Original Article

Changes in the Demographics and Prevalence of Chronic Kidney Disease in Okinawa, Japan (1993 to 2003)

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To compare the risk factor demographics and the prevalence of chronic kidney disease (CKD), we analyzed two databases from the 1993 (*N*=143,948) and 2003 (*N*=154,019) mass screenings in Okinawa, Japan (Okinawa General Health Maintenance Association registry). We estimated the glomerular filtration rate (GFR) using serum creatinine (SCr) levels. SCr was measured by the modified Jaffe method in 1993 and by enzyme assay in 2003; the relation between the two methods was: SCr (Jaffe) = 0.194 + 1.079 × SCr (enzyme). CKD prevalence was compared using the estimated GFR calculated by the abbreviated Modification of Diet in Renal Disease (MDRD) equation. SCr was measured in 66.2% (1993) and 69.8% (2003) of the total screenees. Proteinuria was present in 3.4% (1993) and 4.3% (2003) of the total screened population, respectively. The prevalence of CKD (GFR<60 ml/min/1.73 m^2) was similar between the two databases, being 15.7% in 1993 and 15.1% in 2003. However, the demographics of the CKD risk factors changed during the study period. The mean level of systolic blood pressure decreased, whereas the prevalence of obesity and the mean levels of serum cholesterol and fasting plasma glucose increased. In 2003, the estimated prevalence of metabolic syndrome in the general population of Japan calculated using the modified National Cholesterol Education Program (NCEP) criteria was 19.1%. The prevalence of CKD was significantly associated with that of metabolic syndrome: the age- and sex-adjusted odds ratio was 1.332 (95% confidence interval [CI], 1.277–1.389; *p*<0.0001). In conclusion, the demographics of the participants of the general screenings in Okinawa, Japan differed between the 1993 and 2003 screenings, but the prevalence of CKD seemed to be similar, or at least did not increase substantially, between the two databases. (*Hypertens Res* 2007; 30: 55–62)

***Key Words*: chronic kidney disease (CKD), end-stage renal disease (ESRD), serum creatinine, glomerular filtration rate (GFR)**

Introduction

The number of patients with end-stage renal disease (ESRD) requiring chronic dialysis therapy is increasing worldwide (*1–3*). Within Japan, Okinawa has the highest incidence of ESRD (*1*, *4*). The incidence of ESRD is increasing linearly and the mean age at the start of dialysis is also increasing. Whether this is due to a true increase in chronic kidney disease (CKD) or an increase in the acceptance rate for dialysis therapy is not certain. Several reports have suggested a relatively high prevalence of CKD in screened populations (*5*, *6*). CKD is a causative factor not only for ESRD, but also for cardiovascular disease (CVD) (*7*). CKD patients share similar risk factors for CVD (*8*). Therefore, the increase in ESRD might not simply suggest an increase in CKD; survivors of

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Table 1. Demographics of the Screened Men in 1993 and 2003 in Okinawa, Japan

	Year of screening		*p* value
	1993	2003	
Number	68,564	73,873	
Age (years)			
Mean±SD	48.1±15.6	48.4±16.8	0.0003
Urine test for proteinuria			
Number of data	65,681	72,819	
% of total	95.8%	98.6%	
Proteinuria	3.9%	5.0%	<0.0001
Serum creatinine (mg/dl)			
Number of data	40,157	46,961	
% of total	58.6%	63.6%	
Mean (median)	1.10 (1.10)	1.15 (1.12)	<0.0001
Proteinuria	4.5%	6.0%	<0.0001
Body mass index (kg/m^2)			
Mean±SD	24.3±3.2	24.7±3.5	<0.0001
Obesity (BMI≥25)	39.8%	42.9%	<0.0001
Systolic blood pressure (mmHg)			
Mean±SD	128.8±16.2	126.8±15.9	<0.0001
Serum uric acid (mg/dl)			
Number of data	22,949	41,660	
Mean (median)	6.4 (6.3)	6.5 (6.5)	<0.0001
Serum cholesterol (mg/dl)			
Number of data	63,568	69,493	
Mean (median)	199.6 (197.0)	201.0 (199.0)	<0.0001
Triglyceride (mg/dl)			
Number of data	63,008	69,203	
Mean (median)	166.2 (126.0)	164.8 (126.0)	n.s.
Fasting plasma glucose (mg/dl)			
Number of data	37,197	69,246	
Mean (median)	96.6 (94.0)	106.2 (99.0)	<0.0001

Screening was performed from April 1 in each year to March 31 in the next year. Body mass index (BMI) was calculated by body weight in kg divided by height squared in m. Serum creatinine (SCr) was measure by the modified Jaffe method in 1993, and the enzyme assay in 2003. SCr was calibrated as: SCr (Jaffe) = 0.194 + 1.079 × SCr (enzyme). n.s., not significant.

CVD might also ultimately develop ESRD (*9*, *10*).

Available data suggest that several laboratory variables are significant predictors of ESRD (*11*). Recent progress in pharmacologic therapy for patients with CKD suggests that early detection and appropriate treatment might reduce the incidence of CKD and ESRD (*12–14*). In Japan, several types of health checks and laboratory examinations are routinely performed throughout life, from childhood to old age (*15–17*). To our knowledge, however, there are few data concerning CKD prevalence and its relationship to the ESRD incidence in Japan.

In this study, we compared the changes in the demographics and prevalence of CKD in two screening cohorts, 1993 and 2003, in Okinawa, Japan (*18–20*). ESRD incidence was obtained from the Okinawa Dialysis Study (OKIDS) registry (*21*, *22*) and from the Japanese Society for Dialysis Therapy (*1*). The results demonstrated that the prevalence of CKD did not change over the past 10 years, despite several changes in the demographics of CKD risk factors.

Methods

Screening Program

The Okinawa General Health Maintenance Association (OGHMA), which was formerly under the direction of Y. Ikemiya and is currently under the direction of K. Kinjo, conducts an annual large community-based health examination. The OGHMA is a nonprofit organization founded in 1972 (*18*). Once each year, the staff, doctors, and nurses visit residences and work places throughout the prefecture to perform health examinations. All subjects participate voluntarily in the screening. The OGHMA personnel conduct the mass screening, inform the participants of the results, and make

Table 2. Demographics of the Screened Women in 1993 and 2003 in Okinawa, Japan

	Year of screening		*p* value
	1993	2003	
Number	75,384	80,146	
Age (years)			
Mean±SD	50.8±16.5	51.2±17.6	<0.0001
Urine test for proteinuria			
Number of data	70,177	77,484	
% of total	93.1%	96.7%	
Proteinuria	2.9%	3.6%	<0.0001
Serum creatinine (mg/dl)			
Number of data	55,098	60,547	
% of total	73.1%	75.5%	
Mean (median)	0.89 (0.90)	0.91 (0.88)	<0.0001
Proteinuria	3.3%	4.1%	<0.0001
Body mass index (kg/m^2)			
Mean±SD	23.6±3.5	23.5±3.8	0.0003
Obesity (BMI≥25)	29.8%	30.5%	<0.0001
Systolic blood pressure (mmHg)			
Mean±SD	123.8±17.8	121.3±17.6	<0.0001
Serum uric acid (mg/dl)			
Number of data	25,228	44,237	
Mean (median)	4.8 (4.8)	4.8 (4.7)	<0.0001
Serum cholesterol (mg/dl)			
Number of data	69,770	74,482	
Mean (median)	203.1 (201.0)	205.4 (203.0)	<0.0001
Triglyceride (mg/dl)			
Number of data	69,086	74,185	
Mean (median)	116.5 (94.0)	111.0 (92.0)	<0.0001
Fasting plasma glucose (mg/dl)			
Number of data	41,332	73,861	
Mean (median)	93.8 (90.0)	98.8 (94.0)	<0.0001

Screening was performed from April 1 in each year to March 31 in the next year. Body mass index (BMI) was calculated by body weight in kg divided by height squared in m. Serum creatinine (SCr) was measure by the modified Jaffe method in 1993, and the enzyme assay in 2003. SCr was calibrated as: SCr (Jaffe) = 0.194 + 1.079 × SCr (enzyme).

recommendations for further evaluation or treatment when necessary. This process includes an interview concerning health status, a physical examination, and urine and blood tests. A nurse or doctor measures blood pressure using a standard mercury sphygmomanometer with the subject in a sitting position. Dipstick testing for proteinuria, hematuria, and glucosuria (Ames Dipstick, Tokyo, Japan) is performed in spontaneously voided fresh urine. Proteinuria is defined by a dipstick urinalysis score of 1+ or more, fasting blood is drawn for the laboratory tests, and body mass index (BMI) is calculated as weight (kg) divided by the square of height (m).

Computer-based data were available for 143,948 subjects from April 1, 1993 through March 31, 1994 for the 1993 screening, and for 154,019 subjects from April 1, 2003 through March 31, 2004 for the 2003 screening. These numbers constituted about 17.7% (1993) and 16.1% (2003) of the total adult (20 years or older) population in men and 17.9% (1993) and 16.4% (2003) of the total adult population in women. Serum creatinine (SCr) was measured using a modified Jaffe reaction in an auto-analyzer at the OGHMA laboratory in 1993. The assay method was changed to an enzyme method (SCr-enzyme) in April 2002. The relationship between the two methods was (*23*):

$$\text{SCr (Jaffe)} = 0.194 + 1.079 \times \text{SCr (enzyme)}.$$

This relationship was confirmed in normal subjects at the OGHMA laboratory. Unfortunately, stored samples for SCr were not available for the calibration in both screenings. The estimated glomerular filtration rate (GFR) was calculated using the abbreviated Modification of Diet in Renal Disease (MDRD) equation (*24*, *25*):

$$\text{GFR (ml/min/1.73 m}^2) = 186.3 \times \text{Age}^{-0.203} \times \text{SCr}^{-1.154}$$
$$(\text{if women} \times 0.742).$$

Table 3. Mean (Median) Levels of Serum Creatinine (SCr) According to Sex and Age in the Screened Subjects in 1993, and 2003 in Okinawa, Japan

Age	Year of screening			
	1993	1993#	2003	2003#
Men	*N*=40,157	*N*=19,095	*N*=46,961	*N*=30,029
20–	1.09 (1.10)	1.08 (1.10)	1.15 (1.13)	1.14 (1.13)
30–	1.08 (1.10)	1.07 (1.10)	1.14 (1.12)	1.13 (1.13)
40–	1.07 (1.10)	1.06 (1.00)	1.12 (1.11)	1.12 (1.11)
50–	1.08 (1.10)	1.07 (1.10)	1.14 (1.11)	1.14 (1.11)
60–	1.10 (1.10)	1.08 (1.10)	1.15 (1.12)	1.14 (1.12)
70–	1.15 (1.20)	1.13 (1.10)	1.18 (1.14)	1.17 (1.13)
80–	1.22 (1.20)	1.17 (1.20)	1.24 (1.20)	1.23 (1.19)
Total	1.10 (1.10)	1.08 (1.10)	1.15 (1.12)	1.14 (1.12)
Women	*N*=55,098	*N*=26,118	*N*=60,547	*N*=44,482
20–	0.85 (0.80)	0.84 (0.80)	0.88 (0.87)	0.88 (0.87)
30–	0.84 (0.80)	0.86 (0.80)	0.87 (0.86)	0.87 (0.86)
40–	0.84 (0.80)	0.83 (0.80)	0.87 (0.86)	0.87 (0.86)
50–	0.88 (0.90)	0.86 (0.90)	0.89 (0.87)	0.89 (0.87)
60–	0.90 (0.90)	0.89 (0.90)	0.91 (0.90)	0.91 (0.90)
70–	0.95 (0.90)	0.93 (0.90)	0.95 (0.92)	0.95 (0.92)
80–	1.01 (1.00)	0.98 (1.00)	1.02 (0.97)	1.02 (0.98)
Total	0.89 (0.90)	0.87 (0.90)	0.91 (0.88)	0.90 (0.88)

Data of 2003 was calculated as: SCr (Jaffe) = 0.194 + 1.079 × SCr (enzyme). #Denote data from the screenees without hypertension or diabetes mellitus. Hypertension: systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg. Diabetes mellitus: fasting blood glucose ≥126 mg/dl.

Table 4. Distribution of Renal Function in the Screened Subjects in 1993 and 2003 in Okinawa, Japan

GFR (ml/min/1.73 m^2)	Year of screening	
	1993	2003
Men		
90–	7,720 (19.2%)	4,745 (10.1%)
60–89	28,258 (70.4%)	36,498 (77.7%)
30–59	4,134 (10.3%)	5,585 (11.9%)
15–29	34 (0.1%)	85 (0.2%)
<15	11 (0.03%)	48 (0.1%)
Total	40,157 (100%)	46,961 (100%)
Women		
90–	7,835 (14.2%)	4,338 (7.2%)
60–89	36,532 (66.3%)	45,687 (75.5%)
30–59	10,636 (19.3%)	10,350 (17.1%)
15–29	80 (0.1%)	140 (0.2%)
<15	15 (0.03%)	32 (0.05%)
Total	55,098 (100%)	60,547 (100%)

Stage of glomerular filtration rate (GFR) was defined as K/DOQI guideline. GFR was estimated using the Modification of Diet in Renal Disease (MDRD) formula.

CKD was defined as a GFR of less than 60 ml/min/1.73 m^2. Proteinuria was defined as dipstick proteinuria (≥1+). Diabetes mellitus was diagnosed when the fasting plasma glucose (FPG) levels were at least 126 mg/dl. Subjects who were already on chronic dialysis were excluded from the screening registry.

Metabolic syndrome was defined using the modified criteria recommended in the National Cholesterol Education Program (NCEP) Adult Treatment Panel III guidelines (*26*). Specifically, elevated blood pressure was defined as systolic blood pressure (SBP) of 130 mmHg or more or diastolic blood pressure (DBP) of 85 mmHg or higher; low high-density lipoproteion (HDL)–cholesterol was defined as less than 1.036 mmol/l (40 mg/dl) in men or less than 1.295 mmol/l (50 mg/dl) in women; high serum triglycerides were defined as 1.695 mmol/l (150 mg/dl) or more; and elevated FPG was defined as 6.10 mmol/l (110 mg/dl) or more. Metabolic syndrome was defined as the presence of three or more of these components. We used a BMI of at least 25 kg/m^2 instead of abdominal obesity, because abdominal circumference was not measured at the screenings. The ethics committee of the OGHMA approved the study protocol. Only coded data were used for the study. This study is a part of the Comprehensive Studies on Chronic Kidney Disease Including Dialysis Patients in Okinawa, which have been approved by the ethics committee of the University of the Ryukyus.

Statistical Analysis

The statistical significance of differences in the characteris-

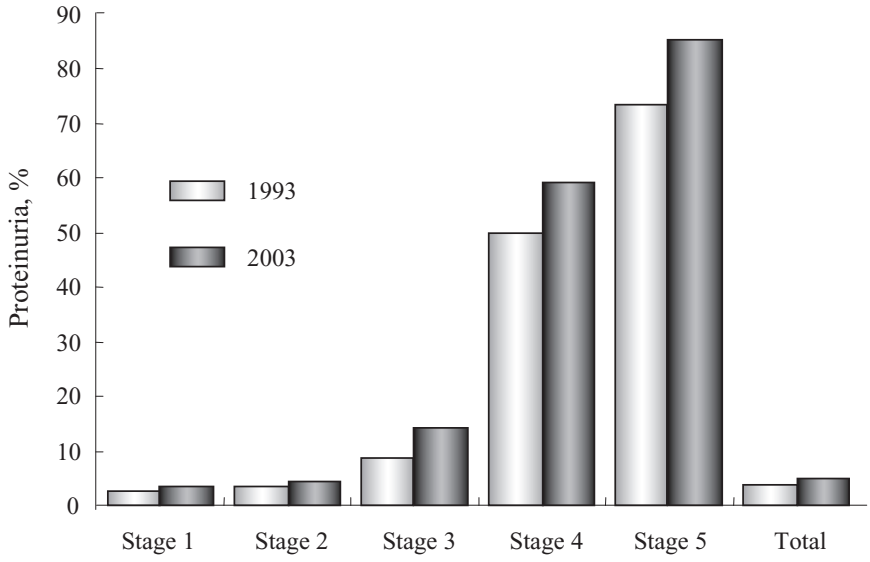

Fig. 1. *Prevalence of proteinuria according to the estimated GFR among the screened subjects in 1993 and 2003 in Okinawa, Japan. GFR was estimated by the MDRD equation as stage 1 (GFR≥90 ml/min/1.73 m^2), stage 2 (60–89 ml/min/1.73 m^2), stage 3 (30–59 ml/min/1.73 m^2), stage 4 (15–29 ml/min/1.73 m^2), or stage 5 (< 15 ml/min/1.73 m^2).*

tics of participants was examined using the Student's *t*-test (continuous variables), and the Wald χ^2 test (categorical variables) was performed using SAS (Version 8.2; SAS Institute Inc., Cary, USA). The odds ratio (95% confidence interval [CI]) was calculated using multivariate logistic regression analysis. A *p* value of less than 0.05 was considered to be statistically significant.

Results

The clinical characteristics of the screened participants are summarized in Table 1 (men) and Table 2 (women). Approximately 17% of the total adult (20 years and over) population in Okinawa was included in the two databases. There was no significant difference in sex ratio between the screenings. In 2003, the mean SCr was obtained using the calibration equation presented in the methods section. The prevalence of obesity increased from 32.9% in 1993 to 36.3% in 2003 ($p<0.0001$): from 39.8% to 42.9% in men ($p<0.0001$, Table 1) and from 29.8% to 30.5% in women ($p<0.0001$, Table 2). Obesity was more common in men than in women. The mean SBP, however, decreased significantly in both men and women. HDL-cholesterol was available only at the 2003 screening. The mean±SD level of HDL-cholesterol was 59.8±14.7 mg/dl, or 55.6±14.0 mg/dl in men and 63.6±14.3 mg/dl in women.

The drift in SCr levels are summarized in Table 3. Both the mean and median values of SCr increased slightly with age in both men and women in the two cohorts. In 1993, the estimated mean (median) GFR was 77.9 (77.8) ml/min/1.73 m^2 in men and 73.5 (72.5) ml/min/1.73 m^2 in women, whereas that of 2003 was 74.1 (74.0) ml/min/1.73 m^2 in men and 71.5 (71.2) ml/min/1.73 m^2 in women. Distributions of GFR are summarized in Table 4. In both sexes, the prevalence of low GFR, defined as <60 ml/min/1.73 m^2, was 15.7% in 1993 and 15.1% in 2003. The prevalence of CKD increased in men, but decreased slightly in women. The prevalence of proteinuria increased sharply in stage 4 and stage 5 CKD (Fig. 1).

In the 2003 screenees, we compared the prevalence of low GFR between those with and those without metabolic syndrome. The mean±SD of GFR was 70.0±13.7 ml/min/1.73 m^2 in those with metabolic syndrome and 73.3±12.9 ml/min/1.73 m^2 in those without metabolic syndrome. Presence of metabolic syndrome was significantly associated with the presence of low GFR: the age and sex adjusted odds ratio (95% CI) was 1.332 (1.277–1.389, $p<0.0001$) (Fig. 2).

Discussion

The present study demonstrated that the prevalence of low GFR (<60 ml/min/1.73 m^2) was similar between two screenings performed 10 years apart in Okinawa, Japan. Proteinuria was less than 5% in both databases. However, significant changes in demographics were observed, suggesting that the increased prevalence of metabolic syndrome or its components were observed. Moreover, the incidence of ESRD increased substantially during this period. The incidence of ESRD requiring dialysis increased from 194 (1990) to 297 (2000) per million population (*22*) and the prevalence was more than 2000 per million population in 2003 (*1*). There are several possible explanations for this observation. The elderly population has rapidly increased and therefore the number of

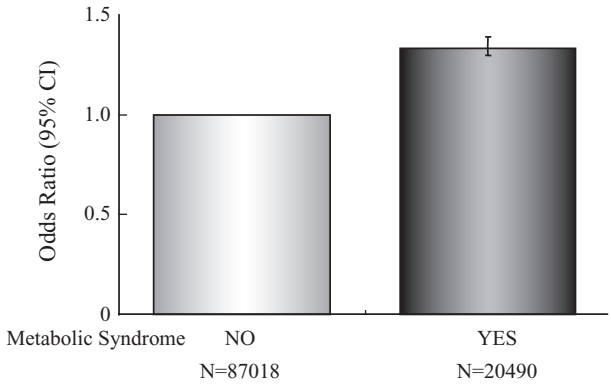

Fig. 2. *Odds ratio and 95% confidence interval (CI) of low GFR according to the presence or absence of metabolic syndrome among the screening subjects in 2003. The odds ratio was adjusted for age and sex. Metabolic syndrome was defined using the modified criteria recommended in the National Cholesterol Education Program (NCEP) Adult Treatment Panel III guidelines (25). We used a body mass index (BMI) of 25 kg/m^2 and over instead of abdominal obesity, because abdominal circumference was not measured in the 2003 screening.*

CKD cases is also higher. With improved general and medical management, people now live longer, even with multiple organ damages such as stroke and acute myocardial infarction. It is also possible that this finding was due to the increase in the number of available dialysis beds during the study period, and the increase in the acceptance rate.

We used the abbreviated MDRD formula to estimate GFR. Using this formula, the prevalence of CKD, from stages 3 to 5, was higher in Okinawa than in the US population (*6*). For this study, we did not use the ethnic factor to correct for GFR, but it would be less than 1.000 (Imai E *et al*., personal communication). Considering reports from Japan (*27*, *28*), Japanese might have a lower GFR than whites and blacks (*24*, *25*). SCr measurements have been performed in the OGHMA laboratory for more than 30 years. Since 2002, the SCr measurement method changed from the modified Jaffe method to an enzyme assay method, resulting in lower values in 2003 (mean SCr 0.76 mg/dl). After converting the SCr measured in 2003 using the equation presented in Methods, the median SCr levels were similar among all age classes in both sexes. Further verification was obtained in subjects without hypertension or diabetes mellitus that were expected to show normal levels of SCr (Table 3). Consequently, we considered that the laboratory data for SCr were very reliable, or at least did not change substantially, during the study period.

The CKD prevalence varies with several factors, such as age, sex, environmental factors, birth weight, and genetic and congenital factors (nephron number). Domrongkitchaiporn *et al*. reported the significance of SBP, serum uric acid, and BMI as risk factors for development of CKD in a Southeast Asian population (*29*). The mean SBP levels were found to be decreased, whereas the mean levels of BMI, serum cholesterol, and fasting plasma glucose were increased, in subjects with CKD in this population. The estimated prevalence of metabolic syndrome was 19.1% in 2003 (*23*), similar to that in the US population (*30*). The stable CKD prevalence in our study could be explained by the combination of demographics changes such as decrease in blood pressure, which may lower the CKD prevalence, and increase in obesity and lipid disturbance, which may act to raise the CKD prevalence.

It is important to recognize CKD and intervene as early as possible to prevent ESRD (*31*). In this regard, dipstick positive proteinuria would be a clue to detect low GFR (Fig. 1). Early intervention is quite effective for preventing the development of microalbuminuria in type 2 diabetes mellitus (*12*). We have identified screened participants who later developed ESRD using the Okinawa Dialysis Study registry (*21*, *22*). However, progression rates or rates of change in GFR are not available. The cumulative incidence of ESRD was significantly lower in those without proteinuria than those with proteinuria despite the similar levels of GFR between these two groups (*32*). Other than developing ESRD, the clinical course of CKD, GFR$<$60 ml/min/1.73 m^2, without proteinuria has yet to be examined.

Obesity is increasingly recognized as a cause of renal damage and ESRD (*33*). We previously reported that BMI is a significant predictor of developing ESRD in men using the 1983 screening registry (*34*). In that study, the prevalence of obesity (BMI$\geq$25 kg/m^2) increased from 32.9% (1993) to 36.3% (2003); this might reflect changes in the life style and dietary habits in Okinawa. The decrease in mean SBP suggests an effect of the public dissemination of information on hypertension as a risk for stroke (*35*).

There are some limitations to the present study. First, the cohort was voluntary, and therefore it was biased by a healthy worker effect and a self-selected database. Those who were already under treatment for CVD or CKD might not have participated. Also, there may have been some cases of undiagnosed renal artery stenosis among the aged participants (*36*). The OGHMA has provided an annual screening for the past 30 years. The number of participants is quite large, and the sex ratio and mean age of the participants are similar in the two databases. Therefore, we believe that it is adequate to examine the trends in the CKD prevalence in Okinawa, which is an isolated subtropical island. The migration in and out of Okinawa is small, but the total population is slightly increasing. To our knowledge, the present study is the first study of trends in the CKD prevalence in Japan. Within Okinawa, we reported that the prevalences of CKD and metabolic syndrome were 13.7% and 21.2% in the hospital-based database (*23*), which are similar to the findings for the 2003 screening in this study (15.1% for CKD and 19.1% for metabolic syndrome).

Second, SCr data was available for two-thirds of the screenees in both screenings. The prevalence of proteinuria was

slightly higher among the participants in the 2003 screening than those in the 1993 screening; individuals with SCr measurements would have similar or slightly higher CKD prevalence. In both screenings, the number of SCr data was quite large and the drift of SCr measurements was small. Third, the cross-sectional study design makes it difficult to infer causality between the metabolic syndrome and risk for CKD or proteinuria. We recently demonstrated, however, that obesity is a significant predictor of developing proteinuria (*37*), CKD (*23*), and ESRD (*34*). Weight reduction is associated with a decrease in proteinuria (*38*, *39*). Fourth, SCr levels and calculated GFR have been used to define CKD (*25*). Although inulin or iothalamate clearance techniques might provide a more sensitive estimate of renal function, SCr is widely used in large epidemiologic studies and in clinical practice for estimating renal function. Therefore, our findings are applicable to clinical and public health practice settings. Ethnic factors for the Japanese are not as well established when using the abbreviated MDRD equation, as for the Chinese (*40*). However, it is estimated that the ethnic factor for the Japanese using this equation would be smaller than 1.000 (Imai E *et al*., submitted). Therefore, our results might have underestimated the CKD prevalence. Another formula to estimate GFR similar to that of MDRD might be necessary in Japanese. In contrast to our database, the CKD prevalence was low among subjects with no metabolic syndrome components in the National Health and Nutrition Examination Survey III (*5*). Fifth, other parameters associated with CKD, such as physical activity (*41*), alcohol consumption (*42*), and smoking habit, were not examined in the present study. Also, it was not known whether the subjects had been treated for hypertension or diabetes mellitus.

In conclusion, the present study demonstrated changes in the demographics and the prevalence of CKD in two population–based screenings in Okinawa, Japan. The prevalence of CKD did not change substantially during the past 10 years. Several of the risk factors for CKD—*i.e.*, high serum cholesterol, fasting plasma glucose, and BMI—became more prevalent over the study period, but one risk factor, high SBP, became less prevalent. We suspect that the decrease in SBP might be explained by increased awareness due to public dissemination of information regarding hypertension as a risk for CVD. Whether the increase in ESRD is related to the increase in acceptance rate for dialysis or the increased progression of CKD remains to be determined. However, more public attention is needed on the renal effects of obesity and metabolic syndrome.

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