history of cardiac disease was defined

by a positive answer to the question “Have you been diagnosed with heart disease?”, and the past history of stroke was also defined by a positive answer to the question “Have you been diagnosed with stroke?” The past history of CVD was defined by the combination of heart disease and stroke.

All data were collected and managed at an independent non-profit data center, the Japan Clinical Research Support Unit.

Statistical Analysis

Continuous variables were expressed as a mean $\pm$ standard deviation (SD) or median (interquartile range), as appropriate, and categorical variables were expressed as a number (proportion). Serum triglyceride levels were logarithmically transformed because of their skewed distribution. The clinical characteristics of subjects with different exercise scores were compared using analysis of variance, Kruskal-Wallis test, and chi-square test, as appropriate. To assess an association between the exercise score and proteinuria, the odds ratio of each exercise score was calculated using univariate and multivariate logistic regression models, with the presence of proteinuria as a dependent variable. A linear association between the exercise score and proteinuria was evaluated by an incorporation of the exercise score as a continuous variable into the models. Multivariate models included age; BMI; MAP; smoking status; drinking status; current treatment for comorbidities; past history of CVD; levels of hemoglobin A1c, serum triglyceride concentration, HDL cholesterol, and eGFR as covariates, in addition to the exercise score. The effect modification by the exercise score and the BMI value was verified by the incorporation of the interaction term for exercise score * BMI into the multivariate models. To clarify the effect modification, multivariate-adjusted odds ratios of each exercise score were calculated for the five subgroups that were stratified in quintiles in terms of BMI.

We defined kidney dysfunction, one of the outcome of interest, as an eGFR less than 45 ml/min/1.73 m² because recent reports demonstrated that an eGFR less than 45 ml/min/1.73 m² was a real risk for CVD and ESRD, resulting in the establishment of CKD stage 3b^{5, 6, 23, 24}. The effect of the exercise score on this outcome was analyzed in a similar way as the analyses using proteinuria as the outcome.

All *P* values were based on two-sided tests of significance, and *P* < 0.05 was considered statistically significant. Statistical analyses were performed using Stata version 11.0 (Stata corp., College Station, Texas, US) and R version 3.0.2 (The R Foundation for Sta-

tistical Computing, <http://www.r-project.org/>).

Results

The clinical characteristics of the 117,692 males and 174,321 females stratified according to their exercise scores are shown in **Table 1** and **Table 2**, respectively. Male subjects with higher exercise scores were likely to be older, non-smokers and rare drinkers, and have no past history of CVD. As a group, they also had lower serum triglyceride levels, higher serum HDL cholesterol levels, a lower eGFR, a lower prevalence of proteinuria, and a lower prevalence of kidney dysfunction (less than 45 ml/min). A similar trend was also observed in the female subjects with higher exercise scores.

In both genders, univariate and multivariate model analyses demonstrated that exercise scores were associated with proteinuria (**Table 3**). The multivariate analysis for proteinuria revealed that a high exercise score was associated with a low prevalence of proteinuria in both males and females (**Table 3**). In male subjects, an exercise score of 1 (lowest exercise score) had a significant association with a low prevalence of proteinuria [vs. exercise score 0, multivariate-adjusted odds ratio 0.86 (95% confidence interval 0.81-0.92), *P* < 0.001], although an exercise score of 1 in female subjects has no association of proteinuria. An exercise score of 2 (middle exercise score) had a significant association with the prevalence of proteinuria in both males [0.84 (0.79-0.90), *P* < 0.001] and females [0.86 (0.80-0.92), *P* < 0.001]. An exercise score of 3 (highest exercise score) had a relatively strong association with the prevalence of proteinuria both in male [0.77 (0.72-0.82), *P* < 0.001] and in female subjects [0.76 (0.70-0.82), *P* < 0.001] (**Table 3**). The association between each component of the exercise score and proteinuria is summarized in **Supplemental Table 1**. The positive answer for “Do you think that you walk faster compared with others of the same age?” associated with a lower prevalence of proteinuria than the other answers both in male and female subjects.

The interactions between the exercise score and each clinical parameter were evaluated, and there was a significant interaction between the exercise score and BMI in male subjects (**Table 3**). Therefore, all male and female subjects were categorized into quintiles according to BMI. The associations between BMI and the exercise score are shown in **Fig. 1**. Both male (**Fig. 1A**) and female (**Fig. 1B**) subjects with a higher BMI tended to have a lower exercise score.

The relationship between exercise and proteinuria is shown in **Fig. 2**. **Fig. 2A** showed the relation-

Table 1. Clinical characteristics of 117,692 males stratified according to Exercise score

	Exercise score				<i>P</i> trend
	0	1	2	3	
<i>N</i>	25,065	31,265	31,383	29,979	
Age (year)	63 (57-70)	63 (58-70)	65 (61-71)	66 (64-71)	<0.001
BMI (kg/m ²)	23.8 ± 3.3	23.7 ± 3.1	23.6 ± 2.9	23.3 ± 2.7	<0.001
MAP (mmHg)	95.3 ± 11.8	95.4 ± 11.7	95.4 ± 11.4	95.6 ± 11.1	<0.001
Currently smoking (<i>n</i> (%))	7965 (31.8)	9185 (29.4)	7625 (24.3)	5400 (18.0)	<0.001
Drinking rarely (<i>n</i> (%))	8143 (32.5)	9227 (29.5)	9186 (29.3)	7909 (26.4)	<0.001*
occasionally (<i>n</i> (%))	5792 (23.1)	7825 (25.0)	7934 (25.3)	7872 (26.6)	<0.001*
every day (<i>n</i> (%))	11130 (44.4)	14213 (45.5)	14263 (45.5)	14198 (47.4)	<0.001*
Current treatment for					
hypertension (<i>n</i> (%))	8417 (33.6)	10126 (32.4)	10861 (34.6)	10229 (34.1)	<0.001
diabetes (<i>n</i> (%))	1840 (7.3)	2043 (6.5)	2484 (7.9)	2270 (7.6)	<0.001
dyslipidemia (<i>n</i> (%))	2987 (11.9)	3649 (11.7)	3884 (12.4)	3735 (12.5)	0.005
Past history of CVD (<i>n</i> (%))	3533 (14.1)	3863 (12.4)	4118 (13.1)	3410 (11.4)	<0.001
Hemoglobin A1c (%)	5.4 ± 0.9	5.4 ± 0.8	5.4 ± 0.8	5.4 ± 0.7	0.063
Triglyceride (mg/dl)	145 (84-173)	141 (82-168)	132 (78-157)	124 (74-148)	<0.001
HDL cholesterol (mg/dl)	55 (45-63)	57 (46-65)	58 (47-66)	60 (48-69)	<0.001
eGFR (ml/min/1.73 m ²)	76.0 ± 17.0	75.7 ± 16.5	74.1 ± 15.9	72.8 ± 15.1	<0.001
Urinary protein by dipstick test					
negative or trace (<i>n</i> (%))	22744 (90.8)	28849 (92.3)	28951 (92.3)	27920 (93.1)	<0.001 [†]
1+	1488 (5.9)	1618 (5.2)	1604 (5.1)	1427 (4.8)	<0.001 [‡]
2+ or more	833 (3.3)	798 (2.6)	828 (2.6)	632 (2.1)	<0.001 [‡]
eGFR < 45 ml/min/1.73 m ²	533 (1.8)	636 (2.0)	559 (1.8)	587 (2.3)	<0.001

Mean ± SD, median (25%, 75%)

BMI, body mass index; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; MAP, mean arterial pressure

*Drinking rarely vs. others

†Drinking every day vs. others.

‡Negative or trace vs. 1+ or more.

§1+ or less vs. 2+ or more.

ship in the whole cohort, **Fig. 2B** showed the relationship in male subjects, and **Fig. 2C** showed the relationship in female subjects.

The associations between the exercise score and prevalence of proteinuria in the five quintiles of the male and female subjects are shown in **Fig. 3**. On the one hand, in female subjects, the association between an exercise score of 3 (highest exercise score) and the prevalence of proteinuria was consistent from the 1st category [0.64 (0.51-0.79), *P* < 0.001] to the 5th category [0.81 (0.69-0.94), *P* = 0.006] (**Fig. 3B**). On the other hand, in male subjects, the association between an exercise score of 3 and the prevalence of proteinuria became progressively weaker and insignificant starting from the 3rd category [0.89 (0.75-1.06), *P* = 0.182], and any association between the exercise score and prevalence of proteinuria was not observed in the 5th category [0.90 (0.85-1.02), *P* = 0.111]. The association between exercise and the prevalence of protein-

uria was attenuated by an increased BMI only in male subjects (**Fig. 3A**). When the sub-group in the 3rd category with an exercise score 0 was treated as a reference, the same effects of exercise on proteinuria were observed (**Supplemental Fig. 1**).

The association between the exercise score and kidney dysfunction in the five quintiles according to the BMI of the male and female subjects are shown in **Fig. 4**. In female subjects, the association between an exercise score of 3 (highest exercise score) and the prevalence of kidney dysfunction was consistent from the 1st category [0.82 (0.59-1.14), *P* = 0.251] to the 5th category [0.85 (0.65-1.11), *P* = 0.240] without significance perhaps because of the small number of outcome (**Fig. 4B**). In male subjects, the association between an exercise score of 3 (highest exercise score) and the prevalence of kidney dysfunction was also consistent from the 1st category [0.53 (0.38-0.74), *P* < 0.001] to the 5th category [0.61 (0.47-0.79), *P* <

Table 2. Clinical characteristics of 174,321 females stratified according to Exercise score

	Exercise score				<i>P</i> trend
	0	1	2	3	
<i>N</i>	42622	50858	45095	35746	
Age (year)	62 (58-70)	63 (59-70)	65 (61-70)	66 (63-71)	<0.001
BMI (kg/m ²)	23.9 ± 3.7	22.7 ± 3.4	22.5 ± 3.3	22.2 ± 3.0	<0.001
MAP (mmHg)	92.3 ± 11.8	92.2 ± 11.7	92.3 ± 11.6	92.6 ± 11.4	<0.001
Currently smoking (<i>n</i> (%))	2903 (6.8)	3448 (6.8)	2498 (5.5)	1500 (4.2)	<0.001
Drinking rarely (<i>n</i> (%))	30854 (72.4)	35949 (70.7)	31745 (70.4)	24111 (67.5)	<0.001*
occasionally (<i>n</i> (%))	8395 (18.7)	10501 (20.7)	9615 (21.3)	8329 (23.3)	<0.001*
every day (<i>n</i> (%))	3373 (7.9)	4408 (8.7)	3735 (8.3)	3306 (9.3)	<0.001*
Current treatment for					
hypertension (<i>n</i> (%))	12130 (28.5)	14125 (27.7)	12659 (28.1)	9715 (27.2)	<0.001
diabetes (<i>n</i> (%))	1576 (3.7)	1810 (3.6)	1807 (4.0)	1525 (4.3)	<0.001
dyslipidemia (<i>n</i> (%))	8441 (19.8)	10367 (20.4)	9919 (22.0)	7995 (22.4)	<0.001
Past history of CVD (<i>n</i> (%))	3560 (8.4)	3943 (7.8)	3417 (7.6)	2361 (6.6)	<0.001
Hemoglobin A1c (%)	5.3 ± 0.6	5.3 ± 0.6	5.3 ± 0.6	5.3 ± 0.6	<0.001
Triglyceride (mg/dl)	113 (71-136)	112 (71-134)	109 (69-130)	106 (68-128)	<0.001
HDL cholesterol (mg/dl)	65 (53-74)	66 (54-75)	67 (55-76)	68 (56-78)	<0.001
eGFR (ml/min/1.73 m ²)	77.7 ± 16.5	76.6 ± 16.0	75.5 ± 15.6	73.9 ± 14.8	<0.001
Urinary protein by dipstick test					
negative or trace (<i>n</i> (%))	40792 (95.7)	48842 (96.0)	43469 (96.4)	34618 (96.6)	<0.001 [†]
1+	1313 (3.1)	1528 (3.0)	1222 (2.7)	861 (2.4)	<0.001 [‡]
2+ or more	517 (1.2)	488 (1.0)	404 (0.9)	267 (0.8)	<0.001 [‡]
eGFR < 45 ml/min/1.73 m ²	364 (1.0)	494 (1.1)	602 (1.2)	535 (1.3)	0.001

Mean ± SD, median (25%, 75%)

BMI, body mass index; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; MAP, mean arterial pressure

*Drinking rarely vs. others

‡Drinking every day vs. others.

†Negative or trace vs. 1+ or more.

‡1+ or less vs. 2+ or more.

Table 3. Associations of Exercise scores and proteinuria in males and females

Gender	Exercise score	Univariate model			Multivariate model*		
		OR [95% CI]	<i>P</i>	<i>P</i> _{trend}	OR [95% CI]	<i>P</i>	<i>P</i> _{trend}
Male	0	1.00 [reference]			1.00 [reference]		
	1	0.82 [0.77-0.87]	<0.001	0.001	0.86 [0.81-0.92]	<0.001	0.001
	2	0.82 [0.77-0.87]	<0.001		0.84 [0.79-0.90]	<0.001**	
	3	0.72 [0.68-0.77]	<0.001		0.77 [0.72-0.82]	<0.001***	
Female	0	1.00 [reference]			1.00 [reference]		
	1	0.92 [0.86-0.98]	0.012	0.001	0.94 [0.88-1.00]	0.056	0.001
	2	0.83 [0.77-0.89]	<0.001		0.86 [0.80-0.92]	<0.001	
	3	0.73 [0.67-0.78]	<0.001		0.76 [0.70-0.82]	<0.001	

OR, odds ratio; CI, confidence interval

*Adjusting for area, age, body mass index, mean arterial pressure, smoking status, drinking status, current treatment for hypertension, dyslipidemia and diabetes, past history of cardiovascular disease, hemoglobin A1c, triglyceride, HDL cholesterol, and estimated glomerular filtration rate.

P* for interaction between Exercise score and body mass index = 0.007*P* for interaction between Exercise score and body mass index = 0.003

Fig. 1. Association between the exercise score and quartiles according to the body mass index in males (A) and in females (B)

0.001] (**Fig. 4B**). The attenuation by an increased BMI was not observed both in male and female subjects (**Fig. 4**).

Discussion

The present cross-sectional study of 292,013 individuals who were undergoing the Specific Health Check and Guidance in Japan revealed that a higher regular exercise regimen has a significant association both with a lower prevalence of proteinuria and with a lower prevalence of kidney dysfunction. There was no association between proteinuria and exercise in male subjects with a higher BMI ($\text{BMI} \geq 23.2 \text{ kg/m}^2$, particularly $\text{BMI} \geq 26.6 \text{ kg/m}^2$), although a consistent association was observed in female subjects, regardless of BMI.

The mechanism of the association between exercise and the lower prevalence of proteinuria and kidney dysfunction is mainly considered to be the amelioration of a metabolic condition such as diabetes

Fig. 2. Multivariate-adjusted odds ratio of 1+ or more of proteinuria by the exercise score in the whole cohort (A), in males (B), and in females (C)

mellitus²⁵), fatty liver²⁶), hyperlipidemia²⁷), or hypertension^{28, 29}), all of which may induce CKD. In the Framingham Offspring cohort, HDL cholesterol, smoking, age, and gender could predict albuminuria³⁰). In the KEEP study, metabolic factors could increase both CKD and CVD³¹). Exercise is well-

Fig. 3. Multivariate-adjusted odds ratio of 1+ or more of proteinuria by the exercise score in quartiles according to the body mass index in males (A) and in females (B)

known to improve the lipid status⁸⁾, glucose status¹⁰⁾, and hypertension status³²⁾, which results in an improvement in the prevalence of proteinuria and kidney dysfunction. In this study, lipid condition, blood pressure, and glucose level (HbA1c) were adjusted for analysis, but these factors may also be improved by the exercise itself; therefore, exercise may improve the prevalence of proteinuria through the amelioration of metabolic factors, except these adjusted factors.

Fig. 4. Multivariate-adjusted odds ratio of kidney dysfunction by the exercise score in quartiles according to the body mass index in males (A) and in females (B)

Another mechanism of the association between exercise and the lower prevalence of proteinuria and kidney dysfunction is the anti-inflammatory effects of exercise^{33, 34)}. The anti-inflammatory effects of exercise are considered to be caused by three distinct pathways: the reduction of fat mass³³⁾, anti-inflammatory cytokines from contracting skeletal muscles³⁴⁾, and the reduction in the expression of Toll-like receptors on monocytes and macrophages³⁵⁾. These anti-inflamma-

tory effects of exercise may have positive effects on the kidneys.

There are several considerable mechanisms that high BMI attenuated the association between the prevalence of proteinuria and exercise score. First, there was the U-shaped association between BMI and proteinuria (**Supplemental Fig. 1**), which was previously reported³⁶. Moreover, the prevalence of proteinuria in the subjects with the lowest BMI at an exercise score 0 was higher than that in the subjects with the highest BMI at an exercise score 0 (**Supplemental Fig. 1**). This phenomenon made reduction of the prevalence of proteinuria by exercise in the lowest BMI category larger than that in the higher BMI category. Second, subjects with a high BMI may have some metabolic factors rather than covariates in this study, resulting in a low effect on the prevalence of proteinuria by exercise as same as the relationship between exercise and CVD¹⁵⁻¹⁸. Third, the attenuation by BMI upon the association between the prevalence of kidney dysfunction and exercise score was not as distinct as the association between proteinuria and the exercise score (**Fig. 4**). Therefore, the effect on CKD by regular exercise may be constant, but some factors, such as proteinuria induced by exercise, may attenuate the association between proteinuria and the exercise score.

There are several limitations to this study. First, we could not infer a causal relationship between exercise and proteinuria because of the cross-sectional nature of the study. Further studies are needed to examine the causality of our findings. Second, the presence of proteinuria was determined by a single measurement by a dipstick test, which may have led to misclassifications. However, the majority of such misclassifications would bias our findings towards the null hypothesis and would thus weaken the associations. In addition, prior studies have shown that even a single dipstick indication for proteinuria is a significant risk factor for all-cause mortality, cardiovascular mortality^{37, 38}, and ESRD^{39, 40}. Third, the exercise habits of the participants were evaluated only by a self-reported questionnaire. Therefore, a reporting bias may exist not only in the male subjects with a high BMI but also in the entire cohort. However, because the participants did not benefit if they answered the questions inaccurately or untruthfully, the correct information was expected.

Conclusion

Exercise may ameliorate the prevalence of proteinuria and kidney dysfunction, and a high BMI may

attenuate this amelioration in male subjects, although further studies are required to confirm our findings.

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Conflict of Interest

None.

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Supplemental Fig. 1. Multivariate-adjusted odds ratio of 1+ or more of proteinuria by the exercise score in quartiles according to the body mass index in males (A) and in females (B) when the sub-group in the 3rd category with an exercise score 0 was treated as a reference

Supplemental Table 1. Univariate and multivariate analysis for proteinuria

Questions	Univariate		Multivariate*	
	OR [95%CI]	P	OR [95%CI]	P
Male				
Do you walk or exercise for more than one hour per day?	0.93 [0.89-0.97]	<0.001	0.93 [0.89-0.98]	0.005
Do you have ≥30 minutes of a sweat-induced workout more than once a week?	0.92 [0.89-0.97]	<0.001	0.90 [0.86-0.95]	<0.001
Do you think that you walk faster compared with others of the same age?	0.75 [0.72-0.79]	<0.001	0.82 [0.79-0.86]	<0.001
Female				
Do you walk or exercise for more than one hour per day?	0.92 [0.88-0.97]	<0.001	0.93 [0.89-0.99]	0.013
Do you have ≥30 minutes of a sweat-induced workout more than once a week?	0.88 [0.84-0.93]	<0.001	0.85 [0.80-0.90]	<0.001
Do you think that you walk faster compared with others of the same age?	0.77 [0.73-0.80]	<0.001	0.82 [0.78-0.87]	<0.001

OR, odds ratio; CI, confidence interval

*Adjusting for area, age, body mass index, mean arterial pressure, smoking status, drinking status, current treatment for hypertension, dyslipidemia and diabetes, past history of cardiovascular disease, hemoglobin A1c, triglyceride, HDL-cholesterol, and estimated glomerular filtration rate.