

Association Between Unhealthy Dietary Habits and Proteinuria Onset in a Japanese General Population: A Retrospective Cohort Study

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Abstract

Background

The relationship between dietary habits and development of chronic kidney disease (CKD) is uncertain. This retrospective cohort study was conducted to examine the association between unhealthy dietary habits and proteinuria onset, a key prognostic factor of CKD.

Methods

We conducted a retrospective cohort study among individuals in a Japanese general population aged ≥ 40 years who underwent annual medical checkups from 1998 to 2014 in Kanazawa City, Japan. The risks of proteinuria onset were estimated based on the status of baseline unhealthy dietary habits (quick eating, late dinner, late evening snack, and skipping breakfast) compared with the status without these habits. We calculated the incidence rates per 1000 person-years based on the presence or absence of each unhealthy dietary habit. Multivariable Cox proportional hazards models were used to estimate the risks of proteinuria onset based on baseline unhealthy dietary habits. Changes in body mass index (BMI) and waist-to-height ratio (WHtR), which were possible intermediate factors in unhealthy dietary habits and proteinuria onset, were estimated using a linear mixed-effects model with random intercept and random slope.

Results

A total of 26,764 subjects were included, with a mean follow-up period of 3.4 years. The most frequent unhealthy dietary habits were quick eating (29%), followed by late dinner (19%), late evening snack (16%), and skipping breakfast (9%). During the follow-up period, 10.6% of the participants developed proteinuria, with an incidence rate of 32.7 per 1000 person-years. Late dinner or skipping breakfast had an increased adjusted risk of proteinuria onset (hazard ratio [HR] 1.12, 95% confidence interval [CI] 1.02 to 1.22, and HR 1.15, 95% CI 1.01 to 1.31, respectively). Each unhealthy dietary habit was not associated with changes in BMI or WHtR.

Conclusion

Our results suggest that late dinner and skipping breakfast were associated with higher risks for proteinuria onset. Unhealthy dietary habits were not associated with changes in BMI or WHtR during the follow-up period.

Introduction

Chronic kidney disease (CKD) is associated with increased risks for all-cause and cardiovascular mortality, which is a major health problem in several countries [1]. The prevention and treatment of CKD include medication [2], smoking cessation [3], and diets. In general, diets include nutrient intake, nutrient balance, and dietary habits. For instance, sodium restriction, a nutrient intake, is a well-known treatment for patients with CKD [4].

Studies conducted to assess the associations between diets and CKD have focused on nutrient intake or nutrient balance. For example, regarding nutrient intake, it has been reported that phosphorus restriction is effective against CKD-associated mineral and bone disorders in patients with CKD stages 3–5 [5]; regarding nutrient balance, a protein-restricted diet was found to be effective in preventing the progression of CKD [6]. In addition to nutrient intake and nutrient balance, dietary habits, including meal times and methods of eating such as the order of dishes, have received attention in recent years [7, 8].

Dietary habits are known to be associated with lifestyle-related diseases. For instance, skipping breakfast is a risk factor for diabetes [9], and late dinner is associated with obesity [10]. Being treatable risk factors, these unhealthy dietary habits are important in the treatment of lifestyle-related diseases, such as diabetes or obesity [11]. Although unhealthy dietary habits causing metabolic disorders are potential risk factors for CKD, the relationship between dietary habits and CKD has not been fully clarified. Therefore, the present study was conducted to investigate the association between unhealthy dietary habits and proteinuria onset, which is a key prognostic factor of CKD [12].

Methods

Study Design and Subjects

We conducted a retrospective cohort study among a Japanese general population aged ≥ 40 years who underwent annual medical checkups from 1998 to 2014 in Kanazawa City, Japan. The inclusion criteria were an estimated glomerular filtration rate (eGFR) at baseline of > 60 mL/min/1.73 m² and a follow-up period of more than 1 year. The exclusion criteria were a baseline urinary protein dipstick result of $\geq 1+$ and unavailability of the status of dietary habits or other covariates.

Measurements of Study Variables

Details regarding unhealthy dietary habits, daily drinking and current smoking status, use of antihypertensive agents, and use of glucose-lowering medication were collected from the self-reported questionnaire used for the annual medical checkups.

Unhealthy dietary habits were defined as follows: late dinner; eating dinner within 2 h of going to bed at a frequency of three or more times a week; skipping breakfast three or more times a week; quick eating, i.e., eating faster than the same generation; and late evening snack, i.e., eating snacks after dinner three or more times a week. Subjects chose from “yes or no” in each questionnaire item, except for quick eating and daily drinking. Participants were classified into the quick eating category when they chose “fast”

from the list of “fast, ordinary, or slow.” They were classified into the daily drinking category when they answered “everyday” from the list of “everyday, sometimes, or rare.”

Body mass index (BMI) was calculated by dividing body weight (kg) by the square of height (m). Waist circumference was measured at navel height in the standing position. Waist-to-height ratio (WHtR), which better reflects visceral fat than waist circumference [13], was calculated by dividing waist circumference (cm) by height (cm). Blood pressure was measured at rest in the sitting position. Urine dipstick test was performed using random spot urine samples and recorded as negative, trace, 1+, 2+, 3+, and 4+; urine dipstick test 1 + corresponds to a proteinuria concentration of 30 mg/dL. eGFR was calculated from serum creatinine using the equation developed by the Japanese Society of Nephrology [14]. In case of subjects taking antihypertensive agents, to obtain the potential blood pressure, we uniformly added 10 mmHg for systolic blood pressure (SBP) and 5 mmHg for diastolic blood pressure [15]. Diabetes was defined as HbA1c \geq 6.5% (National Glycohemoglobin Standardization Program) and/or fasting blood glucose \geq 7 mmol/L [16] or using glucose-lowering medication. Outcome was defined as the time to the onset of dipstick proteinuria \geq 1 + during a follow-up period.

Statistical Analysis

Baseline data with normal distribution were reported as mean and standard deviation, skewed variables were represented as median and interquartile range, and categorical variables were shown as numbers and proportions. Baseline mean BMI and WHtR values were calculated according to the baseline dietary habits using multivariable linear regression analysis. Changes in BMI and WHtR, which were possible intermediate factors in unhealthy dietary habits and proteinuria onset, were estimated using a linear mixed-effects model with random intercept and random slope. For estimating proteinuria onset, we calculated the incidence rates per 1000 person-years based on the presence or absence of each unhealthy dietary habit, and Kaplan–Meier curves were also constructed. Multivariable Cox proportional hazards models were used to estimate the risks of proteinuria onset based on baseline unhealthy dietary habits. Furthermore, to evaluate the potential effect modification based on age, sex, and obesity, which are known as risk factors for CKD [17, 18], we stratified the subjects according to age (< 65 and \geq 65 years), sex, and BMI (< 25 and \geq 25 kg/m²) and tested the interaction terms between unhealthy dietary habits and each of the variables age, sex, and BMI. In the multivariable analysis, each model was adjusted for the following potential confounders based on previous studies: age, sex, BMI, SBP, eGFR, hemoglobin, triglyceride, total cholesterol, HbA1c, serum uric acid, daily drinking, and current smoking [19]. A two-tailed significance level was set at $p < 0.05$. All analyses were performed using the Stata/IC statistical software (version 14; StataCorp LLC, College Station, TX, USA).

Results

Baseline Characteristics of Subjects

Figure 1 shows the flow diagram of the selection of study subjects. Among subjects who underwent a medical checkup between 1998 and 2014, 26,764 subjects met the inclusion criteria and were included in

the analysis.

Table 1 shows the baseline characteristics of the study participants. Mean age was 68 years, and 44% of the participants were men. The most frequent unhealthy dietary habits were quick eating (29%), followed by late dinner (19%), late evening snack (16%), and skipping breakfast (9%). The mean follow-up period was 3.4 years. **Supplementary Table S1** shows the baseline characteristics of the participants according to unhealthy dietary habits.

Changes in BMI and WHtR According to Baseline Unhealthy Dietary Habits

Adjusted baseline BMI and WHtR values were higher in participants with each of the unhealthy dietary habits (**Supplementary Table S2**). Both BMI and WHtR decreased irrespective of each unhealthy dietary habit. Participants with a habit of skipping breakfast exhibited a slightly slower decline in BMI during the follow-up period ($p = 0.049$). The other dietary habits were not associated with changes in BMI or WHtR (**Fig. 2**).

Unhealthy Dietary Habits and Risks for Proteinuria Onset

During the follow-up period, 10.6% of the participants developed proteinuria, with an incidence rate of 32.7 per 1000 person-years. The number, person-years of follow-up, event rates, and hazard ratio of proteinuria onset for each unhealthy dietary habit are shown in **Table 2** and **Supplementary Table S3**.

Figure 3 shows the Kaplan–Meier curves and the hazard ratio of proteinuria onset for each unhealthy dietary habit. Late dinner and skipping breakfast demonstrated significantly higher risks for proteinuria onset after multivariable adjustments ($p = 0.016$ and $p = 0.016$, respectively). To confirm the interaction of late dinner and skipping breakfast, we added a variable multiplied by late dinner and skipping breakfast to the model and analyzed it, but the interaction between late dinner and skipping breakfast was not observed ($p = 0.222$). The habits of quick eating and late evening snack were not associated with increased risks for proteinuria onset ($p = 0.994$ and $p = 0.222$, respectively). The interactions between baseline dietary habits and each of the baseline variables, i.e., age (<65 and ≥ 65 years), sex, and BMI (<25 and ≥ 25 kg/m²), were not significant for any type of unhealthy dietary habit (**Fig. 4**).

Discussion

This retrospective study of a Japanese general population investigated the association between unhealthy dietary habits and proteinuria onset. We found that late dinner and skipping breakfast were associated with higher risks for proteinuria onset. This result was significant even after adjusting for potential confounders, such as BMI and WHtR.

There are a variety of definitions of eating habits, which must be considered when comparing them with previous studies. For example, the participants in our study showed lower proportions of late dinner and skipping breakfast than those in previous studies. A study of South Asian Canadians defined late dinners as after 8 p.m., which was found in 37% of the subjects [20]. In another study of Americans, skipping breakfast was defined as when the meal was taken and the proportions were 17% for men and 24% for women [21, 22]. Not only the differences in the questionnaire, the higher mean age in our study might also have resulted in the lower proportions of unhealthy dietary habits than those in other studies.

Although lifestyle is an important factor in reducing residual risk, compared with established interventions such as antihypertensive therapy and smoking cessation, each lifestyle is characterized by a close relationship between them. An observational study conducted by Katsuma et al. reported that late dinner and skipping breakfast might have interaction for risks of proteinuria [10]. In our study, a status of having both late dinner and skipping breakfast habits showed no increased risk for proteinuria. The reason for this difference is unclear, but it might be due to the different questionnaire or the definitions of unhealthy dietary habits.

Dietary habits, such as late dinner and skipping breakfast, were reported to be associated with obesity or increased waist circumference, which are possible intermediate factors of proteinuria onset. For instance, an observational study conducted by Sakurai et al. reported that skipping breakfast was closely associated with annual changes in BMI and waist circumference among men [23]. In another longitudinal study, late dinner was associated with obesity [24]. It was uncertain why BMI and WHtR were not increased in people with unhealthy dietary habits in our study; however, it implied that they might not be intermediate factors in our study setting. The possibility that weight loss may not serve as an appropriate surrogate for the reduction in the risk of CKD is a point of caution when providing dietary guidance to high-risk individuals.

In this study, we confirmed the importance of these dietary habits and proteinuria onset in a large-scale Japanese general population. Previous studies have reported about dietary habits and risks for kidney injury. A cross-sectional study conducted by Fujibayashi et al. reported that eating irregular meals was associated with 1.40 times higher risks for proteinuria [25]. Another observational study reported that people having two unhealthy lifestyles have 2.04 times higher risks for CKD [26]. The effect sizes associated with dietary habits in our study were slightly small compared to those associated with dietary habits in the previous studies, but they are important for contributing to the reduction of residual risk.

In our study setting, the precise mechanism for the development of proteinuria was uncertain, but unobserved hypertension may be the possible cause. For instance, physiological suppression of cortisol at night is less observed after late dinner [27], and nocturnal cortisol elevation has been reported to be associated with morning hypertension [28]. These mechanisms might be involved in the relationship between late dinner and proteinuria onset. With regard to skipping breakfast and hypertension, Witbracht et al. reported that skipping breakfast can increase blood pressure due to hunger stress [29]. Conversely, Ahuja et al. reported that eating breakfast can reduce the rise in blood pressure [30]. A study of observing

night-time blood pressure and blood pressure in the presence or absence of breakfast might be useful for examining the relationship between late dinner, skipping breakfast, and proteinuria onset.

Our study has several limitations. First, we could not include the changes in unhealthy dietary habits during the follow-up period. Second, nutrient intake and nutrient balance that were not in the questionnaire could not be assessed. Third, it is a well-known fact that renin–angiotensin system inhibitors suppress proteinuria [31], but we were unable to include classes of antihypertensive agents in the model. Fourth, the subjects might have received nutritional guidance during the study period, which was not recorded in our study.

Conclusions

Late dinner and skipping breakfast might be associated with proteinuria onset irrespective of baseline or changes in BMI and WHtR. Considering the aspect of preventive care for the general population, these modifiable dietary habits are important. To make better use of the results of this study for nutritional guidance, an intervention study of dietary habits is necessary.

Declarations

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Authors' contributions

T.Tokumaru conducted conceptualization, data curation, and original draft preparation. T.Toyama conducted validation and original draft preparation. A. Hara and F.K examined methodology. K.K and A. Hashiba collected the original data. Y.Y, S.N, M.O, T.M, K.S and T.W reviewed and edited. N.S, M.S and T.W supervised the project. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author with the permission of the Ethics Committee on reasonable request.

Ethics approval and consent to participate

The study protocol was approved by the ethics committee of Kanazawa University Hospital (approval number: 2287-1). All data were collected and de-identified by the Kanazawa Medical Association. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

All authors have given consent for the paper to be published by the corresponding author.

Competing interests

The authors declare that they have no competing interests.

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References

1. Ortiz A, Covic A, Fliser D, Fouque D, Goldsmith D, Kanbay M, Mallamaci F, Massy ZA, Rossignol P, Vanholder R, et al. Epidemiology, contributors to, and clinical trials of mortality risk in chronic kidney failure. *The Lancet*. 2014;383:1831–43.
2. Whittaker CF, Miklich MA, Patel RS, Fink JC. Medication Safety Principles and Practice in CKD. *Clin J Am Soc Nephrol*. 2018;13:1738–46.

3. Ohkuma T, Nakamura U, Iwase M, Ide H, Fujii H, Jodai T, Kaizu S, Kikuchi Y, Idewaki Y, Sumi A, et al. Effects of smoking and its cessation on creatinine- and cystatin C-based estimated glomerular filtration rates and albuminuria in male patients with type 2 diabetes mellitus: the Fukuoka Diabetes Registry. *Hypertens Res.* 2016;39:744–51.
4. Meuleman Y, Hoekstra T, Dekker FW, Navis G, Vogt L, van der Boog PJM, Bos WJW, van Montfrans GA, van Dijk S, Group ES. Sodium Restriction in Patients With CKD: A Randomized Controlled Trial of Self-management Support. *Am J Kidney Dis.* 2017;69:576–86.
5. Eckardt KU, Kasiske BL: Foreword. *Kidney Int.* 2009;76:113:1–2.
6. Rughooputh MS, Zeng R, Yao Y. Protein Diet Restriction Slows Chronic Kidney Disease Progression in Non-Diabetic and in Type 1 Diabetic Patients, but Not in Type 2 Diabetic Patients: A Meta-Analysis of Randomized Controlled Trials Using Glomerular Filtration Rate as a Surrogate. *PLoS One.* 2015;10:e0145505.
7. Scheer FA, Hilton MF, Mantzoros CS, Shea SA. Adverse metabolic and cardiovascular consequences of circadian misalignment. *Proc Natl Acad Sci U S A.* 2009;106:4453–8.
8. Imai S, Fukui M, Kajiyama S. Effect of eating vegetables before carbohydrates on glucose excursions in patients with type 2 diabetes. *J Clin Biochem Nutr.* 2014;54:7–11.
9. Bi H, Gan Y, Yang C, Chen Y, Tong X, Lu Z. Breakfast skipping and the risk of type 2 diabetes: a meta-analysis of observational studies. *Public Health Nutr.* 2015;18:3013–9.
10. Kutsuma A, Nakajima K, Suwa K. Potential Association between Breakfast Skipping and Concomitant Late-Night-Dinner Eating with Metabolic Syndrome and Proteinuria in the Japanese Population. *Scientifica (Cairo).* 2014;2014:253581.
11. Waxman A, World Health A. WHO global strategy on diet, physical activity and health. *Food Nutr Bull.* 2004;25:292–302.
12. Toyama T, Furuichi K, Ninomiya T, Shimizu M, Hara A, Iwata Y, Kaneko S, Wada T. The impacts of albuminuria and low eGFR on the risk of cardiovascular death, all-cause mortality, and renal events in diabetic patients: meta-analysis. *PLoS One.* 2013;8:e71810.
13. Ashwell M, Cole TJ, Dixon AK. Ratio of waist circumference to height is strong predictor of intra-abdominal fat. *BMJ.* 1996;313:559–60.
14. Matsuo S, Imai E, Horio M, Yasuda Y, Tomita K, Nitta K, Yamagata K, Tomino Y, Yokoyama H, Hishida A. Collaborators developing the Japanese equation for estimated GFR: **Revised equations for estimated GFR from serum creatinine in Japan.** *Am J Kidney Dis.* 2009;53:982–92.
15. Tobin MD, Sheehan NA, Scurrah KJ, Burton PR. Adjusting for treatment effects in studies of quantitative traits: antihypertensive therapy and systolic blood pressure. *Stat Med.* 2005;24:2911–35.
16. American Diabetes A. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2018. *Diabetes Care.* 2018;41:13–27.
17. Imai E, Horio M, Watanabe T, Iseki K, Yamagata K, Hara S, Ura N, Kiyohara Y, Moriyama T, Ando Y, et al. Prevalence of chronic kidney disease in the Japanese general population. *Clin Exp Nephrol.*

- 2009;13:621–30.
18. Ramirez SP, McClellan W, Port FK, Hsu SI. Risk factors for proteinuria in a large, multiracial, southeast Asian population. *J Am Soc Nephrol.* 2002;13:1907–17.
 19. Yamagata K, Ishida K, Sairenchi T, Takahashi H, Ohba S, Shiigai T, Narita M, Koyama A. Risk factors for chronic kidney disease in a community-based population: a 10-year follow-up study. *Kidney Int.* 2007;71:159–66.
 20. Sandhu SK, Tang TS. When's dinner? Does timing of dinner affect the cardiometabolic risk profiles of South-Asian Canadians at risk for diabetes. *Diabet Med.* 2017;34:539–42.
 21. Mekary RA, Giovannucci E, Willett WC, van Dam RM, Hu FB. Eating patterns and type 2 diabetes risk in men: breakfast omission, eating frequency, and snacking. *Am J Clin Nutr.* 2012;95:1182–9.
 22. Mekary RA, Giovannucci E, Cahill L, Willett WC, van Dam RM, Hu FB. Eating patterns and type 2 diabetes risk in older women: breakfast consumption and eating frequency. *Am J Clin Nutr.* 2013;98:436–43.
 23. Sakurai M, Yoshita K, Nakamura K, Miura K, Takamura T, Nagasawa SY, Morikawa Y, Kido T, Naruse Y, Nogawa K, et al. Skipping breakfast and 5-year changes in body mass index and waist circumference in Japanese men and women. *Obes Sci Pract.* 2017;3:162–70.
 24. Yoshida J, Eguchi E, Nagaoka K, Ito T, Ogino K. Association of night eating habits with metabolic syndrome and its components: a longitudinal study. *BMC Public Health.* 2018;18:1366.
 25. Fujibayashi K, Fukuda H, Yokokawa H, Haniu T, Oka F, Ooike M, Gunji T, Sasabe N, Okumura M, Iijima K, et al. Associations between healthy lifestyle behaviors and proteinuria and the estimated glomerular filtration rate (eGFR). *J Atheroscler Thromb.* 2012;19:932–40.
 26. Michishita R, Matsuda T, Kawakami S, Kiyonaga A, Tanaka H, Morito N, Higaki Y. The Association Between Unhealthy Lifestyle Behaviors and the Prevalence of Chronic Kidney Disease (CKD) in Middle-Aged and Older Men. *J Epidemiol.* 2016;26:378–85.
 27. Birketvedt GS, Florholmen J, Sundsfjord J, Osterud B, Dinges D, Bilker W, Stunkard A. Behavioral and neuroendocrine characteristics of the night-eating syndrome. *JAMA.* 1999;282:657–63.
 28. Yen H-W, Lu Y-H, Lin C-C, Lee C-S, Kao W-P, Lee H-C, Voon W-C, Lai W-T, Sheu S-H. **A-002 Association of Lower Endogenous Cortisol Level with Higher Blood Pressure Load in Untreated Hypertensive Patients.** *Journal of Hypertension* 2011, 29.
 29. Witbracht M, Keim NL, Forester S, Widaman A, Laugero K. Female breakfast skippers display a disrupted cortisol rhythm and elevated blood pressure. *Physiol Behav.* 2015;140:215–21.
 30. Ahuja KD, Robertson IK, Ball MJ. Acute effects of food on postprandial blood pressure and measures of arterial stiffness in healthy humans. *Am J Clin Nutr.* 2009;90:298–303.
 31. Sarafidis PA, Khosla N, Bakris GL. Antihypertensive therapy in the presence of proteinuria. *Am J Kidney Dis.* 2007;49:12–26.

Tables

Table 1. Baseline characteristics of participants

Variables	All
N	26,764
Age, year	68 (9)
Men, n (%)	11,690 (44)
Body mass index, kg/m ²	22.8 (3.1)
Waist circumference, cm	83 (9)
Waist-to-height ratio, cm/cm	0.53 (0.06)
Systolic blood pressure, mmHg	132 (18)
Diastolic blood pressure, mmHg	77 (11)
eGFR, mL/min/1.73 m ²	77 (12)
Hemoglobin, g/dL	13.6 (1.4)
Triglyceride, mg/dL	103 [74, 146]
Total cholesterol, mg/dL	204 (33)
HbA1c, %	5.2 [5.0, 5.5]
Quick eating (yes), n (%)	7,659 (29)
Late dinner (yes), n (%)	5,157 (19)
Late evening snack (yes), n (%)	4,218 (16)
Skipping breakfast (yes), n (%)	2,350 (9)
Daily drinking (yes), n (%)	9,225 (34)
Current smoking (yes), n (%)	3,792 (14)

Data are presented in numbers (%), mean (SD), or median [interquartile range].

eGFR, estimated glomerular filtration rate

Table 2. Association between unhealthy dietary habits and hazard ratio of proteinuria onset

	Quick eating		Late dinner	
	Yes	No	Yes	No
Number of events	805 (10.5%)	2,039 (10.7%)	625 (12.1%)	2,219 (10.3%)
Person-years	24,882	62,020	16,582	70,321
Events per 1000 person-years	32.4	32.9	37.7	32.5
Unadjusted HR (95% CI; <i>p</i> -value) (vs. No)	0.98 (0.91, 1.07; <i>p</i> = 0.711)		1.19 (1.09, 1.30; <i>p</i> < 0.001)	
Multivariate-adjusted HR (95% CI; <i>p</i> -value) (vs. No)	1.00 (0.92, 1.09; <i>p</i> = 0.994)		1.12 (1.02, 1.22; <i>p</i> = 0.016)	

	Late evening snack		Skipping breakfast	
	Yes	No	Yes	No
Number of events	469 (11.1%)	2,375 (10.5%)	265 (11.3%)	2,579 (10.6%)
Person-years	13,783	73,120	7,314	79,589
Events per 1000 person-years	34.0	32.5	36.2	32.4
Unadjusted HR (95% CI; <i>p</i> -value) (vs. No)	1.04 (0.95, 1.15; <i>p</i> = 0.396)		1.12 (0.99, 1.27; <i>p</i> = 0.078)	
Multivariate-adjusted HR (95% CI; <i>p</i> -value) (vs. No)	1.06 (0.96, 1.18; <i>p</i> = 0.222)		1.15 (1.01, 1.31; <i>p</i> = 0.016)	

HR, hazard ratio. CI, confidence interval. Adjusted for age, sex, body mass index, systolic blood pressure, estimated glomerular filtration rate, hemoglobin, triglyceride, total cholesterol, HbA1c, serum uric acid, daily drinking, and current smoking

Supplementary Tables

Supplementary Table S1. Baseline characteristics of participants according to unhealthy dietary habits

Variables	All	Quick eating		Late dinner		Late evening snack		Skipping breakfast	
		Yes	No	Yes	No	Yes	No	Yes	No
N (%)	26,764	7,659 (29)	19,105 (71)	5,157 (19)	21,607 (81)	4,218 (16)	22,546 (84)	2,350 (9)	24,414 (91)
Age, year	68 (9)	66 (9)	69 (9)	67 (10)	68 (9)	67 (10)	68 (9)	67 (10)	68 (9)
Men, n (%)	11,690 (44)	3,313 (43)	8,377 (44)	2,925 (57)	8,765 (41)	1,644 (39)	10,046 (45)	1,117 (48)	10,573 (43)
Body mass index, kg/m ²	22.8 (3.1)	23.5 (3.2)	22.5 (3.0)	23.1 (3.2)	22.7 (3.1)	23.0 (3.3)	22.7 (3.1)	22.8 (3.3)	22.7 (3.1)
Waist circumference, cm	83 (9)	85 (9)	82 (9)	84 (9)	83 (9)	83 (9)	84 (10)	83 (10)	83 (9)
Waist-to-height ratio, cm/cm	0.53 (0.06)	0.54 (0.06)	0.53 (0.06)	0.53 (0.06)	0.53 (0.06)	0.53 (0.07)	0.53 (0.06)	0.53 (0.06)	0.53 (0.06)
Systolic blood pressure, mmHg	132 (18)	133 (18)	132 (18)	133 (18)	132 (18)	131 (18)	133 (18)	132 (19)	132 (18)
Diastolic blood pressure, mmHg	77 (11)	78 (11)	77 (11)	78 (11)	77 (11)	77 (11)	78 (11)	78 (11)	77 (11)
eGFR, mL/min/1.73 m ²	77 (12)	78 (12)	77 (12)	79 (13)	77 (12)	78 (12)	78 (12)	80 (13)	77 (12)
Hemoglobin, g/dL	13.6 (1.4)	13.7 (1.4)	13.5 (1.4)	13.8 (1.5)	13.5 (1.4)	13.5 (1.4)	13.6 (1.4)	13.7 (1.4)	13.5 (1.4)
Triglyceride, mg/dL	103 [74, 146]	106 [76, 152]	101 [73, 144]	103 [74, 149]	103 [74, 145]	103 [74, 149]	103 [74, 146]	106 [74, 154]	103 [74, 146]
Total cholesterol, mg/dL	204 (33)	206 (33)	204 (34)	202 (34)	205 (33)	207 (34)	204 (33)	206 (36)	204 (33)
HbA1c, %	5.2 [5.0, 5.5]	5.2 [5.0, 5.5]	5.2 [5.0, 5.5]	5.2 [5.0, 5.5]	5.2 [5.0, 5.5]	5.2 [5.0, 5.5]	5.2 [5.0, 5.5]	5.1 [4.9, 5.4]	5.2 [5.0, 5.5]
Serum uric acid, mg/dL	5.0 (1.3)	5.1 (1.3)	5.0 (1.3)	5.2 (1.3)	5.0 (1.2)	4.9 (1.3)	5.0 (1.3)	5.2 (1.4)	5.0 (1.3)
Daily drinking, n (%)	9,225 (34)	2,709 (35)	6,516 (34)	2,681 (52)	6,544 (30)	1,135 (27)	8,090 (36)	1,011 (43)	8,214 (34)
Current smoking, n (%)	3,792 (14)	1,152 (15)	2,640 (14)	1,147 (22)	2,645 (12)	657 (16)	3,135 (14)	2,350 (9)	3,050 (12)

Data are presented in numbers (%), mean (SD), or median [interquartile range]. eGFR, estimated glomerular filtration rate

Supplementary Table S2. Baseline mean body mass index and waist-to-height ratio according to unhealthy dietary habits

Unhealthy dietary habits	Body mass index (kg/m ²)			Waist-to-height ratio (cm/cm)		
	Yes	No	p-value	Yes	No	p-value
Quick eating	23.3	22.5	< 0.001	0.54	0.53	< 0.001
Late dinner	23.0	22.7	< 0.001	0.54	0.53	< 0.001
Late evening snack	23.1	22.7	< 0.001	0.54	0.53	< 0.001
Skipping breakfast	22.8	22.7	< 0.001	0.53	0.53	< 0.001

Adjusted for age, sex, systolic blood pressure, estimated glomerular filtration rate, hemoglobin, triglyceride, total cholesterol,

HbA1c, serum uric acid, daily drinking, and current smoking

Supplementary Table S3. Hazard ratios of proteinuria onset for late dinner or skipping breakfast along with covariates

Variables	Hazard ratio	(95% CI)	p-value	Variables	Hazard ratio	(95% CI)	p-value
Late dinner (vs. no late dinner)	1.12	(1.02, 1.22)	0.016	Skipping breakfast (vs. no skipping breakfast)	1.15	(1.01, 1.31)	0.032
Age (+1 year)	1.02	(1.01, 1.02)	<0.001	Age (+1 year)	1.02	(1.01, 1.02)	<0.001
Men (vs. women)	1.53	(1.38, 1.69)	<0.001	Men (vs. women)	1.54	(1.39, 1.70)	<0.001
Body mass index (+1 kg/m ²)	1.02	(1.01, 1.03)	0.001	Body mass index (+1 kg/m ²)	1.02	(1.01, 1.04)	0.001
Systolic blood pressure (+5 mm/Hg)	1.05	(1.04, 1.06)	<0.001	Systolic blood pressure (+5 mm/Hg)	1.05	(1.04, 1.06)	<0.001
eGFR (-10 mL/min/1.73 m ²)	1.03	(0.99, 1.06)	0.135	eGFR (-10 mL/min/1.73m ²)	1.02	(0.99, 1.06)	0.139
Hemoglobin (-1 g/dL)	1.08	(1.04, 1.11)	<0.001	Hemoglobin (-1 g/dL)	1.08	(1.04, 1.11)	<0.001
Triglyceride (+10 mg/dL)	1.01	(1.00, 1.01)	0.005	Triglyceride (+10 mg/dL)	1.01	(1.00, 1.01)	0.005
Total cholesterol (+10 mg/dL)	0.98	(0.97, 0.99)	0.005	Total cholesterol (+10 mg/dL)	0.98	(0.97, 0.99)	0.004
HbA1c (+1 %)	1.20	(1.15, 1.26)	<0.001	HbA1c (+1 %)	1.20	(1.15, 1.26)	<0.001
Serum uric acid (+1 mg/dL)	0.99	(0.95, 1.02)	0.398	Serum uric acid (+1 mg/dL)	0.98	(0.95, 1.02)	0.375
Daily drinking (vs. no daily drinking)	0.94	(0.86, 1.02)	0.140	Daily drinking (vs. no daily drinking)	0.95	(0.87, 1.03)	0.215
Current smoking (vs. no current smoking)	1.26	(1.13, 1.40)	<0.001	Current smoking (vs. no current smoking)	1.25	(1.13, 1.39)	<0.001

CI, confidence interval; eGFR, estimated glomerular filtration rate

Figures

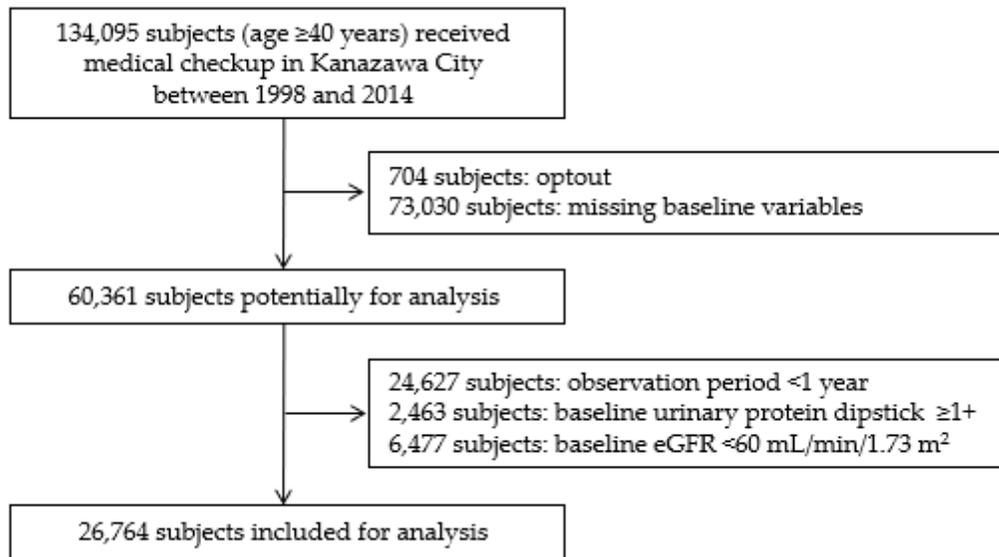


Figure 1

Flow diagram of the study Baseline variables contain unhealthy dietary habits (late dinner, skipping breakfast, quick eating, and late evening snack), height, body weight, waist circumference, blood pressure, urine protein (dipstick measurement), serum creatinine, hemoglobin, triglyceride, total cholesterol, blood glucose, glycated hemoglobin (HbA1c), serum uric acid, daily drinking, current smoking, use of antihypertensive agents, and use of glucose-lowering medication. eGFR, estimated glomerular filtration rate

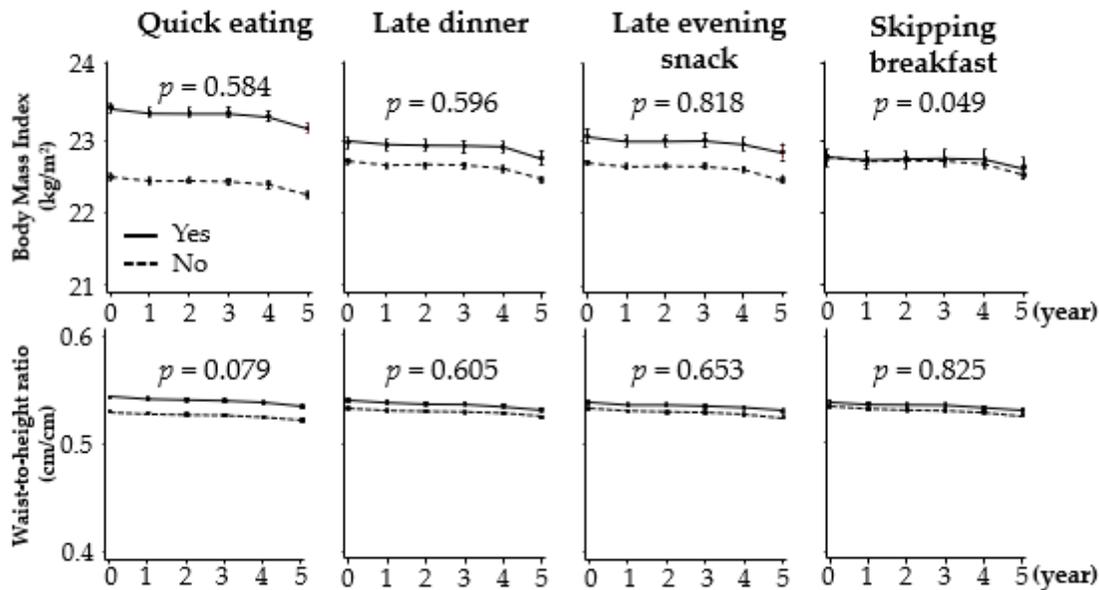


Figure 2

Changes in body mass index and waist-to-height ratio according to baseline unhealthy dietary habits. Adjusted for age, sex, body mass index, systolic blood pressure, estimated glomerular filtration rate, hemoglobin, triglyceride, total cholesterol, HbA1c, serum uric acid, daily drinking, and current smoking. Error bars represent the 95% confidence interval.

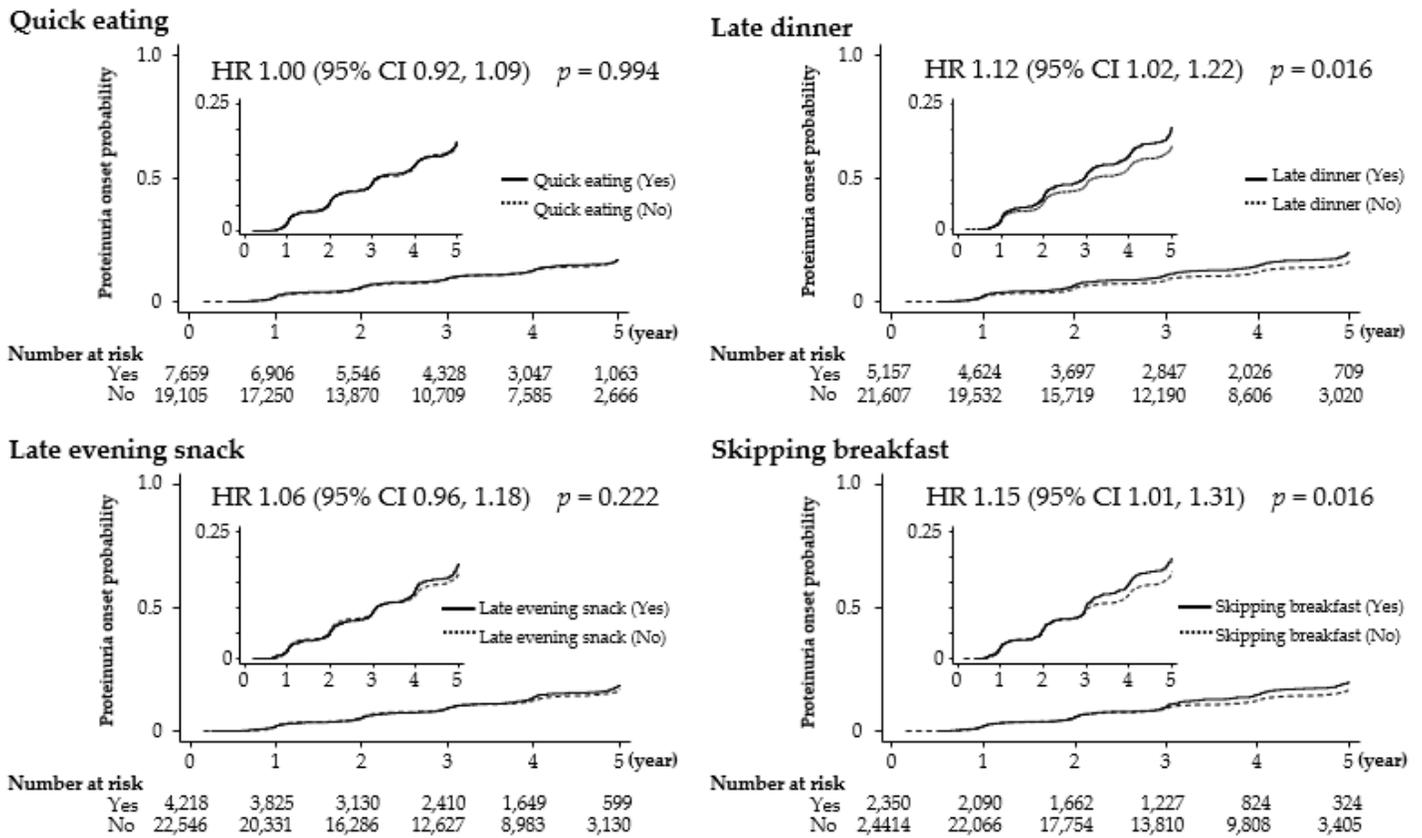


Figure 3

Kaplan–Meier curves and hazard ratio of proteinuria onset for each unhealthy dietary habit. Adjusted for age, sex, body mass index, systolic blood pressure, estimated glomerular filtration rate, hemoglobin, triglyceride, total cholesterol, HbA1c, serum uric acid, daily drinking, and current smoking. HR, hazard ratio; CI, confidence interval

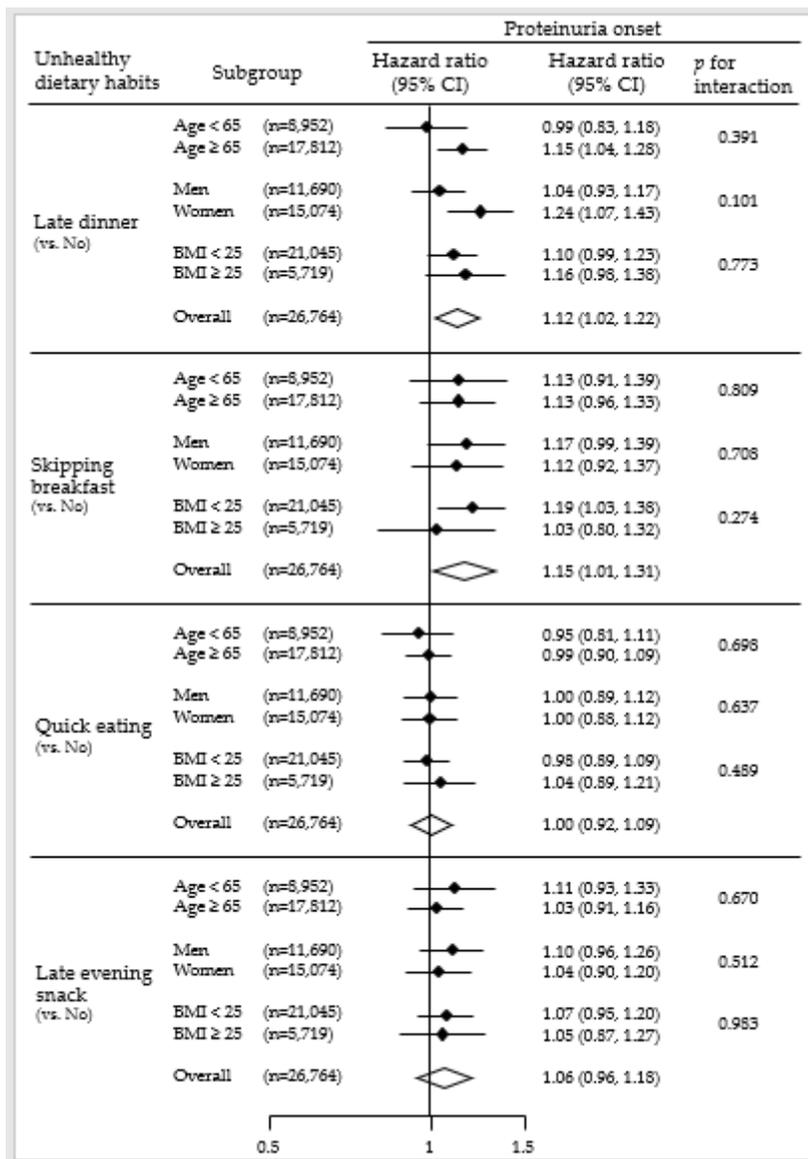


Figure 4

Association between unhealthy dietary habits and proteinuria onset according to the baseline categories of age, sex, and body mass index Adjusted for age, sex, body mass index, systolic blood pressure, estimated glomerular filtration rate, hemoglobin, triglyceride, total cholesterol, HbA1c, serum uric acid, daily drinking, and current smoking. (When the variable of subgroup was included in the explanatory variable, it was excluded from adjustment.) CI, confidence interval; BMI, body mass index

Supplementary Files

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- [supplement1.docx](#)