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Short Communication

Lifestyle Modification Is Associated with Improving Estimated Glomerular Filtration Rate (eGFR) and Proteinuria in Japanese with Proteinuria

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The link between lifestyle modification and changes in both proteinuria and estimated glomerular filtration rates (eGFRs) was evaluated in Japanese subjects with proteinuria who were not taking medications. We used data from 51 men (35.8 ± 10.0 years) and 74 women (38.0 ± 11.0 years) with proteinuria at baseline and a 1-year follow up. eGFR was defined by a new equation developed specifically for Japanese subjects. Subjects were given advice for dietary and lifestyle improvement at the initial appointment. At the 1-year follow up, eGFR was increased in both sexes, but not at significant levels. (men: $p = 0.7709$, women: $p = 0.2180$). Proteinuria was also improved in many subjects. A decrease in proteinuria may be associated with improving eGFR in Japanese.

Key words: proteinuria, estimated glomerular filtration rate (eGFR), lifestyle modification

Chronic kidney disease (CKD) is a common disorder and has become a public health challenge [1]. We previously reported in a cross-sectional study that the estimated glomerular filtration rate (eGFR) [2] in men with abdominal obesity and in women with hypertension was significantly lower than that in subjects without these components of metabolic syndrome [3]. A longitudinal our analysis showed that decreasing systolic blood pressure was associated with improving eGFR in healthy Japanese women [4]. In addition, proteinuria has been closely linked to lower eGFR in Okayama prefecture, Japan [5].

However, whether decreases in proteinuria with lifestyle modification are beneficial for improving eGFR remains to be investigated in a longitudinal study.

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In this study, we evaluate the link between changes in eGFR and changes in proteinuria in Japanese at a 1-year follow up after lifestyle modification counseling was given.

Subjects and Methods

Subjects. We used data for 51 men (35.8 ± 10.0 years) and 74 women (38.0 ± 11.0 years) with proteinuria, who met the following criteria: (1) received a health check-up including special health guidance and a follow-up check-up 1-year later, (2) received anthropometric measurements as part of the annual health check-up, (3) received no medications for diabetes, hypertension, and/or dyslipidemia, and (4) provided written informed consent (Table 1).

At the first health check-up, all subjects were given instructions by well-trained medical staff on how to change their lifestyle as special health guidance. Nutritional instruction was provided with a well-

Table 1 Clinical profiles of enrolled subjects and changes in parameters with lifestyle modification after 1 year

	Men			Women		
	Baseline	Follow up	*p*	Baseline	Follow up	*p*
Number of subjects	51			74		
Age	35.8 ± 10.0			38.0 ± 11.0		
Height (cm)	169.6 ± 5.8			157.0 ± 5.7		
Body weight (kg)	72.7 ± 14.7	71.5 ± 13.2	0.1070	57.1 ± 10.1	56.7 ± 10.2	0.2960
Body mass index (kg/m^2)	25.3 ± 4.7	24.8 ± 4.2	0.0690	23.2 ± 4.0	23.0 ± 4.0	0.1746
Abdominal circumference (cm)	83.1 ± 12.7	82.3 ± 11.1	0.3030	73.1 ± 9.7	73.0 ± 9.9	0.6772
Hip circumference (cm)	95.2 ± 7.4	94.5 ± 6.4	0.1300	91.7 ± 6.2	91.5 ± 5.7	0.5469
Creatinine (mg/dl)	0.84 ± 0.13	0.82 ± 0.11	0.2034	0.63 ± 0.15	0.60 ± 0.10	**0.0247**
eGFR (ml/min/1.73m^2)	87.9 ± 17.9	88.4 ± 14.9	0.7709	89.6 ± 23.9	92.5 ± 20.2	0.2180

Mean ± SD

trained nutritionist, who planned a diet for each subject based on their data and provided simple instructions (*i.e.* not to eat too much and to consider balance when they eat). Exercise instruction was also provided by a well-trained physical therapist, who encouraged each subject to increase their daily amount of steps walked. At the the second health check-up, medical staff subjectively evaluated changes in their lifestyle and subjects with proteinuria were encouraged to receive medications.

Ethical approval for the study was obtained from the Ethical Committee of Okayama Health Foundation, Okayama, Japan.

Anthropometric and body composition measurements. Anthropometric and body compositions were evaluated based on the following parameters: height, body weight and abdominal circumference. Body mass index (BMI) was calculated by weight/[height]^2, in kg/m^2. Abdominal circumference was measured at the umbilical level and the hip was measured at the widest circumference over the trochanter in standing subjects after normal expiration [6].

Urine examination. Urine samples were collected before 10 a.m. as second urine of the day and were subjected to examination within 1 h. The urine examination was performed using urine test strips (BAYER, Tokyo, Japan). The reagent strip was dipped directly into the urine sample. Just after dipping, the sample was graded as negative (−), trace positive (±), or +, 2+, 3+or 4+positive at levels of 30, 100, 300 or 1,000 mg/dl, respectively, based on color chart found on the container's label [7].

Blood sampling and assays. We measured overnight fasting serum levels of creatinine (Cr) (enzymatic method). eGFR was calculated using the following equation: eGFR (ml/min/1.73 m^2)$=194\times$ Cr$^{-1.094}\times$Age$^{-0.287}\times 0.739$ (a constant derived specifically for women) [2]. Reduced eGFR was defined as an eGFR $<$60 ml/min/1.73 m^2.

Statistical analysis. Data are expressed as means ± standard deviations (SDs). Statistical analysis was performed using a paired t test: $p<0.05$ was considered to be statistically significant.

Results

The clinical parameters at baseline and 1-year follow up are summarized in Table 1. Anthropometric and body composition parameters such as body weight, BMI, abdominal circumference and hip circumference were reduced with lifestyle modification after one year, but not at a significant level in both sexes. Cr was significantly decreased in women; eGFR was increased, but not at a significant level in either sex (Table 1). Only one man and 5 women were diagnosed below normal-range eGFR at baseline, and one men and one woman at the 1-year follow up.

We further evaluated the changes in proteinuria (Table 2). At baseline, 36 men and 57 women were diagnosed with trace proteinuria (±), 8 men and 11 women as+, 5 men and 4 women as 2+, and 2 men and 2 women as 3+. However, after lifestyle modifications at the 1-year follow up, 38 men and 56 women were diagnosed as proteinuria negative (−), 7 men and 10 women as trace (±), 2 men and 5 women as+, 3 men and 2 women as 2+, and 1 man and 1 woman as 3+. Proteinuria was increased in only 3 men

Table 2 Changes in proteinuria with lifestyle modification in subjects with proteinuria after 1 year

		Follow up				
Men		Proteinuria (−)	Proteinuria (±)	Proteinuria (+)	Proteinuria (2+)	Proteinuria (3+)
Baseline	Proteinuria (±)	31	3	1	0	1
	Proteinuria (+)	5	1	1	1	0
	Proteinuria (2+)	2	2	0	1	0
	Proteinuria (3+)	0	1	0	1	0
Women						
Baseline	Proteinuria (±)	45	8	3	0	1
	Proteinuria (+)	7	2	1	1	0
	Proteinuria (2+)	2	0	1	1	0
	Proteinuria (3+)	2	0	0	0	0

Table 3 Changes in eGFR in subjects whose proteinuria increased in the 1-year periodr

		Proteinuria		eGFR(ml/min/1.73m^2)	
Subjects	Sex	Baseline	Follow up	Baseline	Follow up
1	Men	+	2+	80.4	75.0
2	Men	±	3+	62.8	52.6
3	Men	±	+	133.2	94.7
4	Women	+	2+	80.8	87.2
5	Women	±	3+	82.1	81.5
6	Women	±	+	69.7	118.9
7	Women	±	+	152.7	133.1
8	Women	±	+	99.1	98.3

eGFR: estimated glomerular filtration rate

(5.9%) and 5 women (6.8%) after 1 year.

Finally, we evaluated the changes in eGFR in the 8 subjects mentioned above with increased proteinuria at the 1-year follow up (Table 3). Their eGFR was decreased at the 1-year follow up, but not at a significant level (Baseline: 95.1±31.8 ml/min/1.73 m^2, Follow up: 92.7±25.2 ml/min/1.73m^2, p=0.7916).

Discussion

The main objective of this study was to explore the link between changes in eGFR and changes in proteinuria in Japanese with proteinuria at a 1-year follow up.

It is well known that an unhealthy lifestyle is closely associated with CKD. Lower physical activity was reported to be a risk for death in patients with CKD [8]. Shankar *et al.* showed that heavy drinking was also closely linked to CKD [9]. In addition, several studies have shown that restriction of protein intake is useful for preventing and improving CKD [10-12]. Swift *et al.* also reported that modest salt reduction reduces blood pressure and urine protein excretion in black hypertensives [13]. Therefore, it seems reasonable to suggest that simple improvements in lifestyle might result in the amelioration of CKD in some Japanese. However, these are few studies on the link between lifestyle modification and CKD using the new equation developed in Japan, so the hypothesis that CKD may be improving by lifestyle modification has not yet been confirmed in the Japanese population.

We previously evaluated the relationship between eGFR and proteinuria in a cross-sectional analysis [5]. The prevalence of proteinuria was closely linked to reduced eGFR. eGFR in subjects with proteinuria at the + level or greater was significantly lower than that in subjects without proteinuria for both sexes. About 15.0% men and women in subjects with proteinuria at the + level or greater were diagnosed as having reduced eGFR. Iseki K *et al.* also identified a strong, graded relationship between end-stage renal disease and dipstick urinalysis positivity for proteinuria, with an adjusted odds ratio was 2.71 [14]. Therefore, proteinuria is a strong, independent predictor of end-stage renal disease. However, in this study, lifestyle modification alone (without medication) in subjects with proteinuria resulted in increased eGFR and improved proteinuria at the one-year follow-up compared to the initial visit. Although we could not evaluate pathophysiological concerns such as IgA nephropathy and nephrotic syndrome, only 8 subjects developed massive proteinuria. Taken together, lifestyle modification alone may be a useful method for improving eGFR in Japanese subjects with proteinuria.

Potential limitations remain in our study. First, the small sample size in our study makes it difficult to infer causality between eGFR and lifestyle modification. eGFR was not significantly improved, especially in men. At the first health check-up, all subjects were given instructions by well-trained medical staff on how to change their lifestyle. However, the changes in participants' lifestyles were not quantitatively evaluated, and the gender differences in lifestyle and improvements in eGFR were also not clearly illuminated. The difference in eGFR between the participants who actually altered their lifestyles and the participants who did not would have been helpful. In addition, eGFR whose proteinuria increased over the one-year period was not significantly decreased in this study. Second, we also could not reveal the mechanism of the linkage between eGFR and lifestyle modification. Third, most of the enrolled subjects were not diagnosed as below-normal-range eGFR at baseline. Therefore, the results in this study may not apply for all patients with CKD.

In conclusion, a decrease in proteinuria with simple lifestyle modification and no medication changes appeared to be associated with an increase in eGFR. Therefore, lifestyle modification alone may be a useful measure for the improvement of CKD.

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References

1. National Kidney Foundation: K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Kidney Disease Outcome Quality Initiative. Am J Kidney Dis (2002) 39: S1–S266.
2. Matsuo S, Imai E, Horio M, Yasuda Y, Tomita K, Nitta K, Yamagata K, Tomino Y, Yokoyama H and Hishida A; on behalf of the collaborators developing the Japanese equation for estimated GFR: Revised equations for estimated GFR from serum creatinine in Japan. Am J Kidney Dis (2009) 53: 982–992.
3. Miyatake N, Shikata K, Makino H and Numata T: Relationship between Estimated Glomerular Filatration Rate (eGFR) and Metabolic Syndrome in the Japanese Population. Acta Med Okayama (2010) 64: 203–208.
4. Miyatake N, Shikata K, Makino H and Numata T: Decreasing systolic blood pressure is associated with improving estimated glomerular filtration rate (eGFR) with lifestyle modification in Japanese healthy women. Acta Med Okayama (2010) 64: 339–343.
5. Miyatake N, Shikata K, Makino H and Numata T: The relation between glomerular filtration rate (eGFR) and Proteinuria in Okayama prefecture, Japan. Environ Health Prev Med (2011) 16: 191–195.
6. Definition and the diagnostic standard for metabolic syndrome—Committee to Evaluate Diagnostic Standards for Metabolic Syndrome, Nippon Naika Gakkai Zasshi (2005) 94: 794–809 (in Japanese).
7. Wallace JF, Pugia MJ, Lott JA, Luke KE, Shihabi ZK, Sheehan M and Bucksa JM: Multisite evaluation of a new dipstick for albumin, protein and creatinine. J Clin Lab Anal (2001) 15: 231–235.
8. Shlipak MG, Fried LF, Cushman M, Manolio TA, Peterson D, Stehman-Breen C, Bleyer A, Newman A, Siscovick D and Psaty B: Cardiovascular mortality risk in chronic kidney disease: comparison of traditional and novel risk factors. JAMA (2005) 293: 1737–1745.
9. Shankar A, Klein R and Klein BE: The association among smoking, heavy drinking, and chronic kidney disease. Am J Epidemiol (2006) 164: 263–271.
10. Fouque D, Wang P, Laville M and Boissel JP: Low protein diets delay end-stage renal disease in non-diabetic adults with chronic renal failure. Nephrol Dial Transplant (2000) 15: 1986–1992.
11. Pedrini MT, Levey AS, Lau J, Chalmers TC and Wang PH: The effect of dietary protein restriction on the progression of diabetic and nondiabetic renal diseases: a meta-analysis. Ann Intern Med (1996) 124: 627–632.
12. Kasiske BL, Lakatua JD, Ma JZ and Louis TA: A meta-analysis of the effects of dietary protein restriction on the rate of decline in renal function. Am J Kidney Dis (1998) 31: 954–961.
13. Swift PA, Markandu ND, Sagnella GA He FJ and MacGregor GA: Modest salt reduction reduces blood pressure and urine protein excretion in black hypertensives: a randomized control trial. Hypertension (2005) 46: 308–312.
14. Iseki K, Ikemiya Y, Iseki C and Takishita S: Proteinuria and the risk of developing end-stage renal disease. Kidney Int (2003) 63: 1468–1474.