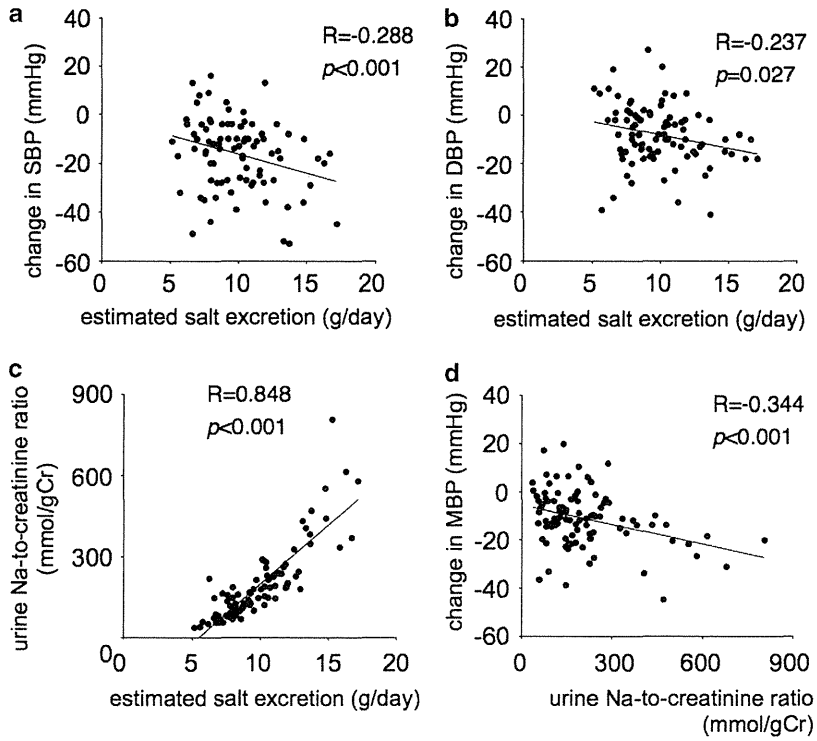

Figure 2 The correlation between estimated salt excretion and changes in systolic or diastolic blood pressure and the correlation between urine Na-to-Cr ratio and estimated salt excretion or changes in mean blood pressure in the 3rd month. The individual correlations between changes in blood pressure during the initial 3 months and baseline eSE were plotted ($n=93$). The relationships between (**a**) baseline eSE and SBP changes and (**b**) baseline eSE and DBP changes were plotted. Correlations between (**c**) baseline NCR and baseline eSE and (**d**) baseline NCR and MBP changes were also plotted. *R* indicates the regression coefficient. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; eSE, estimated salt excretion; NCR, urine Na-to-creatinine ratio.

DISCUSSION

The present study showed that combination therapy with losartan and low-dose hydrochlorothiazide successfully lowered blood pressures in patients whose hypertension was resistant to ARB monotherapy or ARB and CCB combination therapy. As the types and doses of preadministered ARBs varied among the individual patients enrolled in this study, it could be considered that the clinical advantages obtained with the combination therapy did not result from the addition of thiazide alone, but from the concomitant use of losartan and thiazide. The present study also revealed that the clinical efficacy of combination therapy with losartan and thiazide was more prominent in patients with high levels of salt excretion, suggesting that the presumed salt intake and the efficacy of the combination therapy are highly correlated. Simultaneously, the correlation between eSE and MBP changes might indicate that more than a few patients with ARB monotherapy- or ARB and CCB combination-resistant hypertension demonstrated thiazide-responsive, salt-sensitive features.

The clinical effectiveness of thiazide has been examined for many years. The Joint National Council (JNC)-7 guideline positions thiazide at the center of antihypertensive therapy.[20] Similarly, the latest Japanese guideline for hypertension therapy, JSH-2009, recommend that a low dose of thiazide be adopted as a concomitant agent.[19] Multiple clinical studies have elucidated the potential effects of combination therapy with an ARB and thiazide.[25–27] Successful reduction of the proteinuria that remains after ARB monotherapy or ARB-CCB combination therapy has also been reported in a clinical study of patients treated with losartan plus thiazide.[28] The present study clearly shows that hypertensive patients who showed ARB monotherapy-resistant hypertension demonstrated a significant further decrease in blood pressure and a significant reduction in ACR by switching to losartan and thiazide combination therapy, in agreement with previous studies. The combination therapy is considered to be especially beneficial for preventing thiazide-associated hyperuricemia and ARB-associated hyperkalemia because those adverse effects should be canceled by the losartan-associated acceleration of uric acid excretion and the thiazide-associated acceleration of potassium excretion, respectively.[29] Indeed, there was no significant change in the serum concentration of potassium and uric acid throughout the entire observation period in this study.

It seems reasonable to consider that the efficacy of thiazide would be at least somewhat correlated with the amount of salt accumulation in the body or the amount of salt intake, although such a correlation has not been directly demonstrated yet. Uzu *et al.*[30] demonstrated that the antihypertensive effect of thiazide was more obvious in patients with nocturnal blood pressure elevation who showed a large amount of salt excretion compared with cases without nocturnal blood pressure elevation who showed a smaller amount of salt excretion. Although this study did not show a direct correlation between salt excretion and the effectiveness of thiazide, the relationship was indirectly indicated based on clinical observation. In the present study, the advantage of eSE as a parameter to predict

the efficacy of losartan and thiazide combination therapy was shown via stratified, univariate and multivariate analyses, although a rough relationship between thiazide effectiveness and salt excretion or intake has been previously discussed only for stratified groups, such as those with high or low salt intake.[30,31]

Multiple formulas have been proposed for estimating salt excretion. However, we considered that it would be difficult to apply these formulas to this study, because some of them require the measurement of lean body mass[32] or the use of the second urine after awaking as a urine sample.[33] Tanaka *et al.*[23] have reported that sodium excretion for 24 h could be estimated by the use of urine sodium and Cr concentration and the estimated Cr excretion for 24 h, which would be calculated based on the age, body weight and height of individual cases. The Japanese Society of Hypertension recommends using Tanaka's formula.[34] In the present study, estimated sodium excretion was converted to estimated salt excretion, which was considered a reasonable accurate estimate of the salt intake. Indeed, Tanaka *et al.*[23] demonstrated that the estimated salt excretion was highly representative of the salt intake. Therefore, the present study suggests that the effectiveness of combined losartan and thiazide for therapy-resistant hypertension would be significantly affected by salt intake and that the estimation and assessment of salt excretion would be helpful for establishing a strategy for therapy-resistant hypertension.

While salt load causes elevation of blood pressure even in normal subjects,[35] there are individuals who show an especially pronounced blood pressure elevation in response to salt intake, that is, salt-sensitive hypertensives.[2] It is generally believed that the major clinical features of salt-sensitive hypertension are female sex, obesity, insulin resistance and high incidence of diabetes, renal damage (such as microalbuminuria) and dyslipidemia.[2] The National Health and Nutrition Survey of Japan reported that the prevalence of obesity and the average BMI in Japan were 30.4% and 23.1 in males and 20.2% and 22.3 in females,[4] whereas those of the patients enrolled in this study were 32.7% and 24.5 in males and 42.1% and 24.6 in females, indicating that the study subjects had an obesity prevalence that was higher than that of the Japanese population. Similarly, the enrolled patients also showed a higher prevalence of other parameters, such as dyslipidemia, diabetes and CKD.[4] These clinical features of the patients in this study match the clinical profile of salt-sensitive hypertension, which might have contributed to the appearance of a correlation between eSE and MBP change in this study. It is presumed that patients with salt-sensitive hypertension basically suffer from an impairment of renal salt excretion,[36,37] suggesting that their salt intake exceeds their salt excretion. Consequently, a realistic salt intake would be assumed to be more likely than the estimated amount. In any case, patients with salt-sensitive hypertension whose blood pressure is predominantly determined by the salt load or accumulation would be considered resistant to ARB monotherapy, but should respond to the combination of an ARB plus thiazide. Alternately, it might also be suggested that many of the patients with resistance to ARB monotherapy or ARB plus CCB combination therapy might have a higher incidence of salt-sensitive hypertension.

Despite the clinical advantages, daily salt excretion or intake assessments are not realistically straightforward because eSE calculation remains complex in the clinical setting. The present study also showed that NCR might be a more reliable parameter than eSE for estimating daily salt excretion, at least in the patients enrolled in this study. In general, the 95% reliable range for the average population is determined by the following equation:

mean $\pm$ (square root of D) $\times$ k, where D indicates the number of samples divided by the variance of population, and k indicates the reliability coefficient (1.96 for 95% reliability).

Consequently, the 95% reliable range of eSE in the high-responder group would be from 14.5 to 8.4 g per day. An analysis of the correlation between eSE and NCR resulted in the following equation:

NCR = 43.8 $\times$ eSE $-$238.9 (mmol per g of Cr).

Therefore, the 95% reliable range of eSE in the high-responder group would correspond to 396–134 per g of Cr of NCR. Indeed, one study reported that an NCR of 134 mmol per g of Cr might correspond to the salt excretion of Japanese people with average salt intakes, although the study results were based on second urine samples after awaking.[34] Therefore, the study's clinical analysis of NCR suggests that $\sim$130 mmol per g of Cr or more would be a rough standard for cases that might be expected to show a prominent response to combination therapy with losartan and thiazide.

In conclusion, eSE or NCR could be used to assess the efficacy of losartan and low-dose thiazide combination therapy in patients who demonstrate resistance to ARB monotherapy. Combination therapy with losartan and thiazide might be well suited to patients who show ARB resistance and high levels of salt excretion.

Limitations

There were some limitations to this study. First, this study was an observational study in the same population rather than a comparative study. Additionally, the number of enrolled cases was $<$100, and a gender bias existed. These issues raise the possibility that the results obtained in this study are not generally applicable to other populations. However, even in a limited population, the finding of a correlation between estimated salt excretion or intake and efficacy of anti-hypertension therapy using losartan plus thiazide is of clinical importance.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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APPENDIX

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Original Paper

Release From Glomerular Overload by the Addition of Low-dose Thiazide in Patients With Angiotensin Receptor Blocker-Resistant Hypertension

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Key Words
Glomerular filtration rate • Renoprotective effect • Losartan • Thiazide • Albuminuria

Abstract
Background/Aims: This multicenter, prospective, observational study assessed the renoprotective effects of losartan/thiazide combination therapy in terms of lowering the estimated glomerular filtration rate (eGFR). ***Methods:*** Adult patients with angiotensin receptor blocker (ARB)-resistant essential hypertension (n = 104) were enrolled and switched to combination therapy with losartan (50 mg/day) and hydrochlorothiazide (12.5 mg/day). ***Results:*** eGFR values declined significantly during the first 3 months, and changes in eGFR were assessed according to tertiles of the eGFR decrease ratio at 3 months. Only the high eGFR decrease (1st tertile) group showed significantly greater decreases in baseline eGFR and albumin-to-creatinine ratio (ACR) during the first 3 months. Additionally, the assessment according to tertiles of the baseline eGFR showed a significant decrease in eGFR and ACR during the first 3 months in the high baseline eGFR (1st tertile) group, but not in the moderate (2nd tertile) and low baseline eGFR (3rd tertile) groups. ***Conclusion:*** The present results revealed that losartan/thiazide combination therapy attenuated glomerular overload, indicating that this therapy may provide glomerular protection in patients with an elevated GFR without causing prolonged damage to renal function.

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Introduction

Angiotensin receptor blockers (ARBs) are used commonly for anti-hypertension therapy and have been recommended as a first-line therapeutic strategy in several hypertension guidelines [1-3]. The principal advantage of ARBs are that they exert various protective effects in organs in addition to lowering blood pressure [4-8]. Thiazide diuretic agents are used as second-line drugs for hypertensive patients with ARB resistance and they are also recommended for concomitant use with ARBs in several guidelines [1, 2]. Indeed, a large-scale clinical study has reported clinical advantages of an ARB and thiazide combination therapy [9].

We recently conducted a multicenter, prospective, observational study in the Saitama Prefecture of Japan (the Saitama Anti-hypertension Losartan-hydrochlorothiazide Trial: SALT study), wherein we studied the clinical effectiveness of losartan/thiazide combination therapy in patients with hypertension that was resistant to either ARB monotherapy or concomitant ARB + calcium channel blocker (CCB) therapy [10]. The results showed that estimated salt excretion (eSE) at baseline was significantly correlated with the magnitude of blood pressure decrease, and that eSE could predict the efficacy of the combination therapy [10]. The study also demonstrated a significant decrease in the estimated glomerular filtration rate (eGFR) during the first 3 months after the switch to ARB/thiazide combination therapy [10].

It is generally considered that a decrease in the GFR or an increase in serum creatinine (Cr) levels indicates a deterioration in renal function. However, in certain cases, a decreased GFR may indicate attenuation of a pressure overload in the glomerulus. A sub-analysis of the Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) study revealed that an acute decrease in the GFR during the initial period after the switch to losartan predicted a slower decrease in long-term renal function, indicating that the initial decrease in GFR provided a long-term renoprotective effect [11]. In addition, a decrease in the GFR at the onset of losartan/thiazide combination therapy generally predicts a subsequent slower decline in renal function, presumably because it reflects a decrease in glomerular pressure [12]. These results strongly suggest that a decline in the GFR does not necessarily indicate a deterioration in renal function. However, the significance of the GFR decrease caused by combined ARB/thiazide therapy has not been studied sufficiently, particularly its relationship with the associated anti-proteinuric effect.

In this study, we performed a sub-analysis of the SALT study to evaluate the clinical significance of the decline in eGFR. This involved assessing the relationships among the decline in eGFR, the baseline values of eGFR, decrease in blood pressure, and changes in albuminuria. The results showed that a significant decline in the eGFR occurred only in patients with high baseline eGFR values. These patients also showed a significant decrease in albuminuria. The results indicated that the renoprotective effect of losartan/thiazide combination therapy was attributable to amelioration of the hyperfiltration state of glomerular hemodynamics. Our findings thus contribute to knowledge about therapeutic strategies for the clinical management of ARB-resistant hypertension and the renoprotection associated with these strategies.

Materials and Methods

Study subjects

The SALT study was a multicenter, prospective, observational study. The main outcomes and complete study design, organization, clinical measures, exclusion criteria, and baseline characteristics have been published [10]. The study was conducted in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee for Human Studies at Saitama Medical University. We included patients aged 38–85 years with essential hypertension who were administered an ARB with or without the concomitant administration of a CCB over a 1-month period (May 2008 to April 2010). Patients

who did not meet the target blood pressure levels described in the 2004 Japanese Society of Hypertension Guidelines for the Management of Hypertension (≤130/85 mmHg for young and middle-aged adults, ≤ 140/90 mmHg for adults aged > 75 years) [13] after this antihypertension therapy and who provided informed consent were enrolled in the SALT study. As described [10], patients were excluded from the study if they had been administered any type of diuretic or thiazolidinedione agent or if they exhibited advanced renal insufficiency (serum Cr > 2.00 mg/dL or eGFR < 30 mL/min), heart failure (New York Heart Association functional class III or IV for dyspnea at exertion), or severe liver dysfunction.

Study protocol and clinical profile of the participants

A total of 104 patients who underwent SALT study screening were included in the present study. After blood and urine sampling to obtain baseline laboratory data, the ARB treatment in these patients was switched to the daily administration of a tablet of a compound drug (Preminent®) that contains losartan (50 mg) and hydrochlorothiazide (12.5 mg). The first morning urine was collected for biochemical analysis. The enrolled patients visited individual centers for the measurement of blood pressure and medical interviews until the 12th month. At the 3rd- and 12th-month visits, each patient provided blood and urine samples using methods similar to those used for the baseline sample collection. As described [10], 93 and 74 participants completed the 3-month and 12-month observations, respectively. At the baseline, the patients' mean age was 67.7 ± 12.6 years and their mean body mass index (BMI) was 24.6 ± 3.6 kg/m^2 [10]. The ratio of males was 59.1% (55 cases). The prevalence of obesity was 34.4% (n = 32), diabetes 21.5% (n = 20), and dyslipidemia 44.1% (n = 41). The criteria for diagnosing obesity, diabetes, and dyslipidemia were as follows: obesity, body mass index (BMI) ≥ 25.0 kg/m^2; diabetes, use of antihyperglycemic medication or fasting blood glucose levels > 125 mg/dL; dyslipidemia, use of lipid-lowering medication or total cholesterol levels ≥ 220 mg/dL and/or high-density lipoprotein cholesterol levels ≤ 40 mg/dL and/ or triglyceride levels ≥ 150 mg/dL. The ARBs being taken by the patients at enrollment and their mean doses were as follows: olmesartan (n = 25, 26.9%, 20.0 mg/day), losartan (n = 22, 23.7%, 50.0 mg/day), valsartan (n = 18, 19.4%, 92.5 mg/day), telmisartan (n = 14, 15.1%, 38.7 mg/day), candesartan (n = 11, 11.8%, 7.6 mg/day), and irbesartan (n = 3, 3.2%, 100.0 mg/day). Thirty-five patients were receiving concomitant CCB therapy at enrollment in the study, including amlodipine (n = 20; mean dose, 5.6 mg/day), long-acting nifedipine (n = 6, 23.3 mg/day), azelnidipine (n = 5, 12.8 mg/day), benidipine (n = 2, 6.0 mg/day), cilnidipine (n = 1, 10.0 mg/day), and nicardipine (n = 1, 5.0 mg). eSE (g/day) was calculated and assessed as described previously [14]. Briefly, the value was calculated from estimated 24-h Na excretion (24HUNaV) using the following equations proposed by Tanaka et al. [14]:

predicted value of 24-h urine Cr (PRCr, mg/day) =
−2.04 × age + 14.89 × body weight (kg) + 16.14 × height (cm) − 2244.45
24HUNaV (mEq/day) = [21.98 × (uNa/uCr) × PRCr]$^{0.392}$
eSE (g/day) = (58.5 × 24HUNaV)/1000

Statistical analysis

All biochemical parameters except brain natriuretic peptide (BNP) and urine albumin-to-Cr ratio (ACR) are expressed as means ± standard deviations. BNP and ACR values did not have a parametric distribution; therefore, they are expressed as median and 1st- and 3rd-quartile values. We determined the significance of differences in continuous variables with a parametric distribution by paired t-tests if an analysis of variance (ANOVA) demonstrated equal distribution and by Welch's t-test if the ANOVA demonstrated a nonequal distribution. The mean values of unpaired variables with a parametric distribution were analyzed using the two-tailed t-tests for two groups comparison and two-tailed multiple t-test with a Bonferroni correction for multiple group comparisons followed by ANOVA. The significance of paired and unpaired variables with a nonparametric distribution was evaluated using Wilcoxon's signed-rank test and the Mann-Whitney U-test, respectively. All statistical analyses were undertaken using a microcomputer-assisted program with SPSS (ver 20.0) for Windows Xp (SPSS Inc., Chicago, IL, USA). A p-value of < 0.05 was considered significant.

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Table 1. Changes in biochemical parameters

	0 months (n = 93)	3 months (n = 93)	12 months (n = 74)
Blood pressure			
SBP (mmHg)	154.9 ± 14.9	137.4 ± 16.9**	135.2 ± 14.1**
DBP (mmHg)	86.9 ± 12.1	78.6 ± 11.2**	76.2 ± 11.0**
Blood test			
Albumin (g dl^{-1})	4.33 ± 0.39	4.28 ± 0.31	4.25 ± 0.40
Cr (mg dl^{-1})	0.71 ± 0.21	0.80 ± 0.21**	0.80 ± 0.22**
eGFR (ml min^{-1})	78.8 ± 19.8	71.8 ± 19.3**	71.3 ± 0.20.2**
Uric acid (mg dl^{-1})	5.73 ± 1.70	5.63 ± 1.62	5.89 ± 1.73
Na (mEq l^{-1})	141.2 ± 1.6	140.1 ± 2.1	140.6 ± 2.4
K (mEq l^{-1})	4.27 ± 0.57	4.27 ± 0.60	4.16 ± 0.59
Cl (mEq l^{-1})	103.7 ± 2.7	101.9 ± 3.1	102.0 ± 2.5
TC (mg dl^{-1})	202.7 ± 37.7	200.4 ± 35.5	187.8 ± 37.1
TG (mg dl^{-1})	152.7 ± 96.4	159.4 ± 109.5	143.0 ± 76.7
BNP (pg ml^{-1})	22.9 (10.9, 37.7)	16.0 (6.7, 33.6)**	14.4 (5.4, 41.0)**
FBS (mg dl^{-1})	119.4 ± 51.8	110.7 ± 33.0	117.6 ± 39.0
A1c (%)	5.4 ± 1.1	5.5 ± 1.0	5.6 ± 1.1
Urine test			
Creatinine (g l^{-1})	0.84 ± 0.54	0.80 ± 0.22	0.91 ± 0.59
Na (mEq gCr^{-1})	120.8 ± 51.9	130.8 ± 66.5	121.1 ± 57.0
K (mEq l^{-1})	35.9 ± 26.9	40.9 ± 30.4	34.4 ± 23.4
ACR (μg $mgCr^{-1}$)	11.2 (5.8, 46.3)	8.7 (4.6, 16.5)**	4.6 (2.8, 14.9)** ##

The BNP and ACR results are expressed as median values (in parentheses) because these variables did not have a parametric distribution. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; BNP, brain natriuretic peptide; FBS, fasting blood sugar; ACR, albumin-to-creatinine ratio.
* $p < 0.05$ vs. 0 months, ** $p < 0.01$ vs. 0 months, # $p < 0.05$ vs. 3 months, ## $p < 0.01$ vs. 3 months

Results

Physiological and biochemical parameters

The time-related changes in biochemical parameters as measured in the patients' blood and urine samples are listed in Table 1. Both systolic and diastolic blood pressure decreased significantly within the first 3 months, although no significant change was observed over the next 9 months. The majority of biochemical parameters, including serum potassium levels, uric acid levels, and glucose tolerance, showed no significant change during the 1-year observation period. Significant changes in serum Cr levels and eGFR were observed in the first 3 months but not in the next 9 months. BNP levels also showed a significant decrease in the first 3 months. Urine analysis showed that ACR decreased significantly in the first 3 months as well as over the following 9 months.

Stratified analysis of baseline parameters by eGFR decrease ratio at 3 months and the time-differential changes in blood pressure, eGFR and ACR in each group

To elucidate the clinical profile of the patients who showed a decrease in eGFR, we first calculated the decrease ratio of eGFR at 3 months to assess the effects of the losartan/thiazide combination therapy on the changes in eGFR values and the residual albuminuria. The patients were stratified according to tertiles of the eGFR decrease ratio at 3 months. As shown in Table 2, the baseline values of BMI, blood pressure, BNP, ACR, and eSE were not different between the three groups. The baseline eGFR in the high eGFR decrease group (1st tertile) was significantly greater than that in the moderate and low eGFR decrease (2nd and 3rd tertiles) groups. As shown in Fig. 1, the residual albuminuria decreased significantly in the high eGFR decrease group but not in the other two groups. In all three groups, blood pressure showed equal and significant decreases in the first 3 months, with no change over the next 9 months.

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Table 2. Baseline values of parameters in the groups with a high, moderate, and low eGFR decrease ratio

parameters	high eGFR decrease (1st tertitle)	moderate eGFR decrease (2nd tertitle)	low eGFR decrease (3rd tertitle)
n	31	31	31
eGFR-reduction rate	0.74 ± 0.09**##	0.91 ± 0.05	1.09 ± 0.14
baseline BMI (kg m^{-2})	24.6 ± 3.9	24.7 ± 4.1	24.9 ± 3.3
baseline SBP (mmHg)	157.5 ± 15.3	154.2 ± 13.2	149.8 ± 16.3
baseline DBP (mmHg)	87.7 ± 15.1	85.0 ± 9.7	88.3 ± 9.7
baseline eGFR (ml min^{-1})	89.6 ± 31.3**#	71.0 ± 14.5	74.0 ± 14.6
baseline BNP (pg ml^{-1})	25.3 (17.4, 42.4)	27.0 (15.8, 51.0)	21.5 (7.6, 35.0)
baseline ACR (μg mgCr^{-1})	14.2 (5.8, 47.3)	10.1 (6.1, 55.3)	8.6 (4.8, 17.8)
baseline eSE (g day^{-1})	10.08 ± 2.65	10.02 ± 2.86	9.51 ± 2.27

The first and second tertile values of eGFR decrease were 0.85 and 0.99, respectively. The values of BNP and ACR represent the median values (in parentheses) because these variables did not have a parametric distribution. Abbreviations: eGFR, estimated glomerular filtration rate; BNP, brain natriuretic peptide; ACR, albumin-to-creatinine ratio; eSE, estimated salt excretion.
** $p < 0.01$ vs. the moderate eGFR decrease group, # $p < 0.05$ vs. the low eGFR decrease group, ## $p < 0.01$ vs. the low eGFR decrease group

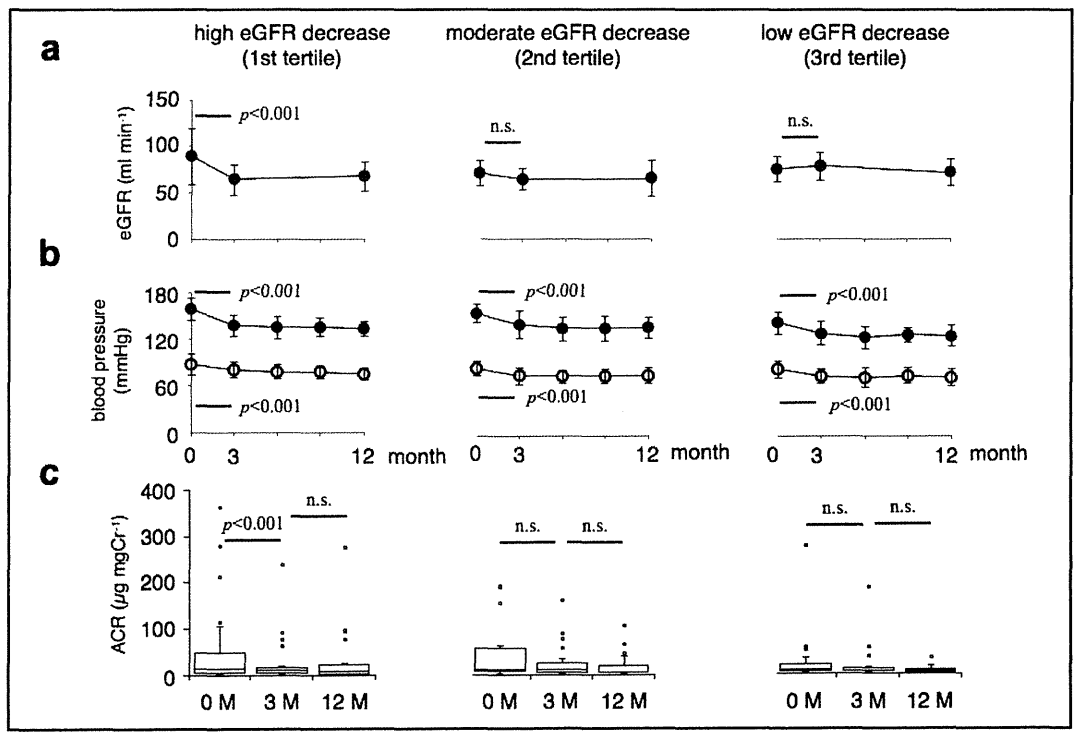

Fig. 1. Tertile analysis of estimated glomerular filtration (eGFR) decrease ratio at the 3rd month. Time-related changes in eGFR at 0, 3, and 12 months (a) and systolic (closed circles) and diastolic (open circles) blood pressure at 0, 3, 6, 9 and 12 months (b) are expressed as mean ± SEM in the 1st, 2nd, and 3rd tertiles of eGFR decrease. The urine albumin-to-creatinine ratio at 0, 3, and 12 months (c) are depicted in the box plot, where the box represents the interquartile range (Q1-Q3).

Stratified analysis of baseline parameters by baseline eGFR and the time-differential changes in blood pressure, eGFR and ACR in each group

Because the decreases in eGFR and albuminuria were related to the significant decrease in high baseline eGFR values, we next divided the patients into three tertiles of baseline eGFR values. As shown in Table 3, there was no significant difference in the baseline value of all other parameters, including albuminuria and eSE. The changes in eGFR, blood pressure, and

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Table 3. Baseline values of parameters in the groups with high, moderate, and low baseline eGFR values

parameters	high baseline eGFR (1st tertile)	moderate baseline eGFR (2nd tertile)	low baseline eGFR (3rd tertile)
n	31	31	31
baseline eGFR (ml min^{-1})	102.2 ± 25.7**##	76.1 ± 5.2	59.3 ± 8.1
baseline BMI (kg m^{-2})	24.6 ± 3.9	24.1 ± 3.7	25.1 ± 3.5
baseline SBP (mmHg)	158.4 ± 16.0	152.0 ± 14.7	151.5 ± 11.8
baseline DBP (mmHg)	90.6 ± 13.8	84.8 ± 11.0	85.8 ± 11.7
baseline BNP (pg ml^{-1})	14.6 (7.8, 29.6)	22.2 (9.6, 47.5)	23.8 (18.8, 36.6)
baseline ACR (μg mgCr^{-1})	12.8 (5.8, 33.6)	10.1 (5.9, 18.9)	7.7 (4.8, 40.6)
baseline eSE (g day^{-1})	9.58 ± 2.85	9.28 ± 2.34	10.53 ± 2.79
age	63.1±12.8	68.7±13.4	70.2±11.6
BMI	24.6±3.9	24.1±3.7	25.1±3.5
incidence of diabetes	20.7%	16.1%	16.7%

The first and second tertile values of baseline eGFR were 85.3 and 68.9 mL/min, respectively. Values of BNP and ACR represent the median values (in parentheses) because these variables did not have a parametric distribution.
Abbreviations: eGFR, estimated glomerular filtration rate; BNP, brain natriuretic peptide; ACR, albumin-to-creatinine ratio; eSE, estimated salt excretion
** $p < 0.01$ vs. The moderate baseline eGFR group, ## $p < 0.01$ vs. the low baseline eGFR group

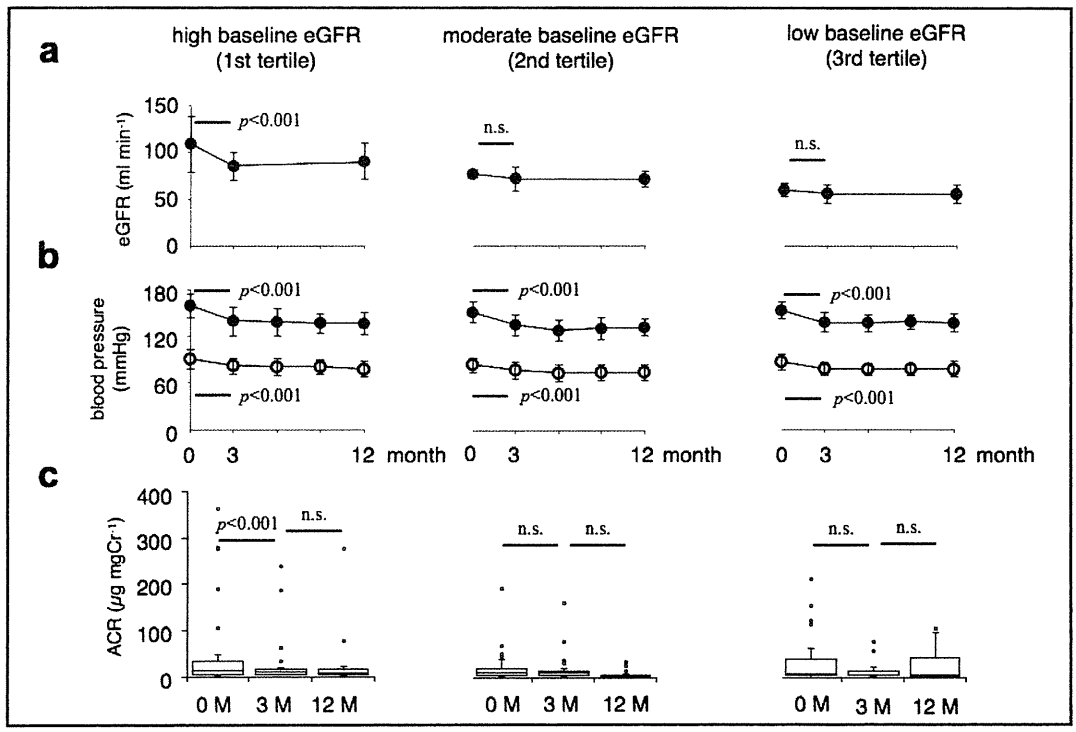

Fig. 2. Tertile analysis of baseline eGFR. Time-related changes in eGFR at 0, 3, and 12 months (a) and systolic (closed circles) and diastolic (open circles) blood pressure at 0, 3, 6, 9, and 12 months (b) are expressed as mean ± SEM in the 1st, 2nd, and 3rd tertiles of baseline eGFR. The urine albumin-to-creatinine ratio at 0, 3, and 12 months (c) are depicted in the box plot, where the box represents the interquartile range (Q1-Q3).

ACR during the observation period are shown in Fig. 2. Patients in the high baseline eGFR group (1st tertile) exhibited a significant decrease in eGFR during the first 3 months, with no change over the next 9 months. In contrast, patients in the moderate baseline eGFR (2nd tertile and 3rd tertile) groups exhibited no significant change in eGFR during the observation period. Both systolic and diastolic blood pressure decreased equally during the first 3 months in all three groups and remained at this level for the next 9 months, indicating that

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the decrease in eGFR observed in the high baseline eGFR group was independent of the decrease in blood pressure. In contrast, the albuminuria that persisted after ARB monotherapy or ARB + CCB combination therapy decreased during the first 3 months only in the high baseline eGFR group.

As demonstrated in Fig. 3, the univariate analysis of the correlation between the baseline eGFR values and the eGFR decrease at the 3rd month showed an inverse correlation between these variables (correlation coefficient = 0.484, $p < 0.01$), indicating that patients with a high baseline eGFR achieved a greater decrease in eGFR by the 3rd month.

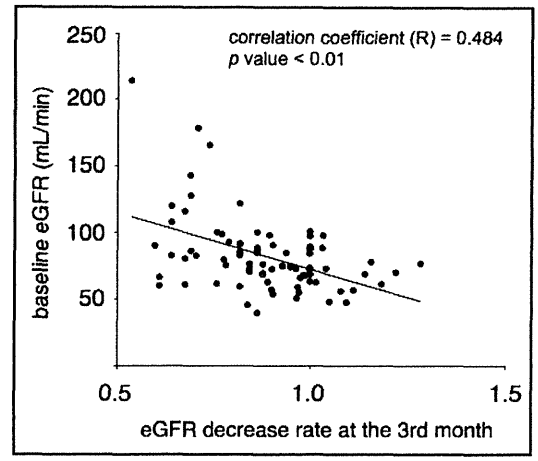

Fig. 3. Correlation between the baseline eGFR and the eGFR decrease ratio at the 3rd month. Individual baseline eGFR values and eGFR decrease ratios at the 3rd month are plotted by a trend line ($n = 93$).

Discussion

This study of patients with ARB- or ARB/CCB-resistant hypertension showed that a significant decrease in the eGFR was achieved by switching to losartan/thiazide combination therapy. We observed that the decrease in the eGFR did not occur in all patients, although it occurred independently of changes in systemic blood pressure in the patients with a high baseline eGFR accompanied by a considerable decrease in the eGFR during the first 3 months. This decrease in eGFR was also associated with a significant decrease in albuminuria, which had persisted even after treatment with either ARB monotherapy or ARB/CCB combination therapy.

The finding of a significant decrease in the eGFR during the first 3 months of losartan/thiazide treatment was in agreement with the results obtained in a previous clinical study [15]. It would be expected that the total body fluid volume would decrease after the addition of thiazide because of the increased elimination of salt. Ito et al. reported that switching to losartan/thiazide combination therapy ameliorated chronic heart failure associated with a decrease in BNP and an increase in Cr levels [16]. These results are compatible with those of the current study. A decrease in body fluid volume and the associated decrease in GFR may be common outcomes after switching to ARB/thiazide treatment.

However, the present study revealed that the decline in ACR was not directly influenced by the decline in body fluid volume and systemic blood pressure. Our stratified analysis of median values of ACR decline during the initial 3 months (3.1 μg/mgCr) showed that the baseline BNP values were not statitically different between the high and low ACR decline groups (17.5 [6.1, 35.9] pg/mL versus 14.9 [8.5, 28.3] pg/mL) although baseline eGFR values were significantly different between the two groups (84.8 ± 29.8 versus 73.9 ± 16.4 mL/min, data not shown in the Result). This observation might indicate that the ACR decline was not directly influenced by the decrease in body fluid volume. The decrease in eGFR values did not occur in all patients in the present study. Our stratified analysis of baseline eGFR values showed a significant decrease only in the patients with the highest baseline values, and the univariate analysis demonstrated an inverse correlation between baseline eGFR values and the eGFR decrease rate at the 3rd month. These results indicate that the switch to losartan/thiazide combination therapy did not cause an equal decrease in eGFR in all patients with ARB-resistant hypertension; this decrease was observed only in the patients with high baseline values or a considerable initial decrease in the eGFR. These patients

would be considered to have glomerular hyperfiltration (GHF), a hemodynamic state that results in podocyte damage [17] and is considered to act as a trigger for a further sequential cascade that leads to glomerular sclerosis [18]. The pathological significance of GHF is that a decrease in high baseline eGFR values does not necessarily indicate the development of renal impairment; rather, it indicates correction of the hyperfiltration state in the glomerulus. The blood pressure-independent decrease in albuminuria, which had persisted even after ARB treatment, in association with the significant decrease in eGFR provides evidence that the decrease in eGFR in patients with high baseline eGFR values appears to be a renoprotective effect.

It has been reported that losartan/thiazide combination therapy may further decrease albuminuria that persists after ARB treatment [19]. In addition, concomitant use of telmisartan and thiazide has been shown to result in a significantly greater decrease in albuminuria compared with telmisartan alone [20]. It is generally accepted that the additive effects of combination therapy with an ARB and thiazide on a further decrease in proteinuria are independent of the decrease in blood pressure. Matsui et al. reported that the concomitant use of olmesartan and thiazide resulted in a more obvious antiproteinuric effect compared to the combination of olmesartan and the CCB azelnidipine, whereas the decline in systemic blood pressure was more evident with the latter combination [21]. The findings of the present study are in agreement with these earlier findings in that the significant decrease in albuminuria was not related to the decrease in blood pressure; rather, it was related to the decrease in the eGFR.

A large-scale clinical study targeting patients without diabetes showed that thiazide treatment alone did not have an antiproteinuric effect [22], indicating that the antiproteinuric effect of ARB/thiazide combination therapy was not caused by thiazide alone but was a consequence of the concomitant use of the ARB. Imanishi et al. reported that the severity of albuminuria did not correlate with systemic blood pressure but showed a significant correlation with glomerular pressure, indicating that an elevated GFR may be involved, at least in part, in the development of albuminuria [23]. It is therefore reasonable to suspect that losartan/thiazide combination therapy provides glomerular protection in patients with an elevated GFR, ultimately leading to further glomerular sclerosis. Zhou et al. [24] demonstrated the superior effects of losartan/thiazide combination therapy on whole kidney and glomerular hemodynamics in spontaneous hypertensive rats (SHRs) treated with NG-nitro-L-arginine methyl ester (L-NAME). These rats are used as an experimental model for hypertensive glomerulopathy. The Zhou study revealed a significant and additive decrease in renal vascular resistance (RVR) and glomerular capillary pressure (P_G) following a concomitant administration of losartan and a thiazide [24]. These results strongly suggest that the combination therapy affected whole kidney and glomerular hemodynamics to an extent that was sufficient to normalize the pressure load in the glomerulus, leading to improved GHF and a decrease in glomerular injury [24]. The clinical advantage of this combination therapy providing glomerular protection by decreasing the GFR has not been demonstrated clearly, although a series of large-scale clinical trials showed that the blood pressure-lowering effect of combination therapy was potentially greater than that of ARB monotherapy [25-28].

Conclusion

The present study of patients with ARB-resistant hypertension and elevated GFR showed that combination ARB/thiazide therapy may normalize glomerular hemodynamics, resulting in a protective effect in the glomerulus. The results of the study may contribute to decision-making in terms of therapeutic strategies for patients with ARB-resistant hypertension.

Conflict of Interests

The authors have no conflict of interest to disclose.

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TH-PO283

Regional Differences in Chronic Kidney Disease Prevalence in Japan: A Japanese Nationwide Health-Check Study Yoshinari Yasuda,[1] Kiyoshi Shibata,[1] Kunitoshi Iseki,[2] Toshiki Moriyama,[2] Kunihiro Yamagata,[2] Kazuhiko Tsuruya,[2] Hideaki Yoshida,[2] Shouichi Fujimoto,[2] Koichi Asahi,[2] Tsuyoshi Watanabe,[2] Seiichi Matsuo.[1] *[1]Nephrology/CKD Initiatives, Nagoya Univ, Nagoya, Japan; [2]Research on the Positioning of CKD in Specific Health, MHWL, Japan.*

Background: Regional variations in the increasing rate of End Stage Kidney Diseases (ESKD) was reported in Japan, however, factors associating these regional differences have not been fully elucidated. In this study, prevalence of Chronic Kidney Disease (CKD) and its risk factors were analyzed in a Japanese nationwide database with a focus on the regional differences.

Methods: Study subjects were 386,517 (163,454 male) participants in a Japanese nationwide health-check including 13 prefectures. Prevalence of CKD and risk factors, including hypertension (HTN), diabetes mellitus (DM), dyslipidemia (DL) and obesity (OB), were analyzed in 4 regions divided by the increasing rate of ESKD as follows; the highest (H), 2 middle (M1 and M2) and the lowest (L) areas. CKD was defined as an estimated glomerular filtration rate less than 60 mL/min/1.73 m^2 and/or proteinuria greater than 1+ by a dipstick method. Odds ratios for CKD were analyzed in 4 areas. Regional differences in optimal treatment rate in HTN, DM and DL were assessed according to each guideline.

Results: CKD prevalence in H, M1, M2 and L areas were 21.4%, 25.5%, 20.9% and 18.5% in male and 18.6%, 15.7%, 16.4% and 11.4% in female, in good agreement with the increasing rate of ESKD. Odds ratios for CKD were significantly high in HTN, DM and OB in all 4 regions. Prevalence of HTN was significantly high in L area, however, the rate of under treatment in HTN and good blood pressure control rate were significantly high in L area. In H area, the rate of no treatment was the highest among 4 areas in HTN, DM and DL.

Conclusions: Association between regional variations in CKD prevalence and those in the increasing rate of ESKD was demonstrated. Although HTN, DM and OB were risk factors for CKD in all 4 areas, the rate of under treatment and good control rate in HTN and DM may affect regional differences.

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SY2-4 CKD診療における生活指導の役割：FROM-J研究での知見を踏まえて—

○山縣邦弘

筑波大学医学医療系腎臓内科学

慢性腎臓病（CKD）患者を対象に「かかりつけ医/非腎臓専門医と腎臓専門医の協力を促進する慢性腎臓病患者の重症化予防の為の診療システムの有用性を検討する研究」（戦略研究；FROM-J）は、大規模臨床介入研究として、2007年より5年間の予定で開始された。この研究では、日本腎臓学会により発行されたCKD診療ガイドに従って、かかりつけ医が主に診療するCKD患者約2500人を、診療目標達成支援ITシステム・受診促進支援センター・栄養ケア・ステーションの支援を受ける群（強介入群）と、支援無し群（弱介入群）の2群にわけ、介入期間3.5年間の研究が行われた。現在は5年間までのフォローアップを日本腎臓学会主導により実施されている。本研究では、1）かかりつけ医、腎臓専門医、コ・メディカルが顔の見える形でCKD重症化予防を討論する場としての地域連携ミーティングを通し、各職種間の緊密な連携の確立、2）生活・食事指導の客観的な評価（チェックリストの客観的な評価）と標準的指導方法の確立、3）生活習慣病関連のCKD患者の行動変容を起こさせるシステムの構築、4）無症状のCKD患者が受診中断しない医療体制の構築などが検討された。その結果をもとにCKDステージ進行抑制、医療費の解析やQOLとの関連調査を通じ、CKDの的確なアウトカム評価を行い、質の高い臨床研究としてのエビデンスを創出することが求められた。本セッションではFROM-Jにより得られた知見ならびに内外の報告から、CKD保存期の非薬物療法としての生活食事指導、腎臓リハビリテーションの位置づけについて考察する。

UNIQUE ENVIRONMENTAL RISK FACTORS OF CKD: LIFE-STYLE RELATED DISORDERS AS RISK FACTORS FOR CHRONIC KIDNEY DISEASE IN A COMMUNITY-BASED POPULATION IN JAPAN

Yohei Maeshima[*1] and Hirofumi Makino[2].

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CKD is associated with increased risk for end-stage renal disease and cardiovascular morbidity and mortality. CKD affects 10–15% of the adult population worldwide. In Japan, the prevalence of CKD significantly increased, especially in male, from the 1970s to the 2000s. During this period, prevalence of obesity has increased, potentially due to societal alterations in lifestyle such as motorized transportation with less walking and high-calorie intake. The prevalence of Chronic Diseases, i.e. hypertension, diabetes mellitus, dyslipidemia and obesity has also increased. Accumulation of these risk factors is associated with the progression of CKD and eventually with cardiovascular morbidity and mortality.
A nationwide screening program of the Specific Health Check-up and Guidance System was initiated in 2008 in Japan. To date, investigation of data from this screening program has led to the identification of several risk factors for CKD such as prehypertension, weight gain after maturity. Recently, we determined the prevalence and the risk factors for CKD in general population of Okayama, Japan. A community-based cohort with 28,132 adults (40-74 yo) who received the Specific Health Checkups and Guidance System in 2011 living in Okayama city was investigated. CKD was determined by eGFR calculated by modified MDRD equation for Japanese, and proteinuria assessed by urine dipstick.
Mean age of participants was 66 yo, 23% had overweight (BMI > 25), 11% were current cigarette smokers, 23.4% exhibited dyslipidemia. The prevalence of CKD was 20.8%. We identified elderly, hyperuricemia, obesity, and past history of cardiovascular events as adjusted risk factors for CKD morbidity. In subjects with hypertension and prehypertension and a normal blood pressure (over 140/90 mmHg), the risk for CKD was significantly greater (OR 1.14) than those with optimal blood pressure (less than 120/80 mmHg). Subjects with hyperuricemia (7.0 mg/dL and greater) exhibited increased risk for CKD (OR 2.13) than those with normal level (less than 5.5). Gender differences, past history of stroke, and HbA1c levels were not identified as significant risk factors. Subjects with risk factors such as moderate renal dysfunction, proteinuria, hypertension, dyslipidemia, impaired glucose tolerance were introduced to clinics or follow-up instruction course. Among those subjects receiving intervention, renal functional deterioration and/or proteinuria were improved in 60% of subjects in the next year. These results suggest that subjects with elderly age, obesity, mildly elevated serum uric acid, hypertension and previous history of cardiovascular events possess increased risk for CKD, and appropriate instruction and follow-ups may improve the outcome.

[SP036] SIGNIFICANCE OF ESTIMATED SALT EXCRETION AS A PREDICTOR FOR ARB/THIAZIDE COMBINATION AND CORRELATION OF GLOMERULAR FILTRATION WITH ANTI-PROTEINURIC EFFECT

Hajime Hasegawa,[1] Koichi Kanozawa,[1] Juko Asakura,[1] Kaori Takayanagi,[1,2] Yosuke Tayama,[1] Shinpei Okazaki,[1] Hiroaki Hara,[1] Tota Kiba,[1] Tomoyuki Mitani,[1] Mizuki Iwanaga,[1] Tomonari Ogawa,[1] Akihiko Matsuda,[1] Tetsuya Mitarai.[1]. [1]Nephrol & Hypertens, Saitama Med Center, Saitama Med Univ, Kawagoe, Japan; [2]Kawagoe Ekimae Clinic, Kawagoe, Japan.

INTRODUCTION AND AIMS:
The purpose of this study was to assess the factors affecting the efficacy of combination therapy of losartan/thiazide by focusing to the significance of salt excretion through the multi-centric observational study, and also to study the underlying mechanism of renoprotective effects of the therapy.
METHODS:
Adult patients with essential hypertension showing therapy resistance to angiotensin receptor blockers (ARBs)-monotherapy or combination with Ca channel blockers (CCB) were enrolled and switched their pre-administered ARBs to Losartan (50 mg/day) concomitant with hydrochlorothiazide (12.5 mg/day). Blood pressure (BP) and biochemical parameters were monitored for a year.
RESULTS:
Baseline BP was significantly lowered at the 3rd month (153.4±14.8/86.4±11.3 vs 137.3±17.4/78.2±11.1 mmHg, n=93), then maintained at this lower level until the 12th month. Baseline value of estimated salt excretion (eSE) was significantly different between the high and low treatment response groups (10.8±2.9 in high responders vs 9.2±2.3 g/day in low responders). Univariate and multivariate analysis indicated significant correlation between eSE and mean BP-decline (R=-0.288, p=0.007), and the significance of eSE as a predictor for mean BP-decline (p=0.021). In addition, estimated glomerular filtration rate (eGFR) was declined during initial 3 but not next 9-months, and urine albumine-to-Cr ratio (ACR) was reduced in both initial 3 and next 9-months. High responders of ACR-decline showed significantly high baseline eGFR (84.8±29.8 vs 73.9±16.4 ml/min). First tertile group of baseline eGFR showed significantly high reduction of ACR and eGFR during initial 3-months (median ACR: 12.8 to 9.0 μg/mgCr, eGFR: 102.2±25.7 to 84.8±15.8 ml/min), but 3rd tertile group did not. Stratified analysis by tertile value of eGFR-reduction ratio also showed significant reduction of ACR and eGFR in only high eGFR-reduction group (1st tertile). There was no significant difference between high and low baseline eGFR groups, or high and low eGFR-reduction groups in other parameters including blood pressure and brain natriuretic peptide.
CONCLUSIONS:
Results might suggest that eSE would be a possible predictors for the efficacy of combination therapy of losartan/thiazide in ARB-resistant patients, and that restoration of glomerular hyperfiltration would evoke the anti-proteinuric effect of the therapy on the remaining proteinuria in ARB-resistant patients.

Session: Poster Session: Hypertension - human studies
Date/Time: Sunday, May 19, 2013 - 10:15 AM

【茨城新聞市民公開セミナーin行方】

防ごうCKD 慢性腎臓病

あなたの腎臓は大丈夫？

国民の８人に１人がかかっているとされる慢性腎臓病は、英語で「Chronic Kidney Disease（クロニック・キドニー・ディジーズ）」と言い、その頭文字を取ってＣＫＤと呼ばれています。茨城新聞市民公開セミナー in 行方「あなたの腎臓は大丈夫？」が２月２日、行方市宇崎のレイクエコーで開かれ、約130人の参加者がＣＫＤについての理解を深めました。セミナーでは医師や保健師４人が尿検査や生活習慣改善の重要性について講演しました。

ほとんどない初期症状

講演1　慢性腎臓病（CKD）とは

森戸　直記　氏

筑波大学腎臓内科学講師

もりと・なおき　医学博士、日本内科学会総合内科専門医、日本腎臓学会専門医、日本透析医学会専門医。1993年筑波大学医学専門学群卒。同年より筑波大学附属病院医員。04年筑波大学大学院人間総合科学研究科研究員。05年ジュネーブ大学（C・M・U）免疫病理学助手。07年筑波大学人間総合科学研究科講師。

腎臓は腰の辺りに２つあるこぶし大ぐらいの臓器です。ＣＫＤは、患者数は1300万人を超え、新たな国民病といわれています。腎臓が悪くなると、さまざまなリスクが発生します。

腎臓の役割は、まず、血液をろ過し老廃物を体から追い出します。腎臓の働きが悪くなると、老廃物を排出できず尿毒症になります。血圧を調節する役割もあります。腎臓の働きが悪くなると高血圧になり、高血圧は腎臓に負担をかけ悪化するという悪循環が起こります。

腎臓からは赤血球をつくる働きを調節する血液ホルモンが出ており、血液をつくる司令官の役割があります。悪くなると「腎性貧血」になります。

腎臓は体液量やイオンバランスを調節し、体に必要なナトリウムやカリウムなどのミネラル類を体内に取り込みます。悪くなると、疲れやすくなり、むくみなどの症状が出ます。

腎臓は活性型ビタミンＤをつくっており、働きが悪くなると、カルシウムが吸収されにくくなり、骨が弱くなります。

ＣＫＤの初期は自覚症状がほとんどなく、腎機能は低下します。早期発見には定期的な健康診断を受けることです。ＣＫＤが進行すると、夜に尿の量が増える夜間尿やむくみ、貧血、倦怠感、息切れなどの症状が出ます。腎臓が十分働かなくなる末期腎不全のリスクが高まります。腎不全になると食事内容や水分を制限する必要があります。さらに悪化すると、腎臓の働きを補う透析や移植を受けることになり、日常生活に大きな支障が出ます。近年、タンパク尿（尿にタンパクが出る）が多いほど、腎機能が悪いほど、脳卒中や心筋梗塞発症のリスクが高くなることが分かってきました。

ＣＫＤは、メタボリックシンドロームや生活習慣病と深く関わっています。メタボリックシンドロームとは、腎臓の機能を低下させる内臓脂肪型肥満に加え高血糖や高血圧、脂質異常などの症状をいいます。そういう方は慢性腎臓病の予備軍といえますから、体重やコレステロール値の適正管理など日常生活の改善が重要になってきます。

生活習慣の見直し重要

講演3　慢性腎臓病（CKD）の予防と治療

植田　敦志　氏

なめがた地域総合病院内科部長

うえだ・あつし　医学博士、日本内科学会総合内科専門医、日本腎臓学会指導医、日本透析学会指導医、茨城県慢性腎臓病対策協議会保存期腎不全委員会責任者。水戸市出身。1992年山形大学卒。同年より筑波大学内科レジデント。2001年なめがた地域総合病院内科科長。10年より同内科部長。12年より筑波大学附属病院臨床准教授兼任。

ＣＫＤは、eGFR（糸球体ろ過量）の状態で５つのステージに分けられます。eGFRが90以下は正常（ステージ１）、90未満60以上は軽度低下（同２）、60未満30以上は中程度低下（同３）、30未満15以上は高度低下（同４）、15以下は腎不全（同５）となります。

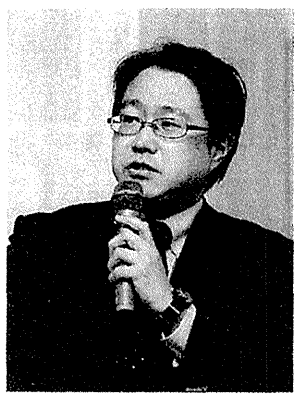
いずれのステージでも、まず腎臓が悪くなった原因となる原疾患を治療します。原疾患は、高血圧、糖尿病、高脂血症、肥満などの生活習慣病が多く、ほかに腎炎などがあります。ステージ１、２は腎不全の予防、ステージ３～５は腎不全の治療を行います。ステージ５でも末期の腎不全になると、透析や移植を検討します。年齢とともに少しずつ腎機能が低下してくることを考慮したうえで、腎機能を維持することを目指します。

ＣＫＤでは、早期から塩分の摂り過ぎに注意します。ステージ３ぐらいからはタンパク質の制限や薬の治療が始まります。腎機能が低下するほど、食事の制限が増えます。

自分でできるＣＫＤの予防や

定期的に尿・血液検査を

講演2 慢性腎臓病（CKD）の検査～尿検査について



錦　健太 氏

筑波大学附属病院水戸地域医療教育センター・水戸協同病院腎臓内科講師

にしき・けんた　医学博士、日本内科学会認定医、日本透析学会専門医。県社会福祉審議会身体障害者福祉専門部会、更生医療審査部会臨時委員。1994年筑波大学卒。同年より筑波大学附属病院医員。日製日立総合病院、水戸済生会総合病院、自治医科大学附属病院などを経て2002年県立中央病院腎臓内科医長。06年県西総合病院腎臓内科医長。09年より現職。

CKDは尿検査のタンパク尿と、血液検査のクレアチニン（血液中の老廃物の一つ）で診断・分類されます。尿検査でタンパク尿陽性、あるいはクレアチニン値と年齢を計算して出したeGFR（糸球体ろ過量）の数値が60％以下、この二つのうちいずれかが、3カ月以上続くとCKDと診断されます。

CKDの検査の前に、要注意だと思われる家庭での変化について紹介します。体に水がたまってきたことが疑われる体重の増加やむくみ、血圧の上昇などです。むくみは足のすねを押すとへこんだままになります。血圧が高いと腎臓が悪くなり、腎臓が悪いと血圧が高くなるという悪循環を止めなくてはいけません。血圧が高い場合は病院で検査を受けることをおすすめします。尿が泡立つときはタンパクが出ている可能性もあります。毎日続くようなら糖尿病や高血圧の方は要注意です。

タンパク尿が続くときは、一見何とも無いように見えても、症状が静かに進行しています。栄養分であるタンパクが尿に出るということは、腎臓のフィルターである糸球体の障害が疑われます。

ただし、正常でも激しい運動や熱が出た後などに一時期的にタンパク尿が出るときがあるため、CKDかどうかは病院の検査が必要です。

クレアチニンは、腎臓が正常ならば、尿として体の外に出されます。血液中のクレアチニンが高いということは、腎機能が低下していることを示します。クレアチニンの値が高いほどeGFRは低く、腎臓の働きは悪くなっています。

尿酸とヘモグロビンもCKDの進行に深く関わっています。尿酸が低い人よりも高い人の方が、腎臓が悪くなる危険度は高くなります。腎臓が弱くなると造血ホルモンが腎臓から出なくなり、貧血を示すヘモグロビンの数値が低くなります。

CKDの初期は症状がほとんどありません。症状が無くても、尿検査でタンパク尿があるかどうか、血液検査でクレアチニン値を定期的にチェックすることが大切です。

治療は喫煙と飲酒を控えること、十分な睡眠、ストレスの解消などがあります。食事は、徐々に薄味にする、酸味のある調味料や香辛料を使うなど、塩分の振り過ぎに注意します。塩分の含有量を正しく理解しましょう。タンパク質やカリウム、カロリーでも食事を工夫します。

運動も自分でできる予防や治療です。血糖値の改善につながります。運動の強さは、心拍数が1分間に100から120回程度。歩くなら1日男性は9200歩、女性は8300歩以上が理想です。車を入り口から遠いところに停めて歩く、階段を使う、食後の体操、掃除など、生活の中に運動を無理なく取り入れてみましょう。

残念ながらCKDに特効薬はありません。高血圧や肥満を治すことが、CKDの治療に結びつきます。食事や薬、運動、喫煙、睡眠などの生活習慣を見直すことも重要です。健康診断をきちんと受けて、CKDの方や、その可能性がある方は、一度腎臓専門医に相談してみるのがよいでしょう。

講演4 地域の健康課題と生活習慣病予防の取り組み

家族みんな健診受けて

一条　千登世 氏

行方市健康増進課・保健師

いちじょう・ちとせ　水戸赤十字看護専門学校卒、茨城県立水戸看護専門学院保健学科卒。1988年旧玉造町役場入職。2005年9月市町村合併後、介護福祉課、地域包括支援センター勤務を経て、現在は行方市保健福祉部健康増進課健康増進グループ特定健診担当。

行方市では、高血圧や糖尿病、脂質異常、肥満などの生活習慣病などが原因で、心筋梗塞や脳梗塞で亡くなる方が多くいます。新しく人工透析を受ける患者は年々増加していて、その主な原因は糖尿病や慢性腎炎、高血圧などです。行方市の健康診断の結果から、人工透析の予備軍が確実にいることが分かっています。市の担当者としては透析になる人を1人でも減らして、少しでも透析になるのを先に延ばすことが課題だと考えています。

平成20年度から40歳から74歳を対象にした特定健診、いわゆるメタボ健診がスタートしました。行方市では、基本項目の尿タンパクのほか、追加項目となるクレアチニン値についても実施しています。

特定健診を受けてメタボリックシンドロームに該当した方に特定保健指導「げんきアップなめがた」というグループ支援を実施しています。それまでの保健指導は1回きりで話を聞いてもらうだけでしたが、現在の保健指導では、グループになって生活習慣の悪い点や改善策について話し合っています。糖尿病の指標となるヘモグロビンA1cを測り、自分の体の状態と生活を振り返っています。

ほかに、「スマート・ダイエット教室」という肥満改善を目的とした生活習慣病予防事業を行っています。約3カ月かけて、減量を目指し、栄養バランスの取れた食生活を指導しています。食事記録をつけるなど、栄養や食事に関する基礎知識を身に付けてもらいます。減量の効果がはっきりと見える教室になっています。

「げんこう応援教室」では、生活の中で運動を習慣化することを目的に、ウオーキングやストレッチ、筋力トレーニングの基本を習得します。教室終了後もウオーキングや筋トレを楽しむグループができ、成果が上がっています。

健康診断は、市町村で必ず実施しています。自分の体の状態を知るために、家族みんなで健康診断を受けて、自分の生活習慣を見直してください。

■主催　茨城新聞社
■協賛　大日本住友製薬
■後援　茨城県、行方市、潮来市、茨城県医師会、水郷医師会、いばらき腎バンク、日本慢性腎臓病対策協議会、茨城慢性腎臓病対策協議会、茨城放送、NHK水戸放送局

企画制作　茨城新聞社営業局

世界腎臓デーに合わせたCKD啓発イベント
『ストップ・ザ・腎不全：～CKD啓発活動とチーム医療～』
講　　演　　会

日本慢性腎臓病対策協議会
J-CKDI

－プログラム(案)－

日　時　：　平成25年3月3日（日）13時～16時30分(予定)

場　所　：　東京ガーデンパレス(TEL：03-3813-6211)
東京都文京区湯島1-7-5
「JR・東京メトロ 御茶の水駅」聖橋口 徒歩5分

13：00
開会の挨拶：　松尾　清一（名古屋大学・日本腎臓学会理事長）

挨　　拶：(予定)

厚生労働省・健康局長	矢島　鉄也
日本医師会・医師会長	横倉　義武 【代読】三上裕司(常任理事)
日本腎臓財団・理事長	浅野　泰
全国腎臓病協議会・会長	宮本　髙宏

【報告の部】

座　長：松尾清一・草野英二

報告１　From-J研究の報告　：山縣　邦弘（筑波大学・教授、J-CKDI・理事）

報告２　世界腎臓デー報告
1) 厚労省秋澤班報告・懸垂幕　：前島　洋平(岡山大学・教授、J-CKDI・監事)
2) YouTube・ノベルティーグッズについて
：安藤　康宏(自治医科大学・教授、J-CKDI・監事)

シンポジウム　：各地域でのCKD対策の発展　[J-CKDI都道府県代表の取り組み]