older in Ibaraki Prefecture showed hypertension, only 41.9% and 49.2% of them, respectively, were receiving antihypertensive treatment [13], and blood pressure was not adequately controlled in about 50% of those who were receiving treatment [14]. Appropriate interventions are assumed to bring about noticeable effects in Japan, in which RAS inhibitors have not been used effectively as antihypertensive therapy, although a slight increase has occurred in recent years [15].

Recently, the CKD Clinical Practice Guide for future treatment methods was developed by the Japanese Society of Nephrology [16], describing the treatment target for every CKD stage. Although all items of the treatment method were supported by clinical evidence, there were no prospective studies showing the effect of practices such as the CKD Clinical Practice Guide targets on renal and cardiovascular outcomes in sufficient number of CKD patients.

In this strategic CKD study, a prospective stratified cluster-randomized trial to examine the effectiveness of a care system designed to prevent progression of CKD through collaboration between nephrologists and general physicians was selected. One of the goals of the study is a 15% reduction in the estimated number of new dialysis patients in 5 years by increasing the rates of compliance with the CKD Clinical Practice Guide. The study also aims to encourage CKD patients to see their family physician, consult a nephrologist, and receive nutritional and lifestyle advice, while discussing health care measures to reduce the number of new dialysis patients.

Hypotheses of study

The study hypothesis encompasses the following four core issues:

1. Clinical practice in accordance with the Japanese CKD Clinical Practice Guide will improve the prognosis of CKD patients and reduce the speed of renal function deterioration.
2. Education-based interventions for CKD patients by registered dietitians and other co-medicals will help achieve strict CKD treatment goals in accordance with the Japanese CKD Clinical Practice Guide.
3. Collaboration concerning clinical practices among general physicians, nephrologists, and co-medicals will reduce the gap between clinical practice and evidence-based care measures, and improve the rate of continued consultation and prognosis in CKD patients.
4. These active interventions to improve CKD treatment will achieve the desired effects in terms of medico-economics.

Subjects and methods

Study organization and duration

Since the increase in the rate of dialysis patients varies from region to region in Japan [17], we divided the country into four regions (Fig. 1) as strata, so that they would

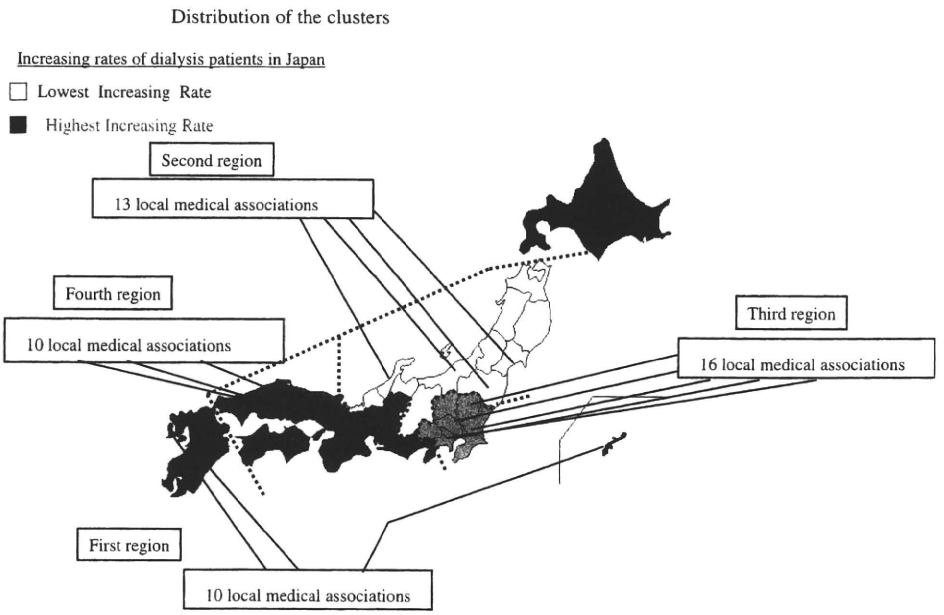

Fig. 1 Distribution of the clusters. We have recruited 49 local medical associations (clusters) in 15 different prefectures, which were classified into four regions (strata) based on the level of increase in the rate of dialysis patients [17]

include at least one managing facility and two or more clusters. The primary intervention study duration is from October 2008 to March 2012.

Rationale for setting the number of patients

This project aims to examine whether or not intervention can reduce the incidence of dialysis patients by 15% over the next 5 years. Regarding the calculation, we estimated the annual decrease in GFR as 0.59 ml/min/year (standard deviation (SD) 0.04 ml/min/year), based on changes in renal function among healthy Japanese people who underwent health checkups [17, 18] and the rate of renal deterioration in patients in CKD stage 3 with diabetes or hypertension [mean serum creatinine = 1.69 mg/dl (SD = 0.57 mg/dl), annual decrease rate = 5.93 ml/min/year (SD 4.321 ml/min/year), $n = 569$] [18, 19]. The required study size was calculated as 2,038 when the unknown intracluster correlation coefficient was assumed to be 0.5. We determined the required number as 2,264 for groups A and B, assuming that 10% would withdraw. We applied the simple number of 2,500 (1,250 for each group) as the target number of patients to perform this study.

Eligible patients

Each registered general physician obtained written informed consent for the study from eligible patients. They were formerly registered after the data center verified their eligibility. Inclusion criterion were: (1) age between 40 and 74 years; (2) in CKD stage 1, 2, 4, or 5; (3) in CKD stage 3 with proteinuria (ratio of urinary protein/urinary creatinine $\geq$0.3, or proteinuria $\geq$1+) and diabetes or hypertension.

Dialysis patients and those who did not consent were excluded from this study.

Assignment and randomization

This trial is a stratified open cluster-randomized study with two intervention groups: group A (weak intervention) and group B (strong intervention). We have recruited 49 local medical associations (clusters) in 15 different prefectures, which were classified into four regions (strata) based on the level of increase in the rate of dialysis patients (Fig. 1). Each local medical association recruited 10–58 general physicians by whom patients in this study has been treated. Local medical associations are randomized when the enrolment period is completed.

Intervention methods

Patients in group A clusters are instructed initially to undergo treatment in accordance with the current CKD treatment guide only, whereas patients in group B clusters are not only instructed in the same fashion but also receive consultations by dietitians visiting the local general practice offices. In addition, the data center closely monitors the treatment status and provides the group B general practice office with comments on the data.

Goals for the treatment of chronic kidney disease (groups A and B)

Participants in the study, or patients, will receive treatment according to the CKD Clinical Practice Guide [16]. Table 1 shows a summary of targets for CKD treatment applied to all patients. In patients with CKD, lifestyle modifications to avoid obesity and stop smoking are necessary. Strict blood pressure control (less than 130/80 mmHg), strict blood sugar control (HbA1c <6.5%), and low-density lipoprotein (LDL)-cholesterol control (LDL-C <120 mg/dl) are shown as targets for CKD treatment. The standards for referral from general physicians to nephrologists are as follows: (1) ratio of urinary protein/urinary creatinine $\geq$0.5, or proteinuria $\geq$1+; (2) estimated GFR (eGFR) <50 ml/min/1.73 m^2; (3) both proteinuria and hematuria positive ($\geq$1+); and (4) when family physicians judge that patients should consult a nephrologist. Estimated GFRs in this study are calculated using the following formula:

$$\mathrm{eGFR}(\mathrm{ml/min/1.73\ m^2}) = 194 \times \mathrm{Age}^{-0.287} \times \mathrm{Cre}^{-1.094} (\times 0.739 \text{ in the case of women}).$$

Monitoring of treatment status by the data center (only group B)

The data center closely monitors the treatment status and provides the group B general practice office with comments on the data. In addition, the data center will provide information on the patients scheduled to visit the office, examinations, and treatment that patients should undergo on their next visit, patients who did not visit hospitals as scheduled, those who are going to receive lifestyle/dietary advice, and those who meet the conditions for referral to nephrologists. The center also monitors patients and their schedules: the next consultation date, required examinations, details of treatment and care provided, and advice on lifestyle and nutrition. The centers will contact patients by mail, telephone, or email a week before the consultation day and encourage those who have not consulted a physician for over 2 months to receive care, trying to prevent their withdrawal from treatment. To facilitate referrals to nephrologists, the centers send a list of patients who meet the criteria for referral to the physicians and clinical research coordinators (CRCs).

Table 1 CKD practice guide target in this study

CKD stages	Lifestyle	Diet	Blood pressure	Blood sugar	Lipid metabolism	Hemoglobin
Stage 1	Smoking cessation BMI <25 kg/m^2	Sodium chloride <6 g/day for hypertensives	<130/80 mmHg	HbA1c <6.5%	LDL-C <120 mg/dl	
Stage 2	Smoking cessation BMI <25 kg/m^2	Sodium chloride <6 g/day for hypertensives	<130/80 mmHg	HbA1c <6.5%	LDL-C <120 mg/dl	
Stage 3	Smoking cessation BMI <25 kg/m^2	Sodium chloride <6 g/day for hypertensives DPI: 0.6-0.8 g/kg/day	<130/80 mmHg	HbA1c <6.5%	LDL-C <120 mg/dl	Hb 10–12 g/dl
Stage 4	Smoking cessation BMI <25 kg/m^2	Sodium chloride <6 g/day for hypertensives DPI: 0.6–0.8 g/kg/day Potassium restriction	<130/80 mmHg	HbA1c <6.5%	LDL-C <120 mg/dl	Hb 10–12 g/dl
Stage 5	Smoking cessation BMI <25 kg/m^2	Sodium chloride <6 g/day for hypertensives DPI: 0.6–0.8 g/kg/day Potassium restriction	<130/80 mmHg	HbA1c <6.5%	LDL-C <120 mg/dl	Hb 10–12 g/dl
Others			<125/75 mmHg If proteinuria >1 g/day			

BMI body mass index, *DPI* dietary protein intake

Nutrition and lifestyle improvement (only group B)

Registered dietitians provide support according to the instructions and advice from family physicians. They help patients achieve their CKD treatment goals, explaining to patients about examination results, achievements in CKD care, and their implications. Registered dietitians receive training so that they will be able to provide integrated and consistent advice.

Data collection

At each consultation, physicians will measure patients' blood pressure, and check their blood pressure conditions at home. Examinations or surveys will be performed every 6 months regarding body weight, abdominal circumference, smoking status, fasting serum creatinine, blood urea nitrogen (BUN), potassium, hemoglobin (Hb), high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), triglyceride (TG), uric acid, total protein, albumin, fasting blood glucose, HbA1c (only in the case of diabetes), urinary creatinine levels, amount of urinary proteins, eGFR, number of patients referred by nephrologists, number of new dialysis patients, and incidence of cardiovascular events.

Parameters for assessment

Primary parameters for assessment are: (1) the rate of continuous clinic visits of CKD patients, (2) the proportion of patients under cotreatment between general physicians and nephrologists, and (3) annual changes in CKD stage.

Secondary parameters are: (1) the proportion of adherence to the complete CKD treatment guide, (2) the rate of achievement of blood pressure goals, (3) the number of subjects with 50% reduction in urinary protein, (4) the number of subjects with a doubling of serum creatinine or 50% reduction in eGFR, (5) yearly changes in the number of patients starting renal replacement therapy, and (6) the incidence of cardiovascular events.

Statistical analysis

Statistical analyses will be performed using an intent-to-treat approach. Differences in primary endpoints between intervention groups are described by their 95% confidence intervals. The declining velocity of eGFR is tested by analysis of variance, using the efficacy of interventions as fixed effects and cluster effects as random effects. We employ a generalized linear model with age, gender, complications, and previous GFR as covariates where appropriate. The significance level on both sides in hypothesis testing is set at 0.05.

For secondary endpoints, we will use analysis of variance with a generalized linear model.

Ethical considerations

This study is being conducted in accordance with the Ethical Guidelines for Clinical Studies (revised on December 28, 2004, of the Ministry of Health, Labor, and Welfare) and the Ethical Guidelines for Epidemiological Studies (revised on August 16, 2007, of the Ministries of Education, Culture, Sports, Science, and Technology/ Health, Labor, and Welfare). All medical professionals involved in this study must comply with these ethical standards. This study is a Central Institutional Review Board (Central IRB) program, and the Committee on Ethics in Strategic Research of the Kidney Foundation, Japan, will examine and approve implementation plans and their revision.

Discussion

The purpose of this study is to enhance cooperation between nephrologists and general physicians, improve lifestyle and dietary advice provided by registered dietitians at general physicians' offices, and offer measures to control blood pressure and other critical parameters in practice, thereby filling the evidence-practice gap, which will slow the progression of kidney disease.

Recently, the concept of chronic kidney disease has been announced not only in Japan, but also throughout the world [9, 10]. There are more than ten million CKD patients in Japan [4], and so CKD is regarded as a public health problem.

CKD guidelines for general physicians or patients have been published in European countries [9, 20–22]. The USA is also preparing similar measures for CKD [23, 24]. In Japan, annual urinalysis for early detection of renal disease started in the 1970s [11, 25], and a serum creatinine test was included in health examinations as early as 1989 to detect kidney failure among adults aged 40 years or older [26]. However, the number of dialysis patients is increasing by approximately 4% each year. It is necessary to implement more appropriate measures to reduce the rate of new dialysis patients in Japan as soon as possible.

In 2007, the Japanese Society of Nephrology established the CKD Clinical Practice Guide to help family physicians provide care for CKD patients. The guide suggests that lifestyle and dietary advice on obesity prevention [27], smoking cessation [28], and a sodium-restricted diet, and treatment for metabolic disorders [29, 30], hypertension [31], and hyperlipidemia [32] are effective to prevent progression of CKD. However, most people are not making sufficient efforts to manage their own health condition [13]. It is necessary to show the effect on the progression of CKD of treatment as part of the Clinical Practice Guide. Our challenge is to obtain sufficient evidence regarding the efficacy of filling the evidence-practice gap in preventing deterioration of renal function among Japanese patients.

We set the following conditions for patient eligibility in this study: CKD patients aged between 40 and 74 years; patients in CKD stage 1, 2, 4 or 5; and patients in CKD stage 3 with a high level of urinary protein and diabetes or hypertension. Proteinuria is known as the strongest predictor of decreasing renal function [13, 33], and the aggressive management of blood pressure and glucose [29, 31] and administration of RAS inhibitors [34–36] prevent the deterioration of renal function. The reason for the condition regarding urinary proteins in stage 3 patients is that we need to register patients showing significant deterioration in renal function [37].

Regarding lifestyle and dietary advice, we have prepared a list of instructions and advice for individual patients on a priority basis, so that registered dietitians can design a guidance schedule based on the priority list and provide consistent advice. In this study, we focus on preventing progression of CKD in the early stage by giving priority to Japanese CKD practice guide goals. We are preparing a long-term guidance method covering a wide range of health management items while seeking ways to reduce the evidence-practice gap as much as possible.

We predict significant positive effects in intervention group B (increased collaboration in clinical practice) in terms of increases in the rate of continued consultation and collaboration between nephrologists and other physicians, and reduced CKD stage progression as a result of instructions and advice from registered dietitians, compared with intervention group A. This study was designed to examine the effectiveness of a support system for collaborative CKD diagnosis and treatment by conducting a cluster-randomized controlled trial. We expect that this study will help improve clinical practices for CKD patients and provide high-quality clinical findings of global standard. Although the number of CKD patients in Japan is estimated to be more than ten million, there are only 3,000 nephrologists. If effective collaboration is established among nephrologists in CKD care, it will have a significant positive impact on renal care systems. In the area of renal care, few large-scale intervention studies have been performed on kidney care systems, except those aimed to assess the efficacy of drug interventions. Little progress has been made in the development of infrastructure for clinical studies and research environments in Japan. This study is expected not only to help develop the infrastructure required for clinical renal studies but also to generate valuable findings.

Progress of the study

Prior to the study, we selected 15 management facilities and 49 local medical associations, registered 491 family physicians (between April and June 2008), and registered 2,494 study participants on a provisional basis (between April and October 15, 2008), 2,413 of whom were randomly divided into intervention groups A (1,211) and B (1,202) in units of medical associations (or clusters) in September 2008. We started the intervention study on October 20, 2008.

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ORIGINAL ARTICLE

Measurement of health-related quality of life in patients with chronic kidney disease in Japan with EuroQol (EQ-5D)

Reiko Tajima · Masahide Kondo · Hirayasu Kai · Chie Saito · Masafumi Okada · Hideto Takahashi · Mariko Doi · Shuichi Tsuruoka · Kunihiro Yamagata

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Abstract
Background Chronic kidney disease (CKD) is a health-related quality-of-life (HRQOL) deteriorating disease which is not only a public health but also a socioeconomic problem. Interest in developing cost-effective interventions to control CKD has increased. The aim of this study was to measure HRQOL in terms of quality-adjustment weights for cost-effectiveness analysis using EQ-5D in patients with CKD. The relationships between the measured HRQOL and clinical indices/complications were also analyzed.
Methods EQ-5D, a generic preference-based instrument, was administered to 569 CKD outpatients at Tsukuba University Hospital between November and December 2008. The response rate was 94.4% (537/569). Data on sex, age, creatinine, hemoglobin, serum albumin and eGFR were obtained from the patients' records. Data on the presence of complications such as hypertension, diabetes, and history of cardiovascular disease (CVD) were also retrieved.
Results Measured quality-adjustment weights by the CKD stage were 0.940 (95% CI 0.915–0.965), 0.918 (0.896–0.940), 0.883 (0.857–0.909), 0.839 (0.794–0.884), and 0.798 (0.757–0.839) for stages 1–5, respectively. The decrease in weight was significant by ANOVA ($P < 0.0001$), and the weight for all stages was 0.885 (0.871–0.898). There was a positive relationship between hemoglobin/serum albumin and the weight. The presence of hypertension lowered the weight from 0.910 (0.885–0.936) to 0.874 (0.858–0.891), diabetes from 0.901 (0.886–0.917) to 0.840 (0.811–0.869), and CVD from 0.892 (0.878–0.906) to 0.783 (0.718–0.848).
Conclusions HRQOL decreases with progression of CKD stage and/or presence of anemia, undernutrition, hypertension, diabetes, or history of CVD.

Keywords Health-related quality of life (HRQOL) · Quality-adjustment weight · Chronic kidney disease (CKD) · EuroQol (EQ-5D)

R. Tajima · H. Kai · C. Saito · S. Tsuruoka · K. Yamagata (✉)
Department of Nephrology, Graduate School of Comprehensive Human Sciences, Institute of Clinical Medicine, University of Tsukuba, 1-1-1 Ten-oudai, Tsukuba 305-8575, Ibaraki, Japan
e-mail: k-yamaga@md.tsukuba.ac.jp

M. Kondo
Department of Health Care Policy and Management, Graduate School of Comprehensive Human Sciences, University of Tsukuba, Tsukuba, Japan

M. Okada · H. Takahashi · M. Doi
Department of Epidemiology, Graduate School of Comprehensive Human Sciences, University of Tsukuba, Tsukuba, Japan

Introduction

Chronic kidney disease (CKD) is not only a worldwide public health problem, but also a global socioeconomic concern, with adverse outcomes including kidney failure, cardiovascular disease (CVD), and premature death. In 2002, the Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation in the United States published a definition and classification system for CKD [1]. The definition and classification of CKD were accepted by the international board of directors of Kidney Disease: Improving Global Outcomes [2]. CKD was classified into five stages based on the appearance of proteinuria and glomerular filtration rate (GFR).

It is estimated that there are more than ten million CKD patients [3], who may progress to ESRD requiring dialysis, and more than 280,000 ESRD patients in Japan [4]. The annual cost of dialysis treatment was more than 130 billion yen in Japan in 2008 [4]. The high morbidity of CKD and high cost of dialysis have promoted interest in developing not only effective but also cost-effective interventions for CKD. Previous studies have suggested that CKD is one of the most important risk factors for CVD among those known: hypertension, diabetes, hyperlipidemia, obesity, smoking, and lifestyle-related diseases [5–8]. Therefore, the early detection of and early initiation of treatment for CKD are important in order to prevent kidney failure as well as cardiovascular complications and death.

To conduct a cost-effective analysis, outcome measurement in terms of quality-adjusted life-years (QALYs) is recommended [9, 10], and is crucial to dealing with QOL-deteriorating diseases including CKD. QALYs are calculated as the sum of the adjusted life-years experienced by a patient, where the adjustment is made by multiplying time by weights linked to the changing health state of the patient. The quality-adjustment weight is a value of between 1 (for perfect health) and 0 (for death), which is a type of health-related quality of life (HRQOL) measurement. The weight, in principle, represents social preference for a certain health state, and so it should be measured in every society. However, there are few reports on such weights in regard to CKD in the literature. Therefore, the first objective of this study was to measure quality-adjustment weights for the health states of CKD patients by stage. Furthermore, Perlman et al. [11] and Leaf et al. [12] identified associations between the HRQOL of CKD patients and clinical indices such as hemoglobin or eGFR. Therefore, we examined the relationship between the measured quality-adjustment weight and clinical indices of CKD patients. The accumulation of comorbidities tends to worsen the patients' HRQOL. We further analyzed the significance of major complications of CKD such as hypertension, diabetes, and history of CVD on the HRQOL of CKD patients.

The results of this study should facilitate the economic evaluation of interventions for CKD, which will contribute to the development of efficient ways to manage the disease. They also inform physicians of how patient HRQOL alters with disease progression, which is helpful for realizing more patient-centered clinical decision-making.

Materials and methods

Instrument for measuring quality-adjustment weights

There are preference-elicitation techniques that can be used when measuring quality-adjustment weights, such as the visual analogue scale (VAS), standard gamble (SG), and time trade-off (TTO) [13]. It is recommended that a representative sample of the community should be recruited when using them [9]. They also require a description of life in a particular state of health that is easy for patients to understand. Describing life at a particular stage of CKD, however, is practically impossible. Therefore, another approach, generic preference-based measures, was employed in this study. Specifically, we used the most widely used instrument, EQ-5D [13], which is standardized and validated for use in Japan [14, 15]. It is administered to representative patients in a particular state of health in Japan, who are asked to grade five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) of their health state as one of three levels ("no problem," "some problems," and "extreme problem"). "No problem" is also referred to as level 1, while "inability or extreme problem" is also referred to as level 3 such that (for example) a health state of 21232 means that the patient has some problems walking, no problem washing and dressing, some problems performing their usual activities, suffers extreme pain or discomfort, and is moderately anxious or depressed. The $3^5 = 243$ possible combinations of responses are converted to weight values according to the Japanese value set [15], and the average is calculated as a quality-adjustment weight for the health state under consideration in Japan. The weight values are based on TTO evaluations. The weight ranges from 1 for perfect health (no problem in any dimension) to 0 for death and −0.111 for severe problems in all dimensions. A positive weight means that the health status is better than dead and a negative weight is worse in EQ-5D.

Study design and subjects

We conducted a cross-sectional outpatient questionnaire survey. All 588 outpatients previously diagnosed with CKD at the Department of Nephrology Tsukuba University Hospital were recruited for this study between November and December 2008. We assumed that they comprised a near-representative sample of CKD patients in Japan to which EQ-5D could be applied, since a lack of knowledge of the descriptive epidemiology of CKD in Japan prevented us from obtaining a representative sample and making appropriate bias corrections during our analyses. The EQ-5D questionnaire was given to them to complete if they signed a written informed consent form when visiting the hospital after receiving an explanation of the purpose of this study. Nineteen patients (3.2%) were not included in this study because they were receiving renal replacement therapy. Thirty-two patients (5.4%) were excluded from the analysis because they did not respond to the questionnaire.

Study variables

From the patient records, sex and age were included in our analysis as demographic baseline characteristics. Creatinine, hemoglobin, and serum albumin on the day of the questionnaire survey were also included as routinely checked clinical indices. GFR was estimated from serum creatinine, age, and sex using the new Japanese equation as follows: eGFR (ml/min/1.73 m^2) = 194 × serum creatinine$^{-1.094}$ × age$^{-0.287}$ × 0.739 (if female) [16]. The presence of complications was also assessed using the records. Hypertension and diabetes were classified based on clinical records. A history of CVD was regarded as present if stroke, congestive heart disease, or ischemic heart disease was recorded.

Statistical analysis

All statistical analyses were performed using SAS. Quality-adjustment weights were calculated as the mean of a group of patients' weight values according to the Japanese value set for EQ-5D, and 95% confidence intervals were computed. The weight differences among CKD stages were tested by ANOVA. Correlation analyses were performed between weights and clinical indices. Multiple regression analysis was also applied to identify indices that determine weights. Nonparametric regression analysis was further applied in order to detect inflection points in the curves of quality adjustment weight versus identified indices. The level of significance was set at $P < 0.05$.

Results

The baseline characteristics of respondents are shown in Table 1. The respondents comprised 282 males (52.5%) and 255 females (47.5%). The overall mean age was 55.2 years old. Mean creatinine was 1.7 mg/dl; mean hemoglobin 12.7 g/dl; mean serum albumin 4.1 g/dl; and mean eGFR 56.1 ml/min/1.73 m^2. Regarding complications, 388 (72.2%) patients had hypertension; 146 (27.0%) patients had diabetes, with a mean HbA1c of 6.0%; and 38 (7.0%) patients had a history of CVD. Proportions of patients at various CKD stages were 15.5, 28.5, 29.4, 13.4 and 13.2% for stages 1–5, respectively. Patients at stages 1 and 2 were relatively young compared to those at stages 3–5.

The EQ-5D questionnaire responses are shown in Table 2. The proportions of the patients who responded "no problem" were 82.8% for mobility, 94.0% for self care, 79.3% for usual activities, 72.8% for pain/discomfort, and 82.1% for anxiety/depression. The frequency of "some problems" was significantly higher for mobility (4.8% in CKD 1 and 36.6% in CKD 5) and usual activities (9.6% in CKD 1 and 39.4% in CKD 5) with progression of the CKD stage. Fewer than 3% of the patients answered "extreme problem" for all dimensions.

Table 1 Baseline characteristics (total $n = 537$)

	Values	SD or %
Male, *n* (%)	282	52.5
Mean age (year), SD	55.2	16.0
Mean creatinine (mg/dl), SD	1.7	1.2
Mean hemoglobin (g/dl), SD	12.7	2.1
Mean albumin (g/dl), SD	4.1	0.6
Mean estimated GFR (ml/min/1.73 m^2), SD	56.1	34.1
Hypertension, *n* (%)	388	72.2
Diabetes, *n* (%)	146	27.0
History of cardiovascular disease, *n* (%)	38	7.0

CKD stage	*n*	%	Mean age	Age range
1 (GFR ≥ 90)	83	15.5	35.6	15–70
2 (60 ≤ GFR < 90)	153	28.5	54.1	27–85
3 (30 ≤ GFR < 60)	158	29.4	60.9	26–87
4 (15 ≤ GFR < 30)	72	13.4	62.1	30–94
5 (GFR < 15)	71	13.2	61.0	28–83

Table 3 shows measured quality-adjustment weights by stage: 0.940 (95% CI 0.915–0.965), 0.918 (0.896–0.940), 0.883 (0.857–0.909), 0.839 (0.794–0.884), and 0.798 (0.757–0.839) for stages 1–5, respectively. Figure 1 illustrates these in a box plot with a mark showing the mean. The decrease in weight was significant by ANOVA ($P = 0.000$), and the weight for all stages was 0.885 (0.871–0.898).

Squares of Pearson's correlation coefficient (R^2) were computed between weights and clinical indices and the patients' age. The age was included in the analysis as a controlling variable because years pass during the progression of the disease. R^2 values were relatively high for hemoglobin 0.1393 ($P = 0.000$), age 0.0737 ($P = 0.000$) and serum albumin 0.0892 ($P = 0.000$), and low for eGFR 0.0527 ($P = 0.000$) and creatinine 0.0406 ($P = 0.000$). Hemoglobin and serum albumin were positively correlated to weights, whereas age was negatively correlated. All correlations were significant upon tests of independence. Table 4 shows the results of multiple linear regression analysis aimed at identifying determinants of the weights. According to forced entry regression, hemoglobin, age, and serum albumin were found to be significant, and were selected as explanatory variables by stepwise regression. Figures 2 and 3 show the relationships between weights and hemoglobin/serum albumin based on nonparametric regression analysis, locally weighted regression, and smoothing scatterplots (LOWESS) [17]. Whereas correlations are

Table 2 Responses to the five dimensions of EQ-5D by CKD stage and complications

	n	Mobility			Self-care			Usual activities			Pain/discomfort			Anxiety/depression		
		No problem (%)	Some problems (%)	Extreme problem (%)	No problem (%)	Some problems (%)	Extreme problem (%)	No problem (%)	Some problems (%)	Extreme problem (%)	No problem (%)	Some problems (%)	Extreme problem (%)	No problem (%)	Some problems (%)	Extreme problem (%)
CKD stage																
1	83	95.2	4.8	–	97.6	2.4	–	89.2	9.6	1.2	89.2	10.8	–	89.2	10.8	–
2	153	91.5	8.5	–	98.0	2.0	–	87.6	11.8	0.7	82.4	15.7	2.0	86.3	13.7	–
3	158	81.7	17.7	0.6	94.3	5.1	0.6	82.3	17.1	0.6	77.9	21.5	0.6	76.6	22.8	0.6
4	72	72.2	25.0	2.8	88.9	8.3	2.8	66.7	27.8	5.6	75.0	25.0	–	84.7	15.3	–
5	71	63.4	36.6	–	85.9	14.1	–	56.3	39.4	4.2	60.6	38.0	1.4	74.7	25.4	–
All stages	537	82.8	16.6	0.6	94.0	5.4	0.6	79.3	18.8	1.9	78.2	20.9	0.9	82.1	17.7	0.2
Presence of HT																
CKD stage																
1	37	97.3	2.7	–	100.0	–	–	89.2	10.8	–	83.8	16.2	–	86.5	13.5	–
2	99	89.9	10.1	–	98.0	2.0	–	87.9	11.1	1.0	78.8	19.2	2.0	84.8	15.2	–
3	122	83.6	16.4	–	94.3	4.9	0.8	82.8	16.4	0.8	79.5	19.7	0.8	78.7	20.5	0.8
4	66	72.7	25.8	1.5	89.4	9.1	1.5	69.7	25.8	4.5	75.8	24.2	–	86.4	13.6	–
5	64	60.9	39.1	–	84.4	15.6	–	53.1	42.2	4.7	57.8	40.6	1.6	73.4	26.6	–
All stages	388	80.9	18.8	0.3	93.3	6.2	0.5	77.6	20.4	0.5	75.5	23.5	1.0	81.4	18.3	0.3
Absence of HT																
CKD stage																
1	45	93.3	6.7	–	95.6	4.4	–	88.9	8.9	2.2	93.3	6.7	–	91.1	8.9	–
2	54	94.4	5.6	–	98.1	1.9	–	87.0	13.0	–	88.9	9.3	1.9	88.9	11.1	–
3	36	75.0	22.2	2.8	94.4	5.6	–	80.6	19.4	–	72.2	27.8	–	69.4	30.6	–
4	6	66.7	16.7	16.7	83.3	–	16.7	33.3	50.0	16.7	66.7	33.3	–	66.7	33.3	–
5	7	85.7	14.3	–	100.0	–	–	85.7	14.3	–	85.7	14.3	–	85.7	14.3	–
All stages	148	87.8	10.8	1.4	95.9	3.4	0.7	83.8	14.9	1.4	85.1	14.2	0.7	83.8	16.2	–
Presence of DM																
CKD stage																
1	14	85.7	14.3	–	92.9	7.1	–	71.4	28.6	–	78.6	21.4	–	92.9	7.1	–
2	35	91.4	8.6	–	97.1	2.9	–	88.6	11.4	–	77.1	20.0	2.9	88.6	11.4	–
3	38	68.4	31.6	–	89.5	7.9	2.6	71.1	26.3	2.6	65.8	34.2	–	65.8	34.2	–
4	25	72.0	24.0	4.0	92.0	8.0	–	68.0	28.0	4.0	80.0	20.0	–	92.0	8.0	–
5	34	55.9	44.1	–	85.3	14.7	–	52.9	38.2	8.8	50.0	50.0	–	64.7	35.3	–

Table 2 continued

	n	Mobility			Self-care			Usual activities			Pain/discomfort			Anxiety/depression		
		No problem (%)	Some problems (%)	Extreme problem (%)	No problem (%)	Some problems (%)	Extreme problem (%)	No problem (%)	Some problems (%)	Extreme problem (%)	No problem (%)	Some problems (%)	Extreme problem (%)	No problem (%)	Some problems (%)	Extreme problem (%)
All stages	146	87.8	10.8	1.4	95.9	3.4	0.7	83.8	14.9	1.4	85.1	14.2	0.7	83.8	16.2	–
Absence of DM																
CKD stage																
1	69	97.1	3.0	–	98.6	1.4	–	92.8	5.8	1.4	91.3	8.7	–	88.4	11.6	–
2	118	91.5	8.4	–	98.3	1.7	–	87.3	11.9	0.8	83.9	14.4	1.7	85.6	14.4	–
3	120	85.8	13.3	0.8	95.8	4.2	–	85.8	14.2	–	81.7	17.5	0.8	80.0	19.2	0.8
4	47	72.3	25.5	2.0	87.2	8.5	4.3	66.0	27.7	6.4	72.3	27.7	–	80.9	19.1	–
5	37	70.2	29.7	–	86.5	13.5	–	59.5	40.5	–	70.3	27.0	2.7	83.8	16.2	–
All stages	391	86.4	13.0	0.5	95.1	4.3	0.5	82.6	16.1	1.3	81.8	17.1	1.0	83.6	16.1	0.3
Presence of CVD																
CKD stage																
1	0	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2	7	85.7	14.3	–	85.7	14.3	–	85.7	14.3	–	85.7	14.3	–	85.7	14.3	–
3	11	54.5	45.5	–	81.8	9.1	9.1	54.5	36.4	9.1	63.6	18.2	9.1	54.5	45.5	–
4	6	66.7	33.3	–	100	–	–	33.3	50	16.7	83.3	16.7	–	100	–	–
5	14	50	50	–	78.6	21.4	–	42.9	50	7.1	35.7	64.3	–	42.9	57.1	–
All stages	38	60.5	39.5	–	84.2	13.2	2.6	52.6	39.5	7.9	60.5	36.8	2.6	63.2	36.8	–
Absence of CVD																
CKD stage																
1	83	95.2	4.8	–	97.6	2.4	–	89.2	9.6	1.2	89.2	10.8	–	89.2	10.8	–
2	146	91.8	8.2	–	98.6	1.4	–	87.7	11.6	0.7	82.2	15.8	2.1	86.3	13.7	–
3	147	83.7	15.6	0.7	95.2	4.8	–	84.4	15.6	–	78.9	21.1	–	78.2	21.1	0.7
4	66	72.7	24.2	3	87.9	9.1	3	69.7	25.8	4.5	74.2	25.8	–	83.3	16.7	–
5	57	66.7	33.3	–	87.7	12.3	–	59.6	36.8	3.5	66.7	31.6	1.8	82.5	17.5	–
All stages	499	84.6	14.8	0.6	94.8	4.8	0.4	81.4	17.2	1.4	79.6	19.6	0.8	83.6	16.2	0.2

Table 3 Quality-adjustment weights by CKD stage

	n	Mean	95% CI	*P* value
CKD stage				
1	83	0.940	0.915–0.965	<0.0001
2	153	0.918	0.896–0.940	
3	158	0.883	0.857–0.909	
4	72	0.839	0.794–0.884	
5	71	0.798	0.757–0.839	
All stages	537	0.885	0.871–0.898	

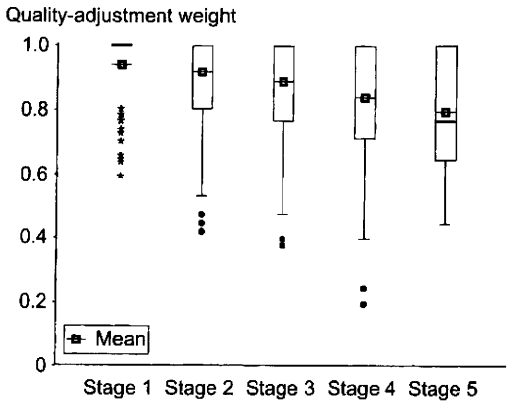

Fig. 1 Box and whisker plots of quality-adjustment weights by CKD stage. Quality-adjustment weights decrease with progression of CKD stage. Quality-adjustment weights at CKD stages 4 and 5 are significantly lower than those at CKD stages 1–3

not very clear when plots of cases are studied, smoothing curves reveal nonlinear relationships. The curves are stable regardless of the chosen bandwidth. Notable inflections in the weight against hemoglobin are seen at around 10.0 and 13.0 g/dl in Fig. 2. Similarly, inflections against serum albumin are seen at around 3.2 and 4.2 g/dl in Fig. 3.

The results from an analysis of the effect of comorbidity on HRQOL are shown in Table 5. The presence of hypertension lowers the weight from 0.910 (0.885–0.936) to 0.874 (0.858–0.891), diabetes from 0.901 (0.886–0.917) to 0.840 (0.811–0.869), and CVD from 0.892 (0.878–0.906) to 0.783 (0.718–0.848). There was a significant relationship between quality-adjustment weights and the presence of complications.

Discussion

We measured the HRQOL in terms of quality-adjustment weight using EQ-5D in patients with CKD. Measured weights by stage were: 0.94 for stage 1, 0.918 for stage 2, 0.883 for stage 3, 0.839 for stage 4, 0.798 for stage 5, and 0.885 for all stages. This is the first report on such weights using EQ-5D, and it can be used in cost-effectiveness analysis with a preferred outcome measure, QALYs, of interventions for CKD. The weights illustrate that CKD patient HRQOL lowers according to the progression of the disease, as expected. We consider that these results show the health-related quality of CKD patients' lives to a certain extent.

Although it is known that a direct international comparison of quality-adjustment weights is not possible, and that the measurement is sensitive to the technique/instrument used, Gorodetskaya et al. [18] report such weights by stage of CKD with TTO and Health Utility Index Mark 3 (HUI3); that is, a generic preference-based measures instrument [19]. TTO yields 0.90 for stages 1 and 2, 0.87 for stage 3, 0.85 for stage 4, 0.85 for stage 4, 0.85 for stage 5, and 0.72 for stage 5D; HUI3 yields 0.67 for stages 1 and 2, 0.67 for stage 3, 0.55 for stage 4, 0.54 for stage 4, 0.54 for stage 5, and 0.72 for stage 5D. The weight decreases along with progression of the stage, which is similar to our results. Gorodetskaya's weights, however, are lower than ours, which may be due to differences in social preferences between Japan and the United States, in the characteristics of the technique/instrument used, or in other factors including measurement errors. A well-designed international comparative study is needed in order to explore the causes of these differences.

There are more reports of weights for ESRD from several countries obtained with various techniques/instruments, although we have not assessed them. The weights for the ESRD range from 0.39 up to 0.93 using TTO, SG, or EQ-5D [20]. Limiting the instrument to EQ-5D, the reported weights were 0.66–0.81 for hemodialysis and 0.71–0.81 for peritoneal dialysis from the Netherlands [21], 0.76 for dialysis from Germany [22], 0.62 for hemodialysis and 0.55 for peritoneal dialysis from Canada [23], and 0.44 for hemodialysis and 0.65 for peritoneal dialysis from Sweden [24]. These values do not raise any concerns over our measurement of 0.798 for stage 5, although no straightforward comparison can be made.

The measured quality-adjustment weights were correlated with routinely checked clinical indices such as hemoglobin, serum albumin, eGFR, and creatinine. Additionally, they significantly depend on hemoglobin and serum albumin after controlling for age. The significance of hemoglobin as a determinant of the HRQOL of CKD patients is consistent with the findings of previous studies, which measured HRQOL along with other measurements, such as SF-36 [11, 12]. The significance of serum albumin has also been pointed out [11]. These results suggest that a patient's HRQOL more closely depends on a general secondary state such as anemia or undernutrition than the primary pathology of CKD, i.e., a low GFR. A notable inflection in the weight at around a hemoglobin level of 10.0 g/dl is also noted in the relationship between the

Table 4 Multiple linear regression analysis of clinical determinants of HRQOL

Variable	Coefficient	SE	*t* Value	*P* value
Forced entry regression[a]				
Alb	0.0465	0.013	3.497	0.001
Hb	0.0148	0.004	3.434	0.001
sCre	−0.0065	0.006	−1.124	0.261
eGFR	−0.0002	0.000	−0.732	0.465
Age	−0.0021	0.001	−4.069	0.000
Sex dummy ("0" for male; "1" for female)	−0.0323	0.015	−2.219	0.027
Constant	0.6607	0.085	7.427	0.000

Step	Variable added	Coefficient	SE	*F* value	Adjusted R^2
Stepwise regression[b]					
1	Hb	0.0165	0.004	79.896	0.133
2	Age	−0.0019	0.000	49.961	0.160
3	Alb	0.0458	0.013	37.584	0.176
4	Sex dummy ("0" for male; "1" for female)	−0.0280	0.014	29.402	0.181

[a] $n = 537$, $R^2 = 0.189$, adjusted $R^2 = 0.180$, $F = 19.785$, $P = 0.000$

[b] Forward selection method, critical $F_{in} = 0.05/F_{out} = 0.1$, other variables considered: sCre, eGFR

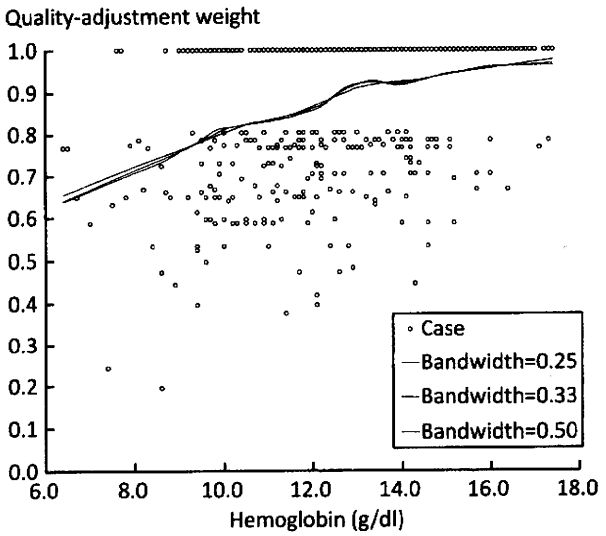

Fig. 2 Smoothing scatterplots of quality-adjustment weight and hemoglobin. Bandwidth is a smoothing parameter that specifies the weighting between the central point and points further away in local linear regressions. The greater the bandwidth, the greater the smoothing. Smoothing curves are stable irrespective of the bandwidth. Inflections in the weight against hemoglobin can be seen at around 10.0 and 13.0 g/dl

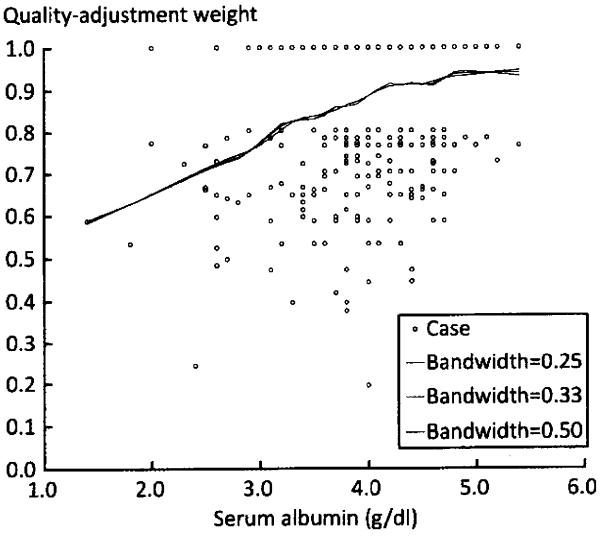

Fig. 3 Smoothing scatterplots of the quality-adjustment weight and serum albumin. Bandwidth is a smoothing parameter that specifies the weighting between the central point and points further away in local linear regressions. The greater the bandwidth, the greater the smoothing. Smoothing curves are stable irrespective of the bandwidth. Inflections in the weight against serum albumin can be seen at around 3.2 and 4.2 g/dl

weight and hemoglobin. This finding corresponds to what Lefebvre et al. [25] reported in an intervention study to improve HRQOL measured by Kidney Disease Questionnaire (KDQ) on the administration of erythropoietin, whereby the maximal gain in HRQL occurred between hemoglobin values of 10 and 12 g/dl. This could be an additional rationale from the viewpoint of HRQOL supporting a target hemoglobin level of 10–12 g/dl for CKD patients as recommended in the CKD Clinical Practice Guideline in Japan of 2007 [26].

The presence of comorbidities such as hypertension, diabetes, or a history of CVD is found to lower quality-adjustment weights, i.e., the HRQOL, of CKD patients, as anticipated. HRQOL deterioration is most severe in the

Table 5 Quality-adjustment weights by CKD stage and complications

	Presence of hypertension				Absence of hypertension			
	n	Mean	95% CI	*P* value	*n*	Mean	95% CI	*P* value
CKD stage								
1	37	0.935	0.896–0.974	0.0000	45	0.942	0.909–0.975	0.0017
2	99	0.909	0.880–0.938		54	0.935	0.901–0.969	
3	122	0.889	0.861–0.917		36	0.862	0.800–0.924	
4	66	0.851	0.807–0.895		6	0.708	0.470–0.946	
5	64	0.782	0.740–0.824		7	0.941	0.825–1.057	
All stages	388	0.874	0.858–0.891	0.0229*	148	0.910	0.885–0.936	
	Presence of diabetes				Absence of diabetes			
	n	Mean	95% CI	*P* value	*n*	Mean	95% CI	*P* value
CKD stage								
1	14	0.867	0.818–0.976	0.0041	69	0.948	0.923–0.973	0.0001
2	35	0.911	0.862–0.960		118	0.920	0.895–0.945	
3	38	0.826	0.767–0.885		120	0.901	0.873–0.929	
4	25	0.843	0.770–0.916		47	0.837	0.780–0.894	
5	34	0.757	0.700–0.814		37	0.836	0.779–0.893	
All stages	146	0.840	0.811–0.869	0.0001*	391	0.901	0.886–0.917	
	Presence of CVD				Absence of CVD			
	n	Mean	95% CI	*P* value	*n*	Mean	95% CI	*P* value
CKD stage								
1	0	–	–		83	0.940	0.915–0.965	0.0000
2	7	0.912	0.793–1.031	0.1731	146	0.918	0.895–0.941	
3	11	0.773	0.633–0.913		147	0.891	0.866–0.916	
4	6	0.816	0.695–0.937		66	0.841	0.793–0.889	
5	14	0.713	0.620–0.806		57	0.819	0.774–0.899	
All stages	38	0.783	0.718–0.848	0.0018*	499	0.892	0.878–0.906	

* *P* value, presence vs. absence of complication at all stages

presence of a history of CVD, and least in the presence of hypertension.

In regard to the presence of diabetes, Sakamaki et al. [27] reported the HRQOL of type 2 diabetes mellitus Japanese patients using EQ-5D. Nephropathy was classified as present with an early-stage urinary albumin/creatinine ratio of >20 mg/g. The quality-adjustment weights of patients with nephropathy were 0.81 (95% CI 0.72–0.90) and 0.87 (0.85–0.89) in those without nephropathy ($P = 0.193$) [27]. In our study, the weights of CKD patients with diabetes were 0.840 (0.811–0.869) and 0.901 (0.886–0.917) in those without diabetes ($P = 0.0001$). We noted slightly higher weights than Sakamaki et al. This may be due to a difference in the age of respondents according to our analysis of weight determinants. The mean age of respondents in our study, 55.2 years old, was younger than that in the report by Sakamaki et al., at 63.3 years old.

This study has several limitations. Firstly, the employment of an established HRQOL measurement tool, EQ-5D [14, 15], improves the reliability of our study and its results. However, its plausibility depends on our sample's representativeness of CKD patients. We made an assumption that outpatients at our department could be considered to comprise a near-representative sample, since a better sampling method such as simple random sampling of CKD patients in the community is not feasible due to the limitations on our epidemiologic knowledge. Therefore, we can neither exclude the possibility of sample selection bias nor implement a bias correction. Further epidemiologic studies are awaited. Secondly, we assessed the effect of the presence or absence of cormobidities (hypertension, diabetes, and CVD) on HRQOL, but not the influence of the severities of these comorbidities on HRQOL.

Finally, the utilization of quality-adjustment weights of CKD patients is a valuable aid when devising an effective

strategy to solve both socioeconomic and public health problems like CKD.

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FROM-J

筑波大学大学院人間総合科学研究科疾患制御医学専攻腎臓病態医学分野

斎藤　知栄，甲斐　平康，山縣　邦弘

KEY WORDS

●慢性腎臓病
●戦略研究
●FROM-J

はじめに

近年，慢性腎臓病(Chronic Kidney Disease；CKD)が注目されるようになった背景には，わが国で1,300万人ものCKD患者が存在すること[1]や，CKDが心血管病のリスクファクターであると証明されたことがある。またわが国で年々増え続ける透析患者数の増加を抑制するためにも，その原因であるCKDの対策が急務である。

CKDは肥満や喫煙，高血圧，糖尿病や脂質異常症と密接な関連があり，生活習慣の是正を行うことでCKDの発症および進展防止につながる可能性は十分にある。そのためにはCKD啓発活動を広く社会や市民，医療従事者に行い，一般住民から医療従事者，行政から医療機関に至るまで相互に連携して行う医療連携が必要となる。こうした連携が普及するためには，全国に汎用できるような診療システムの構築が必要である。

厚生労働省は，2007年度の戦略研究のテーマとして腎臓病を採択し，腎臓病の重症化防止のための方策として，かかりつけ医/非腎臓専門医と腎臓専門医の連携を促進するための診療システムの有用性を検討する研究「腎疾患重症化予防のための戦略研究(Frontier of Renal Outcome Modification in Japan；FROM-J)」が開始された。本稿ではFROM-Jの概略と今後の展望について述べる。

Ⅰ．戦略研究の概要について

戦略研究とは，わが国を支える多くの国民の健康を維持・増進させるために，優先順位の高い慢性疾患・健康障害を標的として，その予防・治療介入および診療の質改善介入など，国民の健康を守る政策に関連するエビデンスを生み出すために実施される大型の臨床介入研究である[2]。これまでに2005年度の「糖尿病予防に関する戦略研究」，

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Chie Saito(講師)
Hirayasu Kai(講師)
Kunihiro Yamagata(教授)

「自殺関連うつ予防に関する戦略研究」に始まり，2006年度の「がん戦略研究」，「エイズ戦略研究」に続き，2007年度に「腎臓病戦略研究」，「感覚器戦略研究」がテーマとして取り上げられてきた。

戦略研究の目標は，「アウトカム研究」あるいは「診療直結研究」である。

「アウトカム研究」とは，実際の医療現場で提供される検査法や治療法などの医療サービスのばらつきと患者アウトカムとの関連，影響を分析する研究であり，発症率・重症化率・死亡率などとともに，QOLや患者満足度，入院・病欠・医療資源活用，費用対効果分析などの指標を取り入れることが特徴である。「アウトカム研究」の意義には，「研究成果が，診療上の意思決定をよりよく行うためのエビデンスとして，診療現場に還元される」こと，「研究成果が，診療現場での臨床家の行動を変える」こと，「研究成果が，医療政策や制度にインパクトを与える」こと，「研究成果により患者や国民の健康アウトカムが改善する」こと，が含まれる。

「診療直結研究」は，臨床医の診療上の疑問を一定の仮説に構造化して検証する研究であり，前述のアウトカム研究とも重複しうる。そのテーマには，「診断法の選択と有効性に関する研究」と，「診療の質測定と改善に関する研究」がある。特に後者は，質の高いエビデンスをできるだけ速やかに臨床の場に普及させる方策を講じ，「エビデンス-診療ギャップ」を解消する方策の1つである。

Ⅱ．研究課題と成果目標

腎臓病が戦略研究のテーマの1つとして採択された背景には，前述のようにCKD対策が急務であることが大きい。今回の腎臓病戦略研究においては，かかりつけ医/非腎臓専門医と腎臓専門医の連携を促進することが重要課題であると厚生労働省より提唱された。かかりつけ医/非腎臓専門医におけるCKDの早期発見および血圧・血糖管理や食事療法の厳格な管理や，腎臓専門医との連携を密接に行うことで，CKDの診療に早期から取り組み進展防止を図ることを目的の1つとしている。そこで本研究の課題名は「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ための診療システムの有用性を検討する研究」と定められ，主要評価項目と副次評価項目が設定された。

主要評価項目は①受診継続率，②かかりつけ医/非腎臓専門医と腎臓専門医の連携達成，③CKDのステージ進行率の3つであり，副次評価項目としては①CKD診療目標の実施率，②血圧の管理目標達成率，③尿蛋白50％減少達成率，④血清クレアチニン値の2倍化到達数，eGFR50%低下到達，⑤新規透析導入患者数の年次推移，⑥心血管系イベントの発生率があげられている。

成果目標はCKD診療ガイドの遵守率，達成目標の達成度を上げることとされ，その結果として5年後の透析導入患者を5年後に予測される導入数の15％減少になることが期待されている。

Ⅲ．研究デザインと体制

FROM-Jの研究実施団体は財団法人日本腎臓財団(酒井　紀理事長)が選定され，研究リーダーは公募により，筑波大学大学院人間総合科学研究科疾患制御医学専攻腎臓病態医学分野 山縣邦弘が選定された。

本研究においては，かかりつけ医と腎臓専門医との連携が評価項目の1つとなっているため，個々の患者の評価を行うだけではなく，地域すなわち地区医師会単位での連携も評価する必要がある。このため研究デザインは地区医師会をクラスターとして，介入方法をクラスターごとに割り付けるクラスターランダム化比較研究が提案された。地区医師会の選定にあたっては，新規透析導入者数の増加率により全国を4つのブロックに分割し，公募により全国から15の幹事施設が選定され，幹事施設により全国で49の参加地区医師会が選定された。

本研究の実施にあたっては日本医師会の協力を得て，都道府県医師会を介して，参加地区医師会へかかりつけ医の参加登録の呼びかけと継続的な研究への協力要請が行われた。またかかりつけ医が円滑に病診連携を達成できるように，腎臓専門医に紹介を広く受け入れる態勢を整えるため，日本腎臓学会より腎臓専門医へ研究への参加協力が要請された。日本栄養士会においては，全国都道府県の病院栄養士協議会とともに，各地区の栄養ケアステーションへ研究への協力を要請し，FROM-Jの生活・食事指導を担う管理栄養士の人選および手配が行われた。このように各方面の強力なサポートの存在が本研究を支えている。

Ⅳ．対象患者と研究期間

FROM-Jで対象となるCKD患者の条件は，①年齢が40歳以上75歳未満，②CKDステージ1，2および4，5の

表．CKDの診療目標

CKDステージ	生活習慣改善	食事指導	血圧管理	血糖管理	脂質管理	貧血管理
ステージ1	禁煙 BMI＜25kg/m^2	高血圧があれば 減塩6.0g/日未満	130/80mmHg未満	HbA_{1c} 6.5％未満	LDL-cho 120mg/dL未満	腎性貧血以外の 原因検索
ステージ2	禁煙 BMI＜25kg/m^2	高血圧があれば 減塩6.0g/日未満	130/80mmHg未満	HbA_{1c} 6.5％未満	LDL-cho 120mg/dL未満	腎性貧血以外の 原因検索
ステージ3	禁煙 BMI＜25kg/m^2	減塩6.0g/日未満 蛋白質制限 0.6～0.8g/kg体重/日	130/80mmHg未満	HbA_{1c} 6.5％未満	LDL-cho 120mg/dL未満	Hb 10g/dL以上 12g/dL未満
ステージ4	禁煙 BMI＜25kg/m^2	減塩6.0g/日未満 蛋白質制限 0.6～0.8g/kg体重/日 高K血症あればK制限	130/80mmHg未満	HbA_{1c} 6.5％未満	LDL-cho 120mg/dL未満	Hb 10g/dL以上 12g/dL未満
ステージ5	禁煙 BMI＜25kg/m^2	減塩6.0g/日未満 蛋白質制限 0.6～0.8g/kg体重/日 高K血症あればK制限	130/80mmHg未満	HbA_{1c} 6.5％未満	LDL-cho 120mg/dL未満	Hb 10g/dL以上 12g/dL未満
備考			蛋白尿1.0g/gCr以上は 125/75mmHg未満			

患者，③CKDステージ3の場合は，尿蛋白を有し，糖尿病あるいは高血圧を有していること，と設定した。CKDステージ3の登録条件の理由は，最も人数の多いCKDステージ3の患者のなかで，腎機能悪化の危険性の高い患者を対象とするためである[3)-5)]。

目標症例数の設定にあたり，成果目標である5年後の新規透析導入数の予測数より15％減少をもとに，介入によりGFRの悪化速度を15％改善させるために必要な症例数の設定を，日本腎臓学会CKD対策委員会疫学ワーキンググループのデータ[6)]および，糖尿病性腎症のGFR低下速度のデータ[7)]より算出したところ，10％の脱落を加味し，全体で2,264例の登録数が必要であることがわかった。そこで今回の目標症例数を2,500例と設定した。研究を開始するにあたり，491名のかかりつけ医，2,494名の参加者の登録連絡があり，2,413名が最終的に登録された。

V．介入方法

FROM-Jでは，CKD診療ガイドに準拠して診療にあたる介入A群と，介入A群の内容に加え，参加者への受診促進支援，かかりつけ医への目標達成度の外部評価を定期的に行い，管理栄養士による生活・食事指導を行う介入B群の2つを設定し，その効果を比較検討する。

2007年に発刊された「CKD診療ガイド」[2)]には，CKDステージごとに生活習慣，食事内容，血圧，血糖，脂質などの診療目標(**表**)や，腎臓専門医への紹介のタイミングが記載されており，本研究では両群において診療目標や紹介基準の達成率と遵守率を評価する。腎臓専門医への紹介の基準はCKD診療ガイドに則り，①尿蛋白2＋以上または尿蛋白が0.5g/gCr以上，②尿蛋白1＋以上かつ尿潜血1＋以上，③推算GFR＜50mL/min/1.73m^2，④その他，医師が必要と認めた場合，の4項目とした。

生活・食事指導では，各地域の栄養ケアステーションに所属する管理栄養士が3ヵ月に1回，かかりつけ医の医療機関内で1回当たり約30分の個別指導を行う。指導内容については，全国の介入B群で均質な指導を行うためのマニュアルや指導講習会の開催を行い，すべての参加管理栄養士に受講を義務付けている。

参加者登録終了後に地区医師会ごとに介入A群，介入B群の割付が行われ，介入A群の参加者数は1,211名，介入B群は参加者数1,202名となった。各介入群の参加者の属性を**図1**，**図2**，**図3**に示す。2008年10月20日よりそれぞれの介入を開始，2012年3月まで継続する予定である(**図4**)。

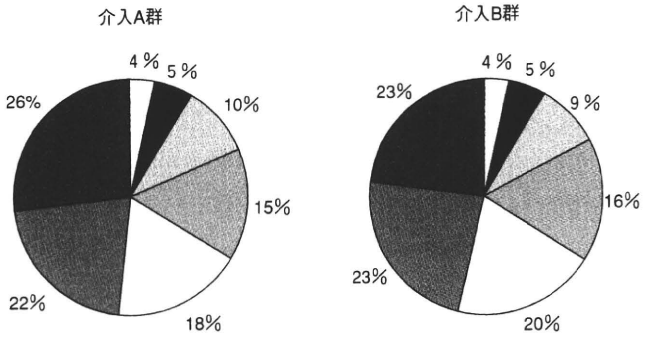

図1．参加者年齢別割合
□：40～44歳，■：45～49歳，▨：50～54歳，▩：55～59歳，
□：60～64歳，▩：65～69歳，■：70～74歳

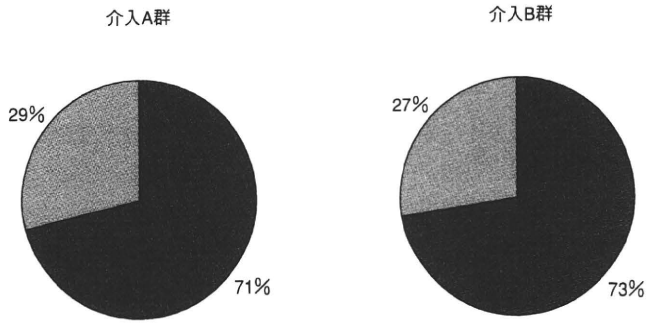

図2．参加者性別割合
■：男，▩：女

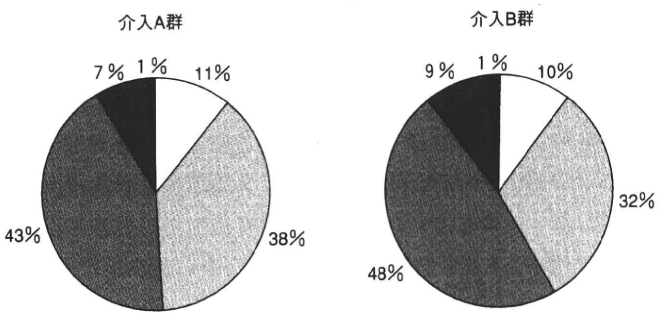

図3．参加者CKDステージ別割合
□：ステージ1，▨：ステージ2，▩：ステージ3，
■：ステージ4，■：ステージ5

Ⅵ．今後の展望

FROM-Jにより，CKDの進行を予防し，透析導入患者を1人でも多く減らすことが主たる目標である。そのための手法として，FROM-Jにおいてかかりつけ医と腎臓専門医との医療連携およびかかりつけ医における管理栄養士の生活・食事指導の体系などCKDの診療連携システムを確立する意義は大きい。研究期間中の医療連携や生活･食事指導の実践と継続については，各地域で定期的に会合を開き検証している。

今後は，かかりつけ医におけるCKD診療をサポートする診療支援のシステムの有用性が本研究により証明されることで，診療システムが全国で普及し，CKD患者の予後が改善されることが期待される。

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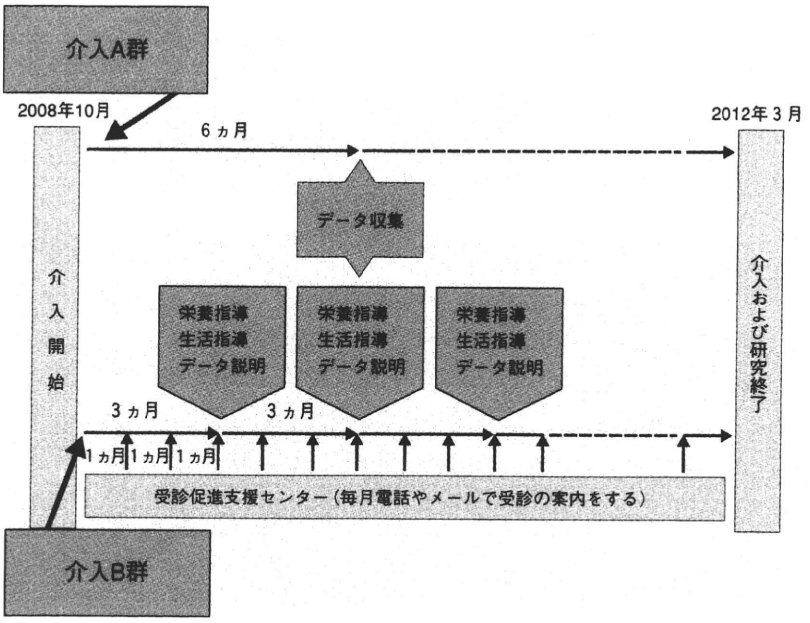

図4．研究のスケジュール

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