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Original Article

Decreasing Abdominal Circumference Is Associated with Improving Estimated Glomerular Filtration Rate (eGFR) with Lifestyle Modification in Japanese Men: A Pilot Study

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The link between changes in a subject's metabolic syndrome components and his estimated glomerular filtration rate (eGFR) was evaluated in healthy Japanese men. We used data from 120 Japanese men (45.5 ± 8.4 years) with a 1-year follow up. eGFR was defined by a new equation developed for Japan. There were no significant differences in eGFR between men with and without metabolic syndrome components at baseline. Subjects were given advice for dietary and lifestyle improvement. At the 1-year follow up, almost all metabolic syndrome components were significantly improved. However, eGFR was significantly decreased. The changes in eGFR were weakly correlated with abdominal circumference ($r = -0.232$, $p = 0.0106$). A decrease in abdominal circumference may be associated with improving eGFR in Japanese men.

Key words: abdominal circumference, estimated glomerular filtration rate (eGFR), metabolic syndrome, lifestyle modification

Chronic kidney disease (CKD) has become a public health challenge and is a common disorder [1]. For example, approximately 20% of adults have CKD, which is defined as kidney damage or a glomerular filtration rate (GFR) < 60 ml/min/1.73 m^2 for at least 3 months, regardless of cause [2]. We have also previously reported in a cross-sectional study that the estimated glomerular filtration rate (eGFR) [3] in men with abdominal obesity and in women with hypertension was significantly lower than that in subjects without these components of metabolic syndrome [4]. In addition, we have shown that decreasing systolic blood pressure is associated with improving eGFR with lifestyle modification in healthy Japanese women [5]. However, whether decreases in metabolic syndrome components are beneficial for improving eGFR, and what effect this has on eGFR remain to be investigated in a longitudinal study in Japanese men.

In this study, we evaluated the link between changes in eGFR and changes in metabolic syndrome components in Japanese men with a 1-year follow up.

Subjects and Methods

Subjects. We used data for 120 Japanese men from a data-base of 16,383 people at the Okayama Southern Institute of Health in Okayama prefecture, Japan, aged 45.5 ± 8.4 years, who met the following criteria: (1) received a health check-up, including

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special health guidance and a follow-up check-up 1-year later; (2) received anthropometric measurements, fasting blood examination, and blood pressure 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-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 number of steps walked.

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

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 in standing subjects after normal expiration [6].

Blood pressure measurements at rest. Resting systolic and diastolic blood pressures were measured indirectly using a mercury sphygmomanometer placed on the right arm of the seated participant after at least 15 min of rest.

Urine examination. Urine samples were collected from the second-morning urine (before 10 a.m.) and 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, +: positive (30 mg/dl), 2+: positive (100 mg/dl), 3+: positive (300 mg/dl), or 4+: positive (1,000 mg/dl) by comparison with a standard color chart found on the container's label.

Blood sampling and assays. We measured overnight fasting serum levels of creatinine (Cr) (enzymatic method), high-density lipoprotein (HDL) cholesterol, triglycerides (L Type Wako Triglyceride・H, Wako Chemical, Osaka, Japan), and blood sugar. eGFR was calculated using the following equation: eGFR (ml/min/1.73 m^2) $= 194 \times Cr^{-1.094} \times Age^{-0.287}$ [3]. Reduced eGFR was defined as an eGFR < 60 ml/min/1.73 m^2.

Definition of metabolic syndrome. Men with an abdominal circumference in excess of 85 cm were defined as having metabolic syndrome if they also had two or more of the following components: 1) Dyslipidemia: triglycerides ≥ 150 mg/dl and/or HDL cholesterol < 40 mg/dl, 2) High blood pressure: blood pressure $\geq 130/85$ mmHg, 3) Impaired glucose tolerance: fasting plasma glucose ≥ 110 mg/dl [6].

Table 1 Clinical characteristics and changes in parameters with 1-year follow up

	Baseline	Follow up	*p*
Number of Subjects	120		
Age	45.5 ± 8.4		
Height (cm)	169.0 ± 5.3		
Body weight (kg)	75.6 ± 11.3	74.0 ± 10.7	**<0.0001**
Body mass index (kg/m^2)	26.5 ± 3.6	25.9 ± 3.4	**<0.0001**
Abdominal circumference (cm)	88.5 ± 9.8	86.3 ± 9.2	**<0.0001**
Systolic blood pressre (mmHg)	131.5 ± 14.6	123.9 ± 12.5	**<0.0001**
Diastolic blood pressure (mmHg)	82.6 ± 11.5	77.0 ± 9.2	**<0.0001**
Triglyceride (mg/dl)	153.3 ± 110.2	121.7 ± 80.3	**0.0011**
HDL cholesterol (mg/dl)	54.2 ± 14.6	56.2 ± 14.9	**0.0390**
Blood sugar (mg/dl)	102.7 ± 18.1	104.2 ± 28.3	0.3710
Cr (mg/dl)	0.81 ± 0.12	0.84 ± 0.12	**0.0012**
eGFR (ml/min/1.73 m^2)	84.0 ± 13.9	80.1 ± 13.1	**<0.0001**

Mean ± SD

Statistical analysis. Data are expressed as means ± standard deviation (SD). A statistical analysis was performed using a paired t test and χ^2 test: $p < 0.05$ was considered to be statistically significant. Pearson's correlation coefficients were calculated and used to test the significance of the linear relationship among continuous variables.

Results

The clinical parameters at the baseline and the 1-year follow up are summarized in Table 1. Anthropometric and body composition parameters such as body weight, BMI, and abdominal circumference were significantly reduced with lifestyle modification after 1 year. Cr was significantly increased, and eGFR was decreased. Thirty-six subjects were diagnosed as having metabolic syndrome at baseline, and 18 subjects were diagnosed as having metabolic syndrome after 1 year, which was a significant reduction ($p < 0.0001$). Two subjects were diagnosed with reduced eGFR at baseline, and 3 subjects were diagnosed with reduced eGFR at the 1-year follow up. In addition, four subjects were identified as trace positive, 2 were identified as positive (+), and one was identified as positive (2+) for proteinuria at baseline, while 5 were identified as trace positive, 4 as positive (+), and 2 as positive (2+) at the 1-year follow up.

In subjects not taking medications, we also compared eGFR levels between the groups with and without each component of the Japanese definition of metabolic syndrome (Table 2). eGFR in men with abdominal obesity was significantly higher than that in men without abdominal obesity. However, there were no significant differences of eGFR between the groups with or without other components of metabolic syndrome. In addition, eGFR in subjects with metabolic syndrome was similar to that in subjects without it.

We further evaluated the relationship between changes in eGFR and changes in clinical parameters. Changes in eGFR were weakly correlated with changes in abdominal circumference ($r = -0.232$, $p = 0.0106$) (Table 3, Fig. 1). After we excluded one subject with abnormal changes in eGFR (-37.7 ml/min/1.73 m^2), changes in eGFR were still weakly correlated with changes in abdominal circumference ($n = 119$, $r = -0.203$, $p = 0.0265$). However, changes in eGFR were not significantly correlated with changes in other metabolic components.

Finally, we investigated the changes in eGFR amongst men with different levels of increased abdominal circumference [Group I: Delta (delta represents positive changes in abdominal circumference) abdominal circumference ≧ 0 cm, Group D: Delta abdominal circumference < 0 cm]. After the 1-year follow up, changes in eGFR in Group I (-6.0 ± 10.2 ml/min/1.73 m^2) were lower than those in Group D (-2.7 ± 8.2 ml/min/1.73 m^2), but not at a significant level ($p = 0.0599$).

Table 2 Comparison of eGFR between men with and without metabolic syndrome

	Abdominal obesity (−)	Abdominal obesity (+)	p
Number of subjects	42	78	
eGFR (ml/min/1.73 m^2)	79.1 ± 13.9	86.6 ± 13.2	**0.0042**
	Impaired glucose torelance (−)	Impaired glucose torelance (+)	
Number of subjects	96	24	
eGFR (ml/min/1.73 m^2)	82.7 ± 13.7	88.8 ± 13.8	0.0535
	Hypertension (−)	Hypertension (+)	
Number of subjects	48	72	
eGFR (ml/min/1.73 m^2)	83.2 ± 14.8	84.5 ± 13.3	0.6326
	Dyslipidemia (−)	Dyslipidemia (+)	
Number of subjects	71	49	
eGFR (ml/min/1.73 m^2)	82.3 ± 14.1	86.2 ± 13.5	0.1348
	Metabolic syndrome (−)	Metabolic syndrome (+)	
Number of subjects	84	36	
eGFR (ml/min/1.73 m^2)	82.4 ± 14.0	87.5 ± 13.2	0.0644

Mean ± SD

Table 3 Simple correlation analysis between changes in eGFR andchanges in clinical parameters with 1-year follow up

	r	*p*
Abdominal circumference (cm)	−0.232	**0.0106**
Systolic blood pressre (mmHg)	0.094	0.3068
Diastolic blood pressure (mmHg)	−0.009	0.9227
Triglyceride (mg/dl)	−0.055	0.5521
HDL cholesterol (mg/dl)	−0.016	0.8616
Blood sugar (mg/dl)	−0.030	0.7458

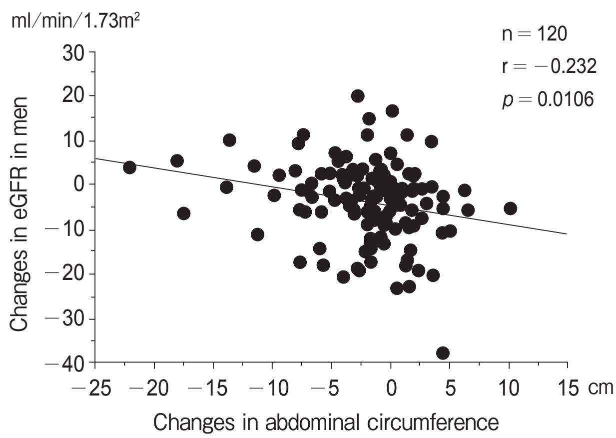

Fig. 1 Simple correlation analysis between changes in eGFR and changes in systolic blood pressure at the 1-year follow up.

Discussion

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

Ninomiya T *et al.* [7], Tanaka *et al.* [8] and Iseki *et al.* [9] reported that metabolic syndrome, using the modified ATP III definition [10], was associated with CKD in the Japanese population. Compared with subjects with 0 or 1 components of metabolic syndrome, subjects with 2, 3, and 4 or more components had odds ratios of 1.13, 1.90, and 2.79 for CKD [7]. In this study, 36 subjects was diagnosed as having metabolic syndrome, using the Japanese criteria, at baseline, and 18 were diagnosed as having metabolic syndrome at the 1-year follow up. We have previously reported a prevalence of 30.7% for metabolic syndrome in Japanese men [11]. In this study, with lifestyle modification after the initial health check-up, metabolic components were significantly improved in men without medications at the 1-year follow-up. Although eGFR was not increased after 1 year, changes in eGFR were negatively correlated with changes in abdominal circumference. Taken together, lifestyle modification targeting reducing abdominal circumference may be a useful method for improving eGFR in Japanese men.

Abdominal obesity contributes to the development of renal injury and end-stage renal disease [12-14]. Bonnet *et al.* have reported that abdominal obesity is related to the development of elevated albuminuria in both sexes, suggesting that the measurement of abdominal circumference might improve the identification of non-diabetic individuals at risk of developing microalbuminuria [12]. In addition, a greater waist-to-hip ratio is associated with a greater risk of diminished filtration, even when corrected for BMI [13]. Yamagata *et al.* have reported that the baseline-adjusted predictor of developing CKD included age, GFR, hematuria, hypertension, diabetes, serum lipids, obesity, smoking status, and consumption of alcohol with a 10-year follow up [14]. In the present study, there were significant differences in eGFR between subjects with and without abdominal obesity at baseline. However, we revealed that, with lifestyle modification, changes in abdominal circumference were weakly correlated with changes in eGFR in men without medications. Changes in other metabolic components were not linked to changes in eGFR. Therefore, the clinical impact of adnominal circumference on eGFR was noted in Japanese men.

Potential limitations remain in our study. First, the 16,383 subjects in our study voluntarily underwent the annual health check-up; they were, therefore, probably more health-conscious than the average person. The selected 120 men underwent an annual health check-up every year with a follow-up duration of 1-year and received no medication; they were, therefore, probably even more health-conscious than most of the subjects in the database, and the small sample size may make it difficult to infer causality between eGFR and abdominal circumference. At baseline, in contrast to our previous report regarding a large sample (n = 11,711) from a cross-sectional study [4], eGFR in men with abdominal obesity was higher than that in men without abdominal obesity. eGFR was not increased with lifestyle modification after 1 year

(−3.9 ml/min/1.73 m^2/year). A link has previously been found between eGFR and age, based on a large sample from a Japanese cohort, with an average decline rate of eGFR of 0.36 ml/min/1.73 m^2/year [15]. Therefore, the decline rate of eGFR in our study was higher than that previously reported. Second, we could not identify the mechanism of the linkage between eGFR and abdominal circumference. Third, most of the enrolled subjects were not diagnosed as CKD at baseline. Therefore, the results in this study may not apply to patients with CKD. Further prospective studies are needed in Japanese subjects.

In conclusion, a decrease in abdominal circumference with lifestyle modification might induce an improvement in eGFR. Therefore, lifestyle modification may be a necessary and useful measure for the prevention of CKD in Japanese men.

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