Original Paper

Depression and Quality of Life in Relation to Decreased Glomerular Filtration Rate Among Adults with Hypertension in Rural Northeast China

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Abstract
Background/Aims: We aim to investigate the extent to which depression and quality of life might be associated with decreased glomerular filtration rate (GFR) in a large hypertensive population in rural Northeast China. ***Methods:*** A total of 5566 hypertensive participants aged 35 years and older were screened with a stratified cluster multistage sampling scheme in rural areas of Liaoning Province during 2012-2013. Decreased GFR was defined as estimated GFR <60 ml/min/1.73 m^2. ***Results:*** The overall prevalence of decreased GFR was 3.2%. In the multivariable regression model, participants with moderate or greater depression had a greater risk for having a decreased GFR (OR: 1.739, 95%CI: 1.004 to 3.014) after full adjustment. Every 1-point increase of all the domains in WHOQOL-BREF, except for physical and environment domains, was significantly related to a lower risk for decreased GFR adjusting for age, gender and race. However, after fully adjustment, only social relations remained significant (OR: 0.899, 95%CI: 0.820 to 0.985). Increasing in total scores of WHOQOL-BREF was a protective factor against decreased GFR after fully adjustment. ***Conclusion:*** We found that moderate or greater depression and lower quality of life were associated with higher risks for developing decreased GFR.

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Introduction

The increasing prevalence of chronic kidney disease (CKD) has become a worldwide public health problem [1]. It has been demonstrated that even minor degrees of renal dysfunction were associated with an enhanced cardiovascular (CV) risk [2-3]. Among hypertensive patients, CKD is much more prevalent [4-6] and is a risk factor for CV events and all-cause mortality [7-9]. Guidelines for the management of hypertension have recognized the relevance of albuminuria and decreased estimated glomerular filtration rate (eGFR) on CV prognosis in hypertensive patients [10, 11]. Considering the large base of hypertensive patients, more attention should be paid to CKD in this population.

In recent years, the Quality of life (QoL) and depression status in patients with CKD have received growing interest. It is evidenced that depression was prevalent and QoL was lower among CKD patients [12-16]. Several studies linked depression or low QoL to increased mortality risk in CKD patients [17-19], indicating the importance and potential effects of depression and QoL during CKD.

Although the treatment for the patients who have already developed CKD is crucial, it is more practical and cost-effective to prevent CKD before it happens, especially in hypertensive patients. To achieve the prevention, comprehensive identification of its risk factors becomes first step to take. To date, there is little information on depression or QoL as risk factors for CKD. Given the evidence on depression and QoL in relation to CKD, we hypothesized that depression and QoL were independent predictors for developing CKD. Therefore, we performed this study to examine the extent to which depression and QoL might be associated with decreased GFR in a large hypertensive population in rural Northeast China.

Subjects and Methods

Study Population

Liaoning Province is located in Northeast China. From January 2012 to August 2013, a representative sample aged ≥ 35 years was selected to describe the prevalence, incidence and natural history of cardiovascular risk factors in rural areas of Liaoning Province. The study adopted a multi-stage, stratified randomly cluster-sampling scheme. In the first stage, 3 counties (Dawa, Zhangwu, and Liaoyang County) were selected from the eastern, southern, and Northern region of Liaoning province. In the second stage, one town was randomly selected from each county (a total of 3 towns). In the third stage, 8-10 rural villages from each town were randomly selected (a total of 26 rural villages). Participants with pregnancy, malignant tumor and mental disorder were excluded from the present study. All the eligible permanent residents aged ≥ 35 years from each village were invited to attend the study, with a response rate of 85.3%. The study was approved by the Ethics Committee of China Medical University (Shenyang, China). All procedures were performed in accordance with the ethical standards. Written consent was obtained in all participants after they had been informed of the objectives, benefits, medical items and confidentiality agreement of personal information. If the participants were illiterate, we obtained the written informed consents from their proxies. In this report, a total of 6077 patients with hypertension were selected. Only participants with a complete set of data regarding the variables analyzed in the present study were included, making a final sample size of 5566 (2730 males and 2836 females).

Depressive Symptoms

Depressive symptoms were assessed using the Patient Health Questionnaire (PHQ-9), which is a 9-item screening instrument with high reliability and validity in the primary care population [20, 21]. Participants were asked how often, over the past 2 weeks, they had been bothered by each of the depressive symptoms with scores ranging from 0 to 27. The severity of depressive disorder is considered mild for scores ranging from 5 to 10, moderate for scores of 10 to 14, moderately severe for scores of 15–19 and severe for scores of 20–27. A PHQ-9 score≥10 has been recommended as the cut-off score for detecting major depressive disorders [20, 22].

Quality of Life

The quality of life was measured with the World Health Organization Quality of Life Brief Scale (WHOQOL-BREF) [23] which is a self-report inventory with 26 original items. The items fall into four domains: the physical health (7 items), the psychological health (6 items), the social relationships (3 items) and the environment (8 items), together with 2 items measuring overall QoL and general health [24]. The scale has demonstrated good internal consistency with Cronbach's alpha ranging from 0.67-0.81 for each domain. Each item is answered on a 5-point response scale, and the range of scores is form 4 to 20 after calculation, with higher scores indicating better QoL.

Glomerular Filtration Rate Assessment

Fasting blood samples were collected in the morning after at least 12 h of fasting for all participants. Blood samples were obtained from an antecubital vein into vacutainer tubes containing EDTA. Blood chemical analyses were performed at a central, certified laboratory. Serum creatinine (SCr) was measured enzymatically on an autoanalyzer. GFR was estimated using the equation originating from the CKD Epidemiology Collaboration (CKD-EPI) equation [25], which is more appropriate than the Modification of Diet in Renal Disease (MDRD) Study group equation [26]. Decreased GFR was defined as estimated GFR (eGFR) <60 ml/min/1.73 m^2.

Covariate Measurements

Information on covariates, such as demographic characteristics, lifestyle risk factors, dietary habits, family income and medical history of hypertension, were collected during a single clinic visit by cardiologists and trained nurses using a standard questionnaire by face-to-face interview. Before the survey was performed, we invited all eligible investigators to attend the organized training. The training contents included the purpose of this study, how to administer the questionnaire, the standard method of measurement, the importance of standardization, and the study procedures. A strict test was evaluated after this training, only those who scored perfectly on the test could become investigators. During data collection, our inspectors had further instructions and support.

According to American Heart Association protocol, blood pressure was measured three times at 2-min intervals after at least 5 min of rest using a standardized automatic electronic sphygmomanometer (HEM-907; Omron), which had already been validated according to the British Hypertension Society protocol [27]. The participants were advised to avoid caffeinated beverages and exercise for at least 30 min before the measurement. During the measurement, the participants were seated with the arm supported at the level of the heart. The mean of three BP measures was calculated and used in all analyses.

Weight and height were measured to the nearest 0.1 kg and 0.1 cm respectively with the participants in light weight clothing and without shoes. Waist circumference (WC) was measured at the umbilicus using a non-elastic tape (to the nearest 0.1 cm), with the participants standing at the end of normal expiration. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters.

Fasting plasma glucose (FPG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), uric acid, hemoglobin and other routine blood biochemical indexes were analyzed enzymatically on an autoanalyzer. All laboratory equipment was calibrated and blinded duplicate samples were used.

Physical activity included occupational and leisure-time physical activity. A detailed description of the methods has been presented elsewhere [28]. Occupational and leisure-time physical activity were merged and regrouped into low, moderate and high levels. Educational level was divided into primary school or below, middle school and high school or above. Family income was classified as ≤5 000, 5 000-20 000 and >20 000 CNY/year. Self-reported sleep duration (including nocturnal and nap duration) was obtained from the questionnaire.

The dietary pattern was assessed using recall of foods eaten in the previous year. The questionnaire included questions on the average consumption of several food items per week. The reported consumption was quantified approximately in terms of grams per week. A special diet score (vegetable consumption score plus meat consumption score) was calculated for each participant (range 0-6). Higher values of the diet score indicate higher meat consumption and lower vegetable consumption and greater adherence to a

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Table 1. Baseline characteristics of study population

| Variables | All (n=5566) | Estimated GFR (ml/min/1.73m²) | | P-value |
		≥60 (n=5388)	<60 (n=178)	
Age (year)	57 ± 10	57 ± 10	69 ± 9	<0.001
Male gender (%)	2730 (49.0)	2664 (49.4)	66 (37.1)	0.001
Race of Han (%)	5265 (94.6)	5090 (94.5)	175 (98.3)	0.026
Spouse (live, %)	5027 (90.3)	4892 (90.8)	135 (75.8)	<0.001
Current smoking status (%)	1953 (35.1)	1906 (35.4)	47 (26.4)	0.014
Current drinking status (%)	1369 (24.6)	1357 (25.2)	12 (6.7)	<0.001
Education (%)				<0.001
Primary school or below	3087 (55.5)	2950 (54.8)	137 (77.0)	
Middle school	1987 (35.7)	1953 (36.2)	34 (19.1)	
High school or above	492 (8.8)	485 (9.0)	7 (3.9)	
Physical activity (%)				<0.001
Low	1862 (33.5)	1744 (32.4)	118 (66.3)	
Moderate	3376 (60.7)	3322 (61.7)	54 (30.3)	
High	328 (5.9)	322 (6.0)	6 (3.4)	
Family income (CNY/year, %)				<0.001
≤5000	847 (15.2)	796 (14.8)	51 (28.7)	
5000-20000	3123 (56.1)	3039 (56.4)	84 (47.2)	
>20000	1596 (28.7)	1553 (28.8)	43 (24.2)	
Diet score	2.3 ± 1.1	2.3 ± 1.1	1.9 ± 1.0	<0.001
Sleep duration (h/d)	7.2 ± 1.8	7.3 ± 1.8	6.6 ± 1.9	<0.001
SBP (mmHg)	158.7 ± 19.6	158.5 ± 19.5	165.1 ± 22.2	<0.001
DBP(mmHg)	88.9 ± 11.2	88.9 ± 11.0	88.1 ± 14.9	0.152
BMI(kg/m²)	25.6 ± 3.7	25.6 ± 3.7	25.4 ± 3.7	0.339
WC (cm)	84.9 ± 9.7	84.9 ± 9.7	85.9 ± 10.4	0.232
TC (mmol/L)	5.4 ± 1.1	5.4 ± 1.1	5.9 ± 1.6	<0.001
TG (mmol/L)	1.8 ± 1.6	1.8 ± 1.6	2.2 ± 1.7	<0.001
LDL-C (mmol/L)	3.1 ± 0.9	3.1 ± 0.9	3.3 ± 1.1	0.005
HDL-C (mmol/L)	1.4 ± 0.4	1.4 ± 0.4	1.3 ± 0.4	<0.001
FPG (mmol/L)	6.2 ± 1.9	6.1 ± 1.9	6.5 ± 2.2	0.087
Uric acid (umol/L)	302.2 ± 87.8	298.7 ± 84.8	406.2 ± 110.9	<0.001
Hemoglobin (g/L)	140.8 ± 18.2	141.1 ± 18.0	130.9 ± 20.4	<0.001
Estimated GFR (ml/min/1.73m²)	90.1 ± 15.4	91.5 ± 13.4	48.5 ± 12.4	<0.001
Antihypertensive medication (%)	1419 (25.5)	1333 (24.7)	86 (48.3)	<0.001
History of heart disease (%)	1045 (18.8)	971 (18.0)	74 (41.6)	<0.001
History of stroke (%)	738 (13.3)	689 (12.8)	49 (27.5)	<0.001
Moderate or greater Depression (%)	375 (6.7)	340 (6.3)	35 (19.7)	<0.001

Data are expressed as the mean ± SD or as n (%).
Abbreviations: GFR, glomerular filtration rate; CNY, China Yuan (1CNY=0.161 USD); SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; WC, waist circumference; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose.

Westernized diet, while lower values indicate adherence to the Chinese-diet. Similar methods for calculating diet score could be found in ATTICA study [29].

Statistical Analysis

Descriptive statistics were calculated for all the variables, including continuous variables (reported as mean values and standard deviations) and categorical variables (reported as numbers and percentages). Differences among categories were evaluated using Student's t-test, ANOVA, non-parametric test or the χ^2-test as appropriate. Multivariate logistic regression analyses were used to identify independent associations between depression or QoL and decreased GFR in different models with odds ratios (ORs) and corresponding 95% confidence intervals (CIs) calculated. Model 1 was adjusted for age, gender and race; model 2 was

Table 2. The mean scores of PHQ-9 and WHOQOL-BREF based on estimated GFR category

	All (n=5566)	Estimated GFR (ml/min/1.73m²)				P-value
		≥90 (n=3019)	60-90 (n=2369)	45-60 (n=134)	<45 (n=44)	
PHQ-9						
All participants	3.17 ± 3.86	2.86 ± 3.64	3.42 ± 3.95	4.74±5.05	6.14 ± 5.71	<0.001
No depression	1.32 ± 1.41	1.27 ± 1.41	1.40 ± 1.42	1.29 ± 1.42	1.10 ± 1.52	0.009
Mild depression	6.56 ± 1.37	6.49 ± 1.34	6.62 ± 1.39	6.42 ± 1.43	7.21 ± 1.48	0.141
Moderate or greater depression	13.63 ± 3.76	13.78 ± 4.10	13.47 ± 3.53	13.40 ± 3.49	14.70 ± 2.87	0.47
WHOQOL-BREF						
Overall quality of life	3.26 ± 0.68	3.29 ± 0.68	3.23 ± 0.68	3.11 ± 0.60	2.89 ± 0.66	<0.001
General health	3.30 ± 0.86	3.37 ± 0.84	3.26 ± 0.87	2.96 ± 0.90	2.50 ± 0.93	<0.001
Physical health	12.69 ± 1.58	12.91 ± 1.53	12.49 ± 1.59	12.00 ± 1.80	11.51 ± 1.49	<0.001
Psychological health	12.71 ± 1.86	12.93 ± 1.76	12.52 ± 1.93	11.80 ± 1.93	11.29 ± 1.67	<0.001
Social relationships	14.49 ± 2.09	14.84 ± 1.94	14.15 ± 2.17	13.13 ± 2.29	12.94 ± 1.81	<0.001
Environment	13.44 ± 2.08	13.47 ± 2.02	13.45 ± 2.14	12.92 ± 2.27	12.30 ± 1.97	<0.001
Total scores	59.90 ±7.00	60.80 ± 6.64	59.09 ± 7.19	55.92 ± 7.55	53.42 ± 6.45	<0.001

Data are expressed as the mean ± SD.
Abbreviations: GFR, glomerular filtration rate; PHQ, Patient Health Questionnaire; WHOQOL-BREF, the World Health Organization Quality of Life Brief Scale.

adjusted for factors in model 1 plus education level, family income, marital status, dietscore, sleep duration, current smoking and drinking status and physical activity; and model 3 was adjusted further for BMI, WC, systolic blood pressre (SBP), diastolic blood pressre (DBP), TC, TG, LDL-C, HDL-C, FPG, uric acid, hemoglobin, antihypertensive medication, history of heart disease and stroke. Depression status and general QoL were adjusted when analyzing each other in all three models. All the statistical analyses were performed using SPSS version 17.0 software, and P values less than 0.05 were considered to be statistically significant.

Fig. 1. Total score of WHOQOL-BREF by quartiles of PHQ-9 score. Error bars represent standard deviation. PHQ-9: Patient Health Questionnaire-9; WHOQOL-BREF: World Health Organization Quality of Life Brief Scale.

Results

A total of 5566 participants (2730 males and 2836 females) were included in the present study with a mean age of 57 ± 10 years. The overall prevalence of decreased GFR (eGFR<60 ml/min/1.73 m²) was 3.2%. There were 375 participants presenting moderate or greater depression. The ethnic composition of the population was predominantly Han Chinese (94.6%).

Table 1 presents baseline characteristics of the studied population. Participants with eGFR<60 ml/min/1.73 m² were more likely to be female, older and Han ethnic compared to those with eGFR≥60 ml/min/1.73 m² (all P<0.05). A lower proportion of current smoking and drinking status was observed in the participants with eGFR<60 ml/min/1.73 m². The mean levels of SBP, TC, TG, LDL-C, FPG and uric acid were significantly higher in the group of decreased GFR. More participants in the group of eGFR<60 ml/min/1.73 m² had a history of heart disease or stroke and moderate or greater depression.

Table 2 describes the scores of PHQ-9 and WHOQOL-BREF according to eGFR category. The mean scores of PHQ-9 and total WHOQOL-BREF were 3.2 ± 3.9 and 59.9 ± 7.0, respectively. As eGFR decreased, scores of PHQ-9 increased and scores for total and every domain of WHOQOL-BREF decreased significantly. Figure 1 shows the total WHOQOL-BREF scores
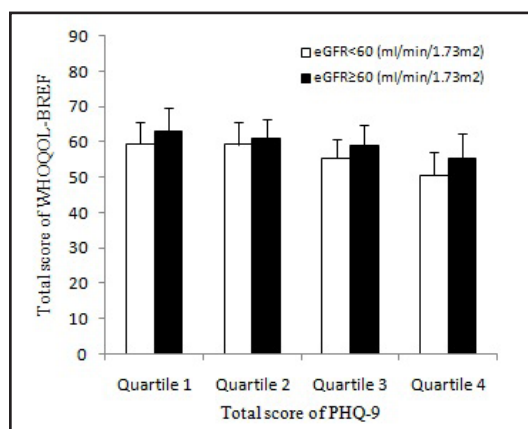
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Table 3. Multivariable logistic regression analyses for associations between depression or quality of life and decreased glomerular filtration rate

	Model 1			Model 2			Model 3		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Moderate or greater depression (yes/no)	1.836	1.175-2.867	0.008	1.666	1.063-2.611	0.026	1.739	1.004-3.014	0.048
Quality of life (every 1-point increase)									
Overall quality of life	0.755	0.590-0.965	0.025	0.784	0.609-1.011	0.061	0.789	0.580-1.072	0.13
General health	0.586	0.486-0.707	<0.001	0.634	0.524-0.768	<0.001	0.817	0.646-1.034	0.092
Physical health	0.912	0.823-1.011	0.08	0.952	0.857-1.058	0.361	0.979	0.862-1.112	0.746
Psychological health	0.853	0.781-0.931	<0.001	0.863	0.789-0.944	0.001	0.904	0.813-1.005	0.063
Social relationships	0.866	0.804-0.933	<0.001	0.877	0.812-0.948	0.001	0.899	0.820-0.985	0.023
Environment	0.947	0.874-1.025	0.179	0.948	0.873-1.030	0.209	0.943	0.856-1.040	0.24
Total scores	0.952	0.929-0.975	<0.001	0.957	0.933-0.982	0.001	0.967	0.938-0.998	0.034

Model 1: adjusted for age, gender and race.

Model 2: adjusted for factors in model 1 and education level, family income, marital status, dietscore, sleep duration, current smoking and drinking status, and physical activity.

Model 3: adjusted for factors in model 2 and body mass index, waist circumference, systolic blood pressure, diastolic blood pressure, total cholesterol, triglyceride, low-densitylipoprotein cholesterol, high-density lipoprotein cholesterol, fasting plasma glucose, uric acid, hemoglobin, antihypertensive medication, and history of heart disease and stroke.

In the analysis for depression, general quality of life was adjusted and in the analysis for quality of life, depression status was adjusted.

Moderate or greater depression defined as PHQ-9 score $\geq$10.

Abbreviations: OR, odds ratio; 95% CI, 95% confidence interval.

according to quartiles of PHQ-9 scores. The scores of QoL were significantly reduced in the upper quartiles of depression scores in both groups of eGFR<60 and $\geq$60ml/min/1.73 m² (both P<0.001).

Figure 2 presents the prevalence of decreased GFR according to quartiles of PHQ-9 and WHOQOL-BREF scores. Upper quartiles of PHQ-9 had higher prevalence of decreased GFR (P<0.001). A decreasing trend of the prevalence was observed as the scores for QoL increased (P<0.001).
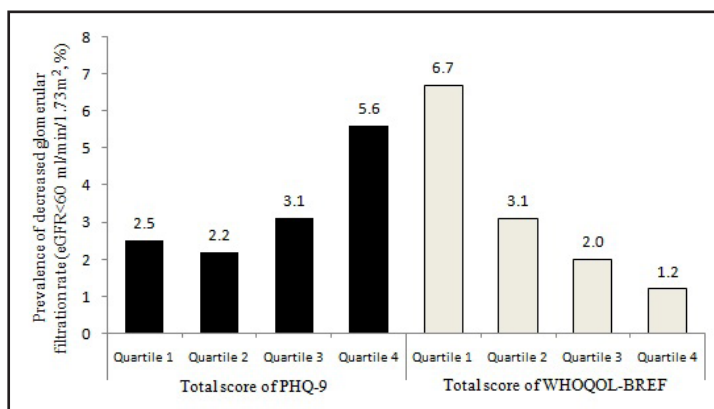

Fig. 2. Prevalence of decreased glomerular filtration rate (eGFR<60 ml/min/1.73m²) according to quartiles of PHQ-9 and WHOQOL-BREF scores. eGFR: estimated glomerular filtration rate; PHQ-9: Patient Health Questionnaire-9; WHOQOL-BREF: World Health Organization Quality of Life Brief Scale.

Table 3 presents multivariable logistic regression analyses on the associations between depression and QoL scores and decreased GFR. Moderate or greater depression (PHQ-9$\geq$10) was associated with a higher risk of decreased GFR (eGFR<60 ml/min/1.73 m²) in all three models. After adjusted for age, gender, race, lifestyle factors, clinical correlates and general quality of life, participants with moderate or greater depression had a 1.7-fold risk for having a decreased GFR (OR: 1.739, 95%CI: 1.004 to 3.014). Every 1-point increase of all the elements in WHOQOL-BREF, except for physical and environment domains, was significantly related to a lower risk for decreased GFR in model 1. However, after fully adjustment, only social relations remained significant (OR: 0.899, 95%CI: 0.820 to 0.985). Increasing in total scores of WHOQOL-BREF was a protective factor against decreased GFR in all three models.

Discussion

To our knowledge, this is the first evaluation of the relationship between depressive symptoms and QoL and kidney disease in a large Chinese hypertensive population. We found that moderate or greater depression increased approximately 1.7-fold risk of developing decreased GFR and higher scores in social relationships and total scores of QoL were significantly associated with lower risks of decreased GFR after fully adjusted for confounders, adding evidence for primary prevention of CKD in hypertensive patients.

Several studies investigated the prevalence of CKD in non-Asian hypertensive populations, with rates for decreased GFR (eGFR<60 ml/min/1.73 m^2) raging from around 10%-30% [5, 30]. The prevalence of decreased GFR we found in Chinese hypertensives was twice as that in general Chinese population [31], though lower than that found in western populations. It is suggested that a much higher number of individuals are at risk of developing CKD when the number of patients with hypertension is taken into account [32], highlighting the significance of preventing CKD in hypertensive population. However, risk factors for developing CKD in hypertensives evaluated by previous studies were confined to traditional correlates, such as blood pressure and lipid disorder.

Although the association between depression and clinical outcomes in patients with CKD were well documented [18, 33], studies focusing on the role of depression as a factor for primary prevention of CKD were rare, especially in hypertensive group. In our study, we found that moderate or greater depression increased the risk for developing decreased GFR in hypertensive patients. Since depression status and QoL had influences on each other, we adjusted one of them when analyzing the other. The mechanism under the positive association between depression and decreased GFR after fully adjustment was unknown. The low threshold to stress, pain and physical activity caused by disturbance of the serotonergic and noradrenergic pathway in depression might serve as one part of the puzzle [34]. In addition, poverty was one of the most significant correlates for major depressive disorder [35, 36], and higher prevalence of reduced eGFR was observed in sites with low economic development [31]. Therefore, it is reasonable to assume that family income might play a role in the correlation between depression and decreased GFR. The effect of family income have been investigated in many previous studies conducted in CKD patients [37, 38], but limited information for the primary prevention of CKD is available. However, in the present study, we failed to find a positive role of family income in the association between depression and decreased GFR after further analysis by stratification of the variable. More studies are expected to investigate this issue. It was also explained that depression was correlated with unhealthy behaviors, such as smoking and drinking, but we had them adjusted in the analyses.

We chose the WHOQOL-BREF to evaluate QoL in the present study because it includes physical, psychological, social relationships and environment domains, the last two of which are more special than other measures of QoL, such Short Form Health Survey (FS-36). Social relationships and environment are frequently affected by policies and cultures, thus WHOQOL-BREF may provide better perspectives of living status in which policies and cultures are taken into consideration. Our study found that increasing in total scores of QoL was associated with a lower risk for decreased GFR, indicating that maintaining or improving QoL should be an important consideration in preventing CKD among hypertensives. Evidence suggested that social support had effects on clinical outcomes in various chronic diseases [39]. In the present study, we found that social relationship was a protective factor for having decreased GFR. The potential mechanism was unexplained. Further researches are needed to explore the mechanisms underlying.

Some limitations should be considered in light of these results. First, the sample in the present study was drawn from a single geographic area, thus data are not representative of population throughout China. Second, urinary albumin was not measured in our study and there might be other unmeasured confounding variables, which could compromise our

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results. In addition, our results were based on a cross-sectional design, thus no cause-and-effect relationships could be established.

Conclusion

In this large Chinese hypertensive population, a population not previously evaluated in the literature and carries a high burden of kidney disease, we found that moderate or greater depression and lower quality of life, especially the aspect of social relationship, were associated with higher risks for developing decreased GFR after adjusting potential confounders. During daily management of hypertension, psychological status and quality of life should be considered to prevent CKD in the hypertensive population.

Disclosure Statement

None

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