ORIGINAL ARTICLE

Effect of chronic kidney disease on individual and population medical expenditures in the Japanese population

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Chronic kidney disease (CKD) is associated with increased risk of cardiovascular disease (CVD), and may also lead to an increase in medical expenditures. The effect of CKD on individual and population medical expenditures was examined in a Japanese cohort study. The participants included 4026 Japanese National Health Insurance beneficiaries aged 40–74 years living in one city, who had no history of major CVD. They were classified into three categories according to their glomerular filtration rate (GFR) at the baseline survey, and their total medical expenditures were followed-up for 3 years. The arithmetic and geometric means of the cumulative medical expenditures were calculated for each category. The geometric mean was also expressed after adjusting for several confounding factors using analysis of covariance. The CKD-related medical expenditures attributable to the participants with mild ($60 \leqslant GFR < 90$) or moderate ($30 \leqslant GFR < 60$) kidney dysfunction were compared with those of participants with normal ($GFR \geqslant 90$) kidney function. There was a negative correlation between the GFR category and the arithmetic and geometric means of personal medical expenditures (adjusted geometric mean: $GFR \geqslant 90$, 167 879 yen; $60 \leqslant GFR < 90$, 210 660 yen; and $30 \leqslant GFR < 60$, 330 050 yen). The CKD-related medical expenditures accounted for 11.5 and 6.5% of the total medical expenditures for the participants with mild and moderate kidney dysfunction, respectively. The prevention of mild CKD is very important for containing medical expenditures. Appropriate strategies, such as regular creatinine measurement, are needed for early detection of CKD.

INTRODUCTION

Chronic kidney disease (CKD) was developed as a concept to prevent end-stage renal disease (ESRD) and other related medical complications.[1] According to the Japanese Society for Dialysis Therapy, the incidence of patients with ESRD starting chronic dialysis therapy has been greater than 2000 per million population since 2005.[1] This large number of ESRD patients could be just the tip of the iceberg of an increasing number of patients with CKD. In the United States, the estimated 19 million persons who have CKD is a significantly larger population than the 450 000 with ESRD.[2]

Earlier studies reported that CKD was associated with increased mortality and morbidity of cardiovascular disease (CVD).[3–5] Considering the large estimated numbers of individuals with CKD and their high risk for CVD, medical expenditures of people with CKD may be an important concern. However, to our knowledge, no study has investigated the medical expenditures of people with CKD in communities.

Accordingly, we investigated the cumulative total medical expenditures after stratification by the estimated glomerular filtration rate (GFR) categories using data of National Health Insurance (NHI) beneficiaries in Tanba City, located in the western part of Japan. Our *a priori* hypothesis was that the estimated GFR was negatively correlated with medical expenditures. Furthermore, we investigated the proportion of the excess cumulative total medical expenditures of participants with CKD.

METHODS

Medical expenditures in Japan

Medical expenditures in Japan were based on a public medical insurance institution,[6,7] which was mainly classified into two insurance systems until March 2008; recently, a third system for elderly persons aged 75 years or more was enrolled. Everyone living in Japan was required to enroll in one of the two insurance systems. One was for employees and their dependents. The other was called the NHI system, which was for self-employed individuals, such as farmers and fishermen, as well as for retirees and their dependents; this system was controlled by local municipalities. The NHI system covered 41% of the total Japanese population in 2005.[8] All prices were strictly controlled by a

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fee schedule that was set by the National Government and calculated on a 'fee-for-service' basis. The fee schedule was constant, independent of the insurance system. Furthermore, the same fee schedule applied to all clinics and hospitals that were approved to provide medical services under the public medical insurance system.

Study population

The study cohort consisted of Japanese NHI beneficiaries, aged 40–74 years, living in Tanba City in Hyogo Prefecture, in the western part of Japan, who had undergone a medical examination in 2002. In this examination, residents under no medication were recommended to participate. In 2002, 4789 individuals participated in the examination. Participants with serious medical conditions, who were expected to be cured soon after the examination, such as those in whom an operation was planned, might initially show high medical expenditures, which would confound the relationship between CKD and medical expenditures; however, it was difficult to detect serious medical conditions by interview at medical health checkups. Accordingly, 4086 participants, who had continuously attended the medical examination in the succeeding year (2003), were enrolled in this study. Thus, the study participants were relatively healthy, community-dwelling residents. Annual NHI claim files for over 3 years after the baseline survey within Tanba City were linked with the baseline survey data. The names and addresses of the participants were deleted from the linked data to protect their privacy. Participants with missing data ($N=7$), and those who had a history of major CVD, such as stroke at baseline ($N=53$), were excluded. Finally, 4026 participants (1735 men and 2291 women) were included in the analysis. The Institutional Review Board of Shiga University of Medical Science for ethical issues approved this study (No. 20-1, 2005).

Baseline examination

The baseline survey was carried out in 2003 using standardized methods in accordance with the Manual for Health Checkups under the Medical Service Law for the Aged, issued by the Japan Public Health Association in 1987.[9] Serum creatinine (mg per 100 ml) was measured using the enzymatic method. GFR (ml min^{-1} per 1.73 m^2) was calculated using the equation developed by the Japanese Society of Nephrology: $194 \times$(serum creatinine (mg per 100 ml))$^{-1.094} \times$(age (years))$^{-0.287} \times$(0.739, if female).[10] On the basis of the National Kidney Foundation (NKF) classification of CKD,[11,12] the participants were classified into three groups according to their GFR: GFR $\geqslant 90$, $60 \leqslant$ GFR < 90 and $30 \leqslant$ GFR < 60. The group with GFR $\geqslant 90$ was defined as having a normal kidney function.[11,12] These classifications were carried out for each calculated value of GFR.

Blood pressure was measured using an automatic sphygmomanometer after a 5-min rest. Hypertension was defined as systolic blood pressure $\geqslant 140$ mm Hg and/or diastolic blood pressure $\geqslant 90$ mm Hg. Diabetes was defined as casual blood glucose $\geqslant 200$ mg per 100 ml. Hypercholesterolemia was defined as total cholesterol $\geqslant 5.69$ mmol l^{-1} (220 mg per 100 ml). The participants' smoking habits were determined from interviews administered by public health nurses, and the Brinkmann index was calculated as number of cigarettes per day × years of smoking.

Data analysis

One-way analysis of variance and the χ^2-test were used to compare risk characteristics at baseline of participants by the three GFR categories (GFR $\geqslant 90$; $60 \leqslant$ GFR < 90 and $30 \leqslant$ GFR < 60). The Kruskal–Wallis test was used to compare the Brinkmann index values.

Cumulative total medical expenditures for 3 years were evaluated for each participant in each of the three GFR categories. The arithmetic mean and median of cumulative total medical expenditures were calculated for each of the three categories. The Kruskal–Wallis test was used to compare the medical expenditures among the three categories. As the distribution of medical expenditures was positively skewed, the data were logarithmically transformed to normalize the distribution; the results were then expressed as geometric means for multivariate analysis. Overall, 126 participants had cumulative total medical expenditures of 0 yen. For participants with expenditures of 0 yen, logarithmic transformations were achieved by replacing 0 yen with 1 yen. To compare cumulative total medical expenditures per person in each category, an

analysis of covariance was carried out after adjusting for systolic blood pressure, plasma glucose, serum total cholesterol, body mass index (BMI) and smoking (the Brinkmann index) with Bonferroni's correction for multiple *post hoc* comparisons.

Furthermore, excess medical expenditures attributable to the GFR category were calculated.[13,14] The excess medical expenditures were estimated as follows: Σ[(the arithmetic mean of the cumulative total expenditures in two of the three groups, except those with GFR $\geqslant 90$, that is, (1) $60 \leqslant$ GFR < 90 and (2) $30 \leqslant$ GFR < 60—the arithmetic mean of the cumulative total medical expenditures in the GFR $\geqslant 90$ group) × (the numbers of individuals in two of the three groups, except those with GFR $\geqslant 90$)]. The proportion of excess cumulative medical expenditures to the entire cumulative total medical expenditures of the population was also examined.

The statistical package, SPSS 15.0J (SPSS, Tokyo, Japan), for Windows was used to carry out these analyses. All P-values were two-tailed, and the significance level was established at $P < 0.05$.

RESULTS

The mean age of the study population was 63.1 years (males, 63.1 years; females, 63.1 years), and the mean GFR value of all participants was 73.8 (males, 73.9; females, 73.7) ml min^{-1} per 1.73 m^2.

Table 1 summarizes the baseline risk characteristics of the participants classified into three groups on the basis of GFR according to the definition of CKD; 17.7% of participants had CKD with GFR < 60 at baseline. The mean values of age, serum total cholesterol and BMI for both sexes were higher in participants with decreased GFR. Systolic blood pressure and the prevalence of hypertension were higher in male participants with CKD than in participants without CKD, whereas the Brinkmann index in male participants and the casual plasma glucose in female participants were lower in participants with decreased GFR.

Table 2 shows the cumulative total medical expenditures per person (Japanese yen) grouped by sex and GFR. The median of the medical expenditures showed significant differences among the three categories. The geometric means of the medical expenditures after adjusting for several confounding factors also showed significant differences among the three categories. Bonferroni's correction for multiple *post hoc* comparisons showed a significant difference between the adjusted geometric mean of the participants with GFR $\geqslant 90$ and that of the participants with $60 \leqslant$ GFR < 90 and those with $30 \leqslant$ GFR < 60.

The calculated excess cumulative total medical expenditures attributable to the $60 \leqslant$ GFR < 90 group and to the $30 \leqslant$ GFR < 60 group were 303 947 460 yen and 171 774 756 yen, respectively. Figure 1 shows the excess cumulative total medical expenditure related to CKD for each group as a proportion of the cumulative total medical expenditures of the entire population. The proportion of the excess cumulative total medical expenditures related to CKD for the participants with $60 \leqslant$ GFR < 90 ($n=2670$) was 11.5%, and that for the participants with $30 \leqslant$ GFR < 60 ($n=711$) was 6.5%.

As the estimation of GFR tends to be underestimated among those with GFR > 60, we divided the source population into two groups (GFR $\geqslant 60$ and GFR < 60). The arithmetic mean was 209 238 yen in GFR $\geqslant 60$ and 259 208 yen in GFR < 60. The adjusted geometric mean was 69 703 yen in GFR $\geqslant 60$ and 112 308 yen in GFR < 60. The proportion of excess medical expenditure was 4.0% in GFR < 60.

DISCUSSION

In this study, there was a negative correlation between GFR and the arithmetic and geometric means of personal medical expenditures. However, the excess total medical expenditures might be higher among the participants with $60 \leqslant$ GFR < 90 than among those with

Table 1 Baseline risk characteristics of 4026 participants by sex and kidney function in 2003 in Tanba City, Japan

	GFR (ml min^{-1} per 1.73 m^2)			P-value
	GFR $\geqslant$ 90	60 $\leqslant$ GFR < 90	30 $\leqslant$ GFR < 60 (CKD)	
Male				
No. of participants	207	1198	330	
Age (years)	58.0 ± 10.2	63.1 ± 8.5	66.7 ± 5.7	<0.001
GFR (ml min^{-1} per 1.73 m^2)	101.2 ± 9.2	74.6 ± 8.0	54.0 ± 6.0	<0.001
Serum creatinine (mg per 100 ml)	0.63 ± 0.06	0.81 ± 0.08	1.08 ± 0.14	<0.001
Systolic blood pressure (mm Hg)	134 ± 20	135 ± 19	139 ± 21	<0.01
Serum total cholesterol (mg per 100 ml)	199 ± 37	205 ± 33	206 ± 32	<0.05
Plasma glucose (mg per 100 ml)	105 ± 35	101 ± 23	101 ± 31	0.13
Body mass index (kg m^{-2})	22.7 ± 3.0	23.2 ± 3.0	23.8 ± 2.8	<0.001
Brinkmann index[a]	477	444	300	<0.001
Hypertension (%)	39.6	46.2	51.2	<0.05
Diabetes mellitus (%)	2.4	0.9	2.1	0.08
Hypercholesterolemia (%)	12.1	14.4	13.6	0.65
Female				
No. of participants	438	1472	381	
Age (years)	61.1 ± 7.8	63.3 ± 7.8	64.8 ± 6.3	<0.001
GFR (ml min^{-1} per 1.73 m^2)	98.0 ± 11.3	72.2 ± 7.2	51.8 ± 5.6	<0.001
Serum creatinine (mg per 100 ml)	0.48 ± 0.04	0.63 ± 0.06	0.86 ± 0.10	<0.001
Systolic blood pressure (mm Hg)	133 ± 19	134 ± 19	134 ± 19	0.56
Serum total cholesterol (mg per 100 ml)	216 ± 35	222 ± 33	225 ± 34	<0.001
Plasma glucose (mg per 100 ml)	100 ± 20	96 ± 16	93 ± 19	<0.001
Body mass index (kg m^{-2})	22.5 ± 3.0	22.8 ± 3.1	23.2 ± 3.2	<0.01
Brinkmann index[a]	3.0	7.4	5.9	0.22
Hypertension (%)	41.6	40.5	39.6	0.85
Diabetes mellitus (%)	0.7	0.1	0.3	0.09
Hypercholesterolemia (%)	24.0	27.9	30.7	0.14

Abbreviation: GFR, glomerular filtration rate.
Values are mean ± s.d. or the % of participants in that category. One-way analysis of variance for continuous variables, χ^2-test for categorical variables.
[a]Kruskal–Wallis test.

30 $\leqslant$ GFR < 60, because the number of participants with 60 $\leqslant$ GFR < 90 was much higher than that of participants with 30 $\leqslant$ GFR < 60. Accordingly, the prevention of mild CKD is very important from the viewpoint of national medical expenditures.

In this study, the equation developed by the Japanese Society of Nephrology for GFR estimation[10] was used, and the definition of CKD from The Kidney Disease Outcome Quality Initiative (K/DOQI) practice guideline that was published in 2002 by the National Kidney Foundation (NKF)[11,12] was adopted. According to earlier community-based population studies in Japan,[4,5,15] which used the equation developed at the Cleveland Clinic laboratory for the MDRD (Modification of Diet in Renal Disease) study for GFR estimation,[16,17] the prevalence of CKD was ∼10% or less. In this study, the prevalence of CKD was 17.7%. This difference might be explained by the equation or by the high mean age of the participants in this study. Zhang *et al.*[18] reported that the median prevalence of CKD was 7.2% in persons aged 30 years or older, and the prevalence of CKD varied from 23.4 to 35.8% in persons aged 64 years or older. Considering the mean age of our participants (63.1 years), our result was essentially consistent with the result of Zhang's study. Accordingly, the present result may be representative of medical expenditure data among participants for health checkups in Japanese local cities, where the mean age of the residents is relatively high.

There was an inverse correlation between GFR and the arithmetic mean of the total medical expenditures. Furthermore, after adjusting for several confounding factors, such as systolic blood pressure and plasma glucose, the geometric means of the medical expenditures also showed an inverse correlation with GFR category. According to earlier studies, CKD is associated with cardiovascular mortality and morbidity.[3–5] The etiology of the increased risk of CVD in CKD patients is still unknown, but it may be in part because of shared CVD risk factors, including hypertension, diabetes, obesity, lipid abnormalities and smoking.[19–23] Acute CVD related to CKD, such as stroke and myocardial infarction, may increase medical expenditures because of hospitalization and intensive care. Accordingly, an individual with CKD faces high future medical expenditures. Furthermore, although the residents taking no medication were recommended to participate in the baseline survey, no information about the details of medication after the baseline survey was available. Some participants with decreased GFR might have had treatment for CVD risk factors, such as hypertension and diabetes. The treatment of CVD risk factors may be another reason for increased medical expenditures among individuals with CKD.

Nevertheless, from the perspective of the entire population, the participants with 60 $\leqslant$ GFR < 90 have a large medical economic effect, because the number of participants with 60 $\leqslant$ GFR < 90 was very large. Early screening of mild kidney dysfunction by serum creatinine measurement and early intervention to stop progression are important. Moreover, we would expect an 18% reduction in total population medical expenditures if each individual were to maintain a normal GFR by controlling CKD.

Table 2 Cumulative total medical expenditures per person grouped by sex and GFR, after 3 years of follow-up in Tanba City, Japan

		Cumulative total medical expenditures per person (Japanese yen)		
GFR category	No. of participants	Arithmetic mean	Median	Adjusted geometric mean
Male and female				
GFR ⩾ 90	645	536 027	308 570	167 879
60 ⩽ GFR < 90	2670	649 865	403 850	210 660*
30 ⩽ GFR < 60	711	777 623	511 050	330 050*
			P<0.001ª	P<0.001ᵇ
Male				
GFR ⩾ 90	207	457 775	229 700	132 720
60 ⩽ GFR < 90	1198	648 106	351 665	157 157
30 ⩽ GFR < 60	330	813 277	552 025	319 017*
			P<0.001ª	P<0.001ᵇ
Female				
GFR ⩾ 90	438	573 010	362 010	190 118
60 ⩽ GFR < 90	1472	651 296	439 510	265 375*
30 ⩽ GFR < 60	381	746 741	475 330	343 898*
			P<0.001ª	P<0.001ᵇ

Abbreviation: GFR, glomerular filtration rate.
*Bonferroni correction for multiple post hoc comparisons. Significance, between GFR ⩾90 and other categories, P<0.05.
ªKruskal–Wallis test.
ᵇMultivariate analysis of covariance adjusted for systolic blood pressure (mm Hg), plasma glucose(mg per 100 ml), serum total cholesterol (mg per 100 ml), body mass index and smoking habit (Brinkmann index).
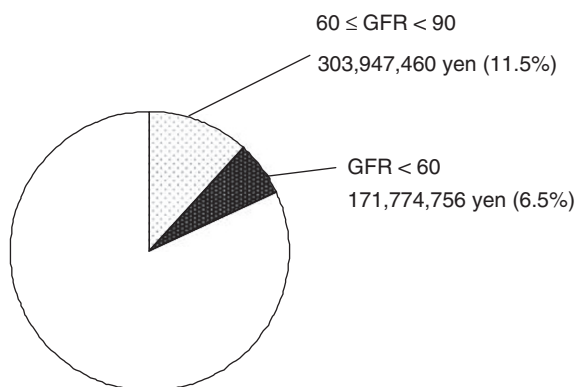

Figure 1 Proportion (%) of excess medical expenditures related to chronic kidney disease (CKD) in the whole population after a 3-year follow-up in Tanba City, Japan. White area represents predicted medical expenditures if all participants were of glomerular filtration rate (GFR) ⩾90 ml min⁻¹ per 1.73 m².

The interplay between CKD and CVD risk factors leads to enhanced cardiovascular risk.[24–26] Accordingly, the prevention of hypertension and diabetes mellitus by lifestyle modification, such as reducing dietary salt intake, decreasing body weight, increasing physical activity and reducing alcohol intake,[27–31] is very important for preventing CKD. Furthermore, angiotensin-converting enzyme inhibitors or angiotensin II type I blockers, which lower intra-glomerular pressure, protect against renal injury[32] and lower the risk of CVD mortality in individuals with hypertension or diabetes mellitus.[33,34]

In this study, only the residents with no medication were invited to participate. However, practically, CKD is often accompanied by diseases, such as hypertension, diabetes and CVDs, which were not taken into consideration in this study. Therefore, the medical expenditure examined in this study reflects only a certain part of the whole expenditure for CKD.

This study has several limitations. First, the medical expenditures of persons who died or moved during the follow-up period could not be determined. As earlier studies showed that CKD is a risk factor for CVD or all-cause mortality,[35–37] the effect of CKD on medical expenditures in this study was underestimated. In addition, the tendency of the relationship between kidney function and medical expenditures was the same in the result of this study when we analyzed the medical expenditures by each year of follow-up. Second, none of the participants had severely decreased kidney function (GFR<30), because such individuals did not participate in the medical examination. Therefore, the relationship between CKD and medical expenditures was also underestimated. Third, the details of the participants' medication status were not available in this study. However, participants taking no medications were invited to participate in the baseline survey. Fourth, the estimation of GFR may be underestimated among the participants with GFR>60.[10] The development of the new equation might be needed to estimate the accurate GFR of the individuals with GFR>60. Finally, the details of the names of diseases causing increased medical expenditures were unknown.

In conclusion, CKD may be an important predictor for excess medical expenditures for individuals and for the population as a whole. To maintain kidney function and contain medical expenditures, appropriate strategies, such as regular serum creatinine screening, are needed to identify CKD and intervene in high-risk individuals with CKD.

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