Acta Med. Okayama, 2010
Vol. 64, No. 5, pp. 339-343

Acta Medica Okayama
http://escholarship.lib.okayama-u.ac.jp/amo/

Short Communication

Decreasing Systolic Blood Pressure Is Associated with Improving Estimated Glomerular Filtration Rate (eGFR) with Lifestyle Modification in Japanese Healthy Women

Nobuyuki Miyatake[a]*, Kenichi Shikata[b], Hirofumi Makino[b], and Takeyuki Numata[c]

[a]*Department of Hygiene, Faculty of Medicine, Kagawa University, Miki, Kagawa, 761-0793, Japan,*
[b]*Department of Medicine and Clinical Science, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, 700-8558, Japan, and*
[c]*Okayama Southern Institute of Health, Okayama Health Foundation, Okayama 700-0952, Japan*

The link between changes in a subject's metabolic syndrome components and her estimated glomerular filtration rate (eGFR) was evaluated in healthy Japanese women. We used data for 53 Japanese women (46.0 ± 10.9 years) with a 1-year follow up. eGFR was defined by a new equation developed for Japan. There were no significant relationships between eGFR and clinical parameters at baseline. Subjects were given advice for dietary and lifestyle improvement. At the 1-year follow up, eGFR was significantly increased. In addition, changes in eGFR were weakly correlated with systolic blood pressure ($r = -0.306$, $p = 0.0260$). A decrease in systolic blood pressure may be associated with improving eGFR in Japanese women.

Key words: systolic blood pressure, estimated glomerular filtration rate (eGFR), metabolic syndrome, lifestyle modification

Chronic kidney disease (CKD) is a common disorder and has become a public health challenge [1]. For example, about 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, and 4.1% have moderate or severe CKD [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]. However, whether decreases in metabolic syndrome components are beneficial for improving eGFR, and what effects this has on eGFR remain to be investigated in a longitudinal study.

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

Subjects and Methods

Subjects. We used data for 53 Japanese women, aged 46.0 ± 10.9 years, 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, 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).

Received April 16, 2010; accepted June 1, 2010.
*Corresponding author. Phone: +81-87-891-2465; Fax: +81-87-891-2134
E-mail: miyarin@med.kagawa-u.ac.jp (N. Miyatake)

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

	Baseline	Follow up	p
Number of Subjects	53		
Age	46.0 ± 10.9		
Height (cm)	156.1 ± 4.3		
Body weight (kg)	62.4 ± 8.8	60.9 ± 8.5	0.0002
Body mass index (kg/m^2)	25.6 ± 3.3	25.0 ± 3.3	0.0002
Abdominal circumference (cm)	78.7 ± 8.1	76.6 ± 8.3	0.0005
Systolic blood pressre (mmHg)	121.5 ± 14.1	119.8 ± 15.4	0.2772
Diastolic blood pressure (mmHg)	76.2 ± 9.4	74.6 ± 10.8	0.2245
Triglyceride (mg/dl)	98.2 ± 65.8	95.8 ± 62.1	0.7065
HDL cholesterol (mg/dl)	64.5 ± 14.5	64.6 ± 14.9	0.9362
Blood sugar (mg/dl)	95.1 ± 9.4	93.8 ± 9.3	0.2018
Cr (mg/dl)	0.58 ± 0.09	0.56 ± 0.10	0.0148
eGFR (ml/min/1.73m^2)	90.0 ± 17.9	94.2 ± 19.9	0.0215

Mean ± SD

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 amount of steps walked.

Ethical approval for the study was obtained from the Ethical Committee of 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 [5].

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 plasma glucose. eGFR was calculated using the following equation: eGFR (ml/min/1.73m^2) $= 194 \times \mathrm{Cr}^{-1.094} \times \mathrm{Age}^{-0.287} \times 0.739$ (a constant derived specifically for women) [3]. Reduced eGFR was defined as an eGFR < 60 ml/min/1.73 m^2.

Definition of metabolic syndrome. Women with an abdominal circumference in excess of 90 cm were defined as having metabolic syndrome if they also had 2 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 [5].

Statistical analysis. Data are expressed as means ± standard deviation (SD). A statistical analysis was performed using a paired t 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; stepwise multiple regression analysis was also used.

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 decreased and eGFR was significantly increased. No subject was diagnosed as having metabolic syndrome and only one subject was diagnosed with reduced eGFR from baseline to the 1-year follow up. In addition, 2 subjects were identified as positive (+) for proteinuria at baseline and 4 subjects were identified as trace positive at the 1-year follow up.

The relationship between eGFR and clinical parameters at baseline was evaluated. There were no significant relationships between eGFR and other clinical parameters at baseline (Table 2).

Table 2 Simple correlation analysis between eGFR and clinical parameters at baseline

	r	*p*
Body weight (kg)	0.082	0.5594
Body mass index (kg/m^2)	0.033	0.8165
Abdominal circumference (cm)	−0.154	0.2708
Systolic blood pressre (mmHg)	−0.167	0.2333
Diastolic blood pressure (mmHg)	−0.119	0.3958
Triglyceride (mg/dl)	0.123	0.3785
HDL cholesterol (mg/dl)	−0.063	0.6566
Blood sugar (mg/dl)	−0.193	0.1662

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

	r	*p*
Body weight (kg)	0.188	0.1775
Body mass index (kg/m^2)	0.181	0.1945
Abdominal circumference (cm)	0.253	0.0672
Systolic blood pressre (mmHg)	−0.306	0.0260
Diastolic blood pressure (mmHg)	−0.112	0.4325
Triglyceride (mg/dl)	0.095	0.5006
HDL cholesterol (mg/dl)	0.227	0.1015
Blood sugar (mg/dl)	−0.214	0.1232

We further evaluated the relationship between changes in eGFR and changes in clinical parameters. Changes in eGFR were weakly correlated with changes in systolic blood pressure ($r = -0.306$, $p = 0.0260$) (Table 3, Fig. 1). However, changes in eGFR were not significantly correlated with changes in other metabolic components. We also used stepwise multiple regression analysis to evaluate the effect of changes in clinical parameters, *i.e.* body weight, BMI, abdominal circumference, systolic blood pressure, diastolic blood pressure, triglyceride, HDL cholesterol and blood sugar, on the change in eGFR, and found that only change in systolic blood pressure was significant [Change in eGFR = 3.632 − 0.349 (change in systolic blood pressure), $r^2 = 0.093$, $p = 0.0260$].

Finally, we further investigated the difference of change in eGFR between subjects who had different levels of systolic blood pressure at baseline [Group L, systolic blood pressure < 140 mmHg; Group H, systolic blood pressure ≥ 140 mmHg]. The changes in systolic blood pressure in Group H subjects (−1.20 ml/min/1.73 m^2) was lower than that in Group L subjects (4.9 ml/min/1.73 m^2) after 1 year, but not at a significant level ($p = 0.2822$).

Discussion

The main objective of this study was to explore the link between changes in eGFR and changes in metabolic syndrome components in Japanese women with a

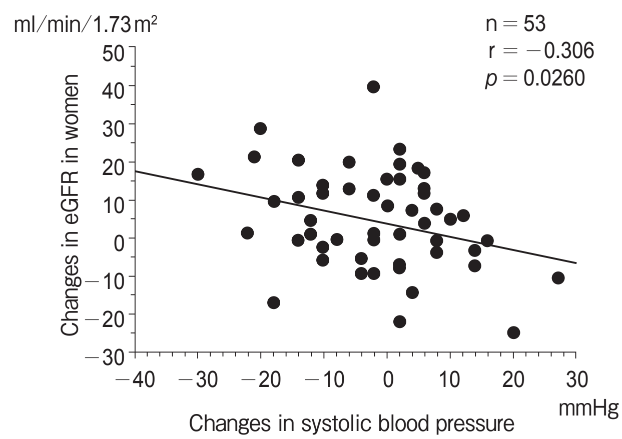

Fig. 1 Simple correlation analysis between changes in eGFR and changes in systolic blood pressure at 1-year follow up.

1-year follow up.

Tanaka *et al.* [6], Ninomiya T *et al.* [7] and Iseki *et al.* [8] reported that metabolic syndrome, using the modified ATP III definition [9], was associated with CKD in the Japanese population. Compared with subjects with 0 or 1 component 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, no subject was diagnosed as having metabolic syndrome, using the Japanese criteria, either at baseline or at the 1-year follow up. We have previously reported that the prevalence of metabolic syndrome was 3.6% in Japanese women [10]. However, with lifestyle modification after the initial health check-up, eGFR was significantly increased even in women without metabolic syndrome at the 1-year follow-up.

Hypertension contributes to the development of renal injury and end-stage renal disease [11-15]. Even high-normal blood pressure has been shown to be significantly associated with development of CKD in both sexes. Yamagata *et al.* 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 10-year follow up [11]. Tozawa *et al.* also reported a relative risk of 1.34 for end-stage renal failure for every increase of 10 mmHg in systolic blood pressure in 51,878 women investigated [12]. In the present study, there was no significant relationship between eGFR and systolic blood pressure at baseline. However, we revealed that, with lifestyle modification, changes in systolic blood pressure were correlated with changes in eGFR in women without metabolic syndrome. Therefore, the clinical impact of hypertension was noted.

Potential limitations remain in our study. First, the small sample size in our study makes it difficult to infer causality between eGFR and hypertension. Second, we also could not reveal the mechanism of the linkage between eGFR and hypertension. Further prospective studies are needed in Japanese subjects. Third, most of the enrolled subjects were not diagnosed as CKD at baseline. Therefore, the results in this study may not apply for patients with CKD.

In conclusion, a decrease in systolic blood pressure with lifestyle modification was associated with an increase in eGFR. Therefore, lifestyle modification may be a necessary and useful measure for the prevention of CKD.

Acknowledgments. This research was supported in part by Health and Labor Sciences Research Grants from the Ministry of Health, Labor and Welfare, Japan.

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. Imai E, Horio M, Iseki K, Yamagata K, Watanabe T, Hara S, Ura N, Kiyohara Y, Hirakata H, Moriyama T, Ando Y, Nitta K, Inaguma D, Narita I, Iso H, Wakai K, Yasuda Y, Tsukamoto Y, Ito S, Makino H, Hishida A and Matsuo S: Prevalence of chronic kidney disease (CKD) in the Japanese general population predicted by the MDRD equation modified by a Japanese coefficient. Clin Exp Nephrol (2007) 11: 156-163.
3. 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.
4. 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.
5. 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).
6. Tanaka H, Shiohira Y, Uezu Y, Higa A and Iseki K: Metabolic syndrome and chronic kidney disease in Okinawa, Japan. Kidney Int (2006) 69: 369-374.
7. Ninomiya T, Kiyohara Y, Kubo M, Yonemoto K, Tanizaki Y, Doi Y, Hirakata H and Iida M: Metabolic syndrome and CKD in a general Japanese population: the Hisayama Study. Am J Kidney Dis (2006) 48: 383-391.
8. Iseki K, Kohagura K, Sakime A, Iseki C, Kinjo K, Ikeyama Y and Takishita S: Changes in the demographics and prevalence of chronic kidney disease in Okinawa, Japan (1993 to 2003). Hypertens Res (2007) 30: 55-62.
9. Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults: Executive Summary of the Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel Ⅲ). JAMA (2001) 285: 2486-2497.
10. Miyatake N, Kawasaki Y, Nishikawa H, Takenami S and Numata T: Prevalence of metabolic syndrome in Okayama prefecture, Japan. Intern Med (2006) 45: 107-108.
11. Yamagata K, Ishida K, Sairenchi T, Takahashi H, Ohba S, Shiigai T, Narita M and Koyama A: Risk factors for chronic kidney disease in a community-based population: a 10-year follow-up study. Kidney Int (2007) 71: 159-166.
12. Tozawa M, Iseki K, Iseki C, Kinjo K, Ikemiya Y and Takishita S: Blood pressure predicts risk of developing end-stage renal disease in men and women. Hypertension (2003) 41: 1341-1345.

13. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Ford CE, Shulman NB and Stamler J: Blood pressure and end-stage renal disease in men. N Engl J Med (1996) 334: 13–18.
14. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL and Stamler J: End-stage renal disease in African-American and white men. 16-year MRFIT findings. JAMA (1997) 277: 1293–1298.
15. Reynolds K, Gu D, Muntner P, Kusek JW, Chen J, Wu X, Duan X, Chen CS, Klag MJ, Whelton PK and He J: A population-based, prospective study of blood pressure and risk for end-stage renal disease in China. J Am Soc Nephrol (2007) 18: 1928–1935.