Published in final edited form as:
Nephron Clin Pract. 2006 ; 103(1): c1–c7. doi:10.1159/000090112.

Depression, Stress, and Quality of Life in Persons with Chronic Kidney Disease: The Heart and Soul Study

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Abstract

Background—The effect of mild chronic kidney disease (CKD) on depression, stress, quality of life (QOL), and health status is not well understood. We compared these outcomes in subjects with and without CKD.

Methods—We performed a cross-sectional study of 967 outpatients enrolled in the Heart and Soul Study. CKD was defined as a measured creatinine clearance <60 ml/min. Outcome measures included depressive symptoms measured using the Patient Health Questionnaire (PHQ), stress measured using the Perceived Stress Scale (PSS), and QOL and overall health rated as excellent, very good, good, fair, or poor.

Results—The prevalence of depressive symptoms (17 vs. 19%, p = 0.4) or perceived stress (11 vs. 16%, p = 0.09) did not vary significantly by CKD. The prevalence of fair or poor QOL was not significantly different in subjects with CKD, compared with those without CKD (24 vs. 23%, p = 0.65). Age-adjusted analyses revealed a significant association of CKD with QOL (p = 0.003), however, this association no longer reached statistical significance after adjustment for confounders (p = 0.06). Subjects with CKD were more likely to report poor or fair overall health than subjects without CKD (42 vs. 34%, p = 0.03). After multivariate adjustment, CKD remained significantly associated with worse overall health (OR = 1.65, 95% CI 1.21–2.24, p = 0.001), and modestly associated with QOL (OR = 1.31, 95% CI 0.99–1.75, p = 0.06), but had no association with depression (p = 0.48) or stress (p = 0.24).

Conclusion—In this study of persons with coronary artery disease, subjects with CKD had reduced overall health and modestly reduced QOL; however, mental health was similar in those with and without CKD. These findings suggest that self-assessed overall health may decline at earlier stages of renal dysfunction than mental health outcomes or QOL.

Keywords

Chronic kidney disease; Kidney disease, depression; Kidney disease, stress; Kidney disease, quality of life

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Introduction

Advanced kidney disease is associated with poor quality of life (QOL), due to the effects of uremia on physical and mental health. End-stage renal disease (ESRD) leads to loss in mobility, exercise capacity, and self-assessed physical function, and is further associated with reduced ability to work and function in daily life [1–4]. In addition, many studies have found that a significant proportion of patients with ESRD suffer from depression [5–9]. The Modification of Diet in Renal Disease (MDRD) Study, a cohort of patients with moderate to severe chronic kidney disease (CKD), found decreased renal function to be associated with psychological distress and impaired health-related QOL [10].

A few studies have examined the physical component of QOL in subjects with mild to moderate renal dysfunction. In a prior analysis from the Heart and Soul Study, we found CKD was associated with self-assessed physical limitation [11]. Investigators from the Cardiovascular Health Study found elderly persons with CKD to have an increased prevalence of frailty [12]. In the African-American Study of Kidney Disease and Hypertension (AASK) Trial, the mean physical health score of the cohort was observed to be lower than in the general US population [13]. However, despite these recent findings, mental health outcomes and overall QOL in subjects with mild to moderate CKD have not been well characterized. Increasing interest in the association of ESRD with QOL has highlighted the relative paucity of similar evidence in subjects with CKD [14,15].

The goal of this study was to determine whether moderate kidney disease is associated with reduced mental health outcomes and overall QOL in a population of ambulatory adults with chronic illness. Because QOL is a balance of health and psychosocial factors, we evaluated the relative effects of CKD in four different domains. Specifically, we compared depressive symptoms, perceived stress, QOL, and overall health, among participants with and without CKD in the Heart and Soul Study.

Subjects and Methods

Subjects

The Heart and Soul Study is a prospective cohort designed to examine the influence of psychosocial factors on cardiac outcomes in participants with known coronary disease. From September 2000 to December 2002, subjects were recruited from the San Francisco Veterans Affairs Medical Center, the Veterans Affairs Palo Alto Health Care System, the University of California, San Francisco Medical Center, and nine public health clinics in the Community Health Network of San Francisco. Subjects were eligible to participate if they had one of the following inclusion criteria: history of myocardial infarction, angiographic evidence of >50% stenosis in one or more coronary vessels, evidence of exercise-induced ischemia by treadmill or nuclear testing, history of coronary revascularization, or documented diagnosis of coronary artery disease by an internist or cardiologist. Subjects were excluded if they had a myocardial infarction in the past 6 months, were unable to walk one block, or were planning to move out of the area in the next 3 years.

From 15,438 potential subjects, 1,024 were enrolled. Additional descriptions of the cohort have been previously published [16,17]. For this analysis, we excluded subjects who did not have 24-hour urine collection data (n = 57). All participants provided written informed consent, and the protocol was approved by the appropriate institutional review boards.

Measurements

Predictors

Primary: CKD was defined a priori as a creatinine clearance <60 ml/min [18–20]. Creatinine clearance was measured, based on 24-hour urine collection, using the following formula: [Urine Cr (mg/dl)·24-hour urine volume (ml)] / [Serum Cr (mg/dl)·1,440 (min/day)]. At the intake appointment, subjects were given a 3-liter collection jug and instructed to save all urine between the end of their intake appointment and the time when a researcher recovered the urine. Research personnel visited the subjects' homes exactly 24 h after their intake appointments to ensure accurately timed specimens. If the sample was reported to be incomplete, subjects were asked to repeat the collection, and research personnel returned 24 h later to re-collect the urine. Similarly, if the 3-liter collection jug was completely full, subjects were given two new jugs and asked to repeat the collection to insure that no urine was inadvertently discarded. If subjects were unable to collect all urine for any reason or had urinary incontinence, their samples were deemed inadequate and no urine creatinine data were recorded for these subjects.

Secondary: Age, sex, race, marital status, income, education, medical history, smoking status, and alcohol use were determined by self-report. We measured height and weight, and calculated body mass index (BMI). Serum samples were collected for measurement of hemoglobin, albumin, and creatinine.

Outcomes—Depressive symptoms were measured using the 9-item Patient Health Questionnaire (PHQ) [21]. We categorized patients with a score of 10 or higher as having depressive symptoms [22]. Stress was measured using the 4-item Perceived Stress Scale (PSS), and we considered patients to have stress if they scored 9 or greater on the 16-point scale [23]. As a measure of overall QOL, we asked patients, 'Compared with other people your age, how would you rate your overall quality of life?' [24,25]. Subjects could respond with one of the following choices: excellent, very good, good, fair, or poor. We also asked patients, 'Compared with other people your age, how would you rate your overall health?' Subjects had the same choice of responses as for the overall QOL question.

Statistical Analyses

We evaluated baseline characteristics of subjects by the presence of kidney disease using a t test for continuous variables and χ^2 statistic for dichotomous variables. We compared prevalence of depressive symptoms and stress by presence of CKD using a χ^2 statistic. For the overall health and QOL questions, we compared the responses of excellent, very good, and good, fair, and poor using a χ^2 statistic.

We used logistic regression to determine the association of CKD with depressive symptoms or stress. To determine the association of the CKD with overall health and QOL, we used ordered logit regression. This method was chosen as it allows the outcome to be modeled as an ordinal variable (excellent, very good, good, fair/poor), rather than a dichotomous outcome. We added the secondary predictors listed above into the ordered logistic and logit regression models to determine the independent association of CKD with each outcome. To further explore the association of kidney function with self-reported QOL and health status, we calculated age-adjusted and multivariate-adjusted mean creatinine clearance in each outcome category, based on the parameter estimates from linear regression models. Backward stepwise regression was used with a criterion of $p < 0.10$ for inclusion. We tested for interactions between CKD and age and race, for predicting each outcome. All analyses were performed using Stata 8.0 (Stata Corp., College Station, Tex., USA).

Results

Of the 967 eligible Heart and Soul Study participants, 236 (24%) had CKD. Compared with participants who had normal renal function, those with CKD were older, and were more likely to have anemia, hypertension, heart failure, hypoalbuminuria, and had a lower BMI (table 1). Subjects with CKD were also more likely to have a history of myocardial infarction, or stroke.

The 17% (40/236) prevalence of depressive symptoms in subjects with CKD was similar to the 19% (142/731) prevalence in subjects without CKD (p = 0.40). Perceived stress also did not significantly differ by renal function: 27/239 (11%) with CKD vs. 117/731 (16%) without CKD, p = 0.09. Using logistic regression, we found that CKD was not significantly associated with the mental health outcomes of depressive symptoms and stress in age-adjusted or adjusted analyses (table 2).

Of 236 subjects with CKD, 57 (24%) reported fair or poor QOL vs. 166 (23%) subjects without CKD (p = 0.65). 100 (42%) subjects with CKD reported fair or poor overall health compared with 251 (34%) with no CKD (p = 0.03). Age-adjusted models revealed a significant association between QOL and CKD, however this association no longer reached statistical significance after adjustment for confounders (table 2). In comparison, CKD was strongly associated with worse overall health in age-adjusted and multivariate-adjusted models. There was a significant trend of worsening kidney function across decreasing self-reported QOL and health status, however, this trend only remained significant in multivariate-adjusted analyses for health status (table 3).

We found no significant interactions between CKD and race for predicting any of the outcomes. We found an interaction of CKD and age for predicting depressive symptoms. In adjusted analyses, CKD was associated with a 0.37 (95% CI 0.14–0.98) odds for depressive symptoms in those subjects<60 years, 0.88 (95% CI 0.40–1.94) odds for depressive symptoms in those 60 to <70, and 1.31 (95% CI 0.72–2.39) odds for those over 70 years (p for interaction = 0.01). Overall the prevalence of depressive symptoms decreased in each increasing age group, particularly in subjects without CKD. (fig. 1) We found no interactions between CKD and age for predicting overall health, QOL, or stress.

Discussion

After adjustment for age, subjects with CKD were more likely to have reduced QOL and poor overall health in the Heart and Soul Study compared with subjects with normal kidney function. Adjustment for confounders attenuated the association of CKD and QOL, however the relationship with health status remained significant. In contrast, we did not find an association of CKD with depressive symptoms, or perceived stress. Our findings suggest that mild to moderate CKD is associated with reduced self-assessed health and modestly decreased QOL, but that mental health outcomes do not appear to be affected by moderate reductions in renal function.

Our findings should be interpreted in the context of prior studies. In the MDRD Study (mean GFR 33 ml/min), multivariate analyses showed a significant positive correlation between measured GFR and Quality of Well-Being score, a measure of health-related QOL [10]. However, in contrast to our study, a significant inverse relationship was found between measured GFR and the Symptom Checklist-90R scores, suggesting worsened mental health in subjects with reduced GFR. Shidler et al. [26] evaluated persons with moderate to severe kidney disease (mean creatinine clearance 37 ml/min) and did not find depressive symptoms to be correlated to serum creatinine concentration. The AASK Trial (mean GFR 46 ml/min) reported similar results to our study [13]; subjects in this cohort had lower physical component summary scores on the SF-36 than the general US population, however, the mental summary scores of

the cohort were slightly higher than in the general population. A prior publication from the Heart and Soul Study found that CKD (creatinine clearance <60 ml/min) was associated with self-assessed physical limitation [11]. Thus, it appears that physical health declines at earlier stages of renal dysfunction than mental health.

Considering the physical symptoms that accompany CKD, it is not surprising that we found an association of CKD with worsened overall health. However, it is interesting that moderate kidney disease appeared to be associated with decrements in overall health, and that mental health outcomes appeared similar in subjects with and without CKD. The association of CKD with QOL, although significant in age-adjusted analyses, was less robust than that of CKD with health status. It may be that subjects equate their overall health predominantly with physical health, while QOL encompasses a broader range of factors, including psychosocial outcomes. It is commonly accepted that QOL is reduced in persons with ESRD [2,15] and depression is thought to be the most common psychological disorder in ESRD patients [27, 28], with estimated prevalence rates in excess of one-third [9,29]. However, the prevalence of depression in subjects with CKD has not been well studied [14]. Depression has been associated with the response to a loss of some kind [27] and stress is often a response to a change in a person's life [30]. Persons with advanced kidney disease have not only reduced physical function, but their loss in mobility may affect employment, familial roles, and social networks. These losses, coupled with the stress of dealing with the changes in the patients' lifestyle, may lead to the high prevalence of psychological illness in subjects with ESRD.

Mental health may remain unchanged in persons with moderate CKD because the burden of their illness has not yet grown to represent a change or loss. While these patients have a reduction in physical health, it may not substantially limit their performance in their daily life. Therefore, although physical health is affected, mental health outcomes appear to remain stable in the setting of moderate CKD. This may explain why we found a smaller reduction in overall QOL, compared with health status, because it reflects a combination of mental and physical health. Interestingly, the association of CKD with QOL appeared to be an average of the associations of CKD with overall health and the mental health outcomes.

We found an interesting interaction of age and CKD for predicting depressive symptoms. Although somewhat unexpected, previous studies have found an inverse association between age and depression, with depression being more prevalent in the young than in the elderly [31,32]. It is possible that despite declining physical health, such as coronary artery disease or CKD, the elderly adapt to their life situations more effectively. We also must consider the possibility that the interaction of age and CKD for predicting depressive symptoms may have been a chance finding.

A strength of our study is that, unlike most previous studies, we included persons with normal renal function as a comparison group. The data that exist regarding the association of health-related QOL and CKD are predominantly in cohorts with renal disease, and therefore do not include comparison groups without CKD. Another strength is the measurement of creatinine clearance by 24-hour urine collection, rather than a one-time measurement of serum creatinine.

Our study also has some limitations that must be considered. This was a cross-sectional analysis which limits our ability to determine causation. We cannot assume that CKD would be associated with the development of worsened health status over time. In addition, there may have been unmeasured confounding variables that may have affected the associations of CKD with our outcome variables. We cannot exclude the possibility that our positive or negative findings may have been due to chance. The Heart and Soul Study was a cohort of predominantly male patients with coronary artery disease, therefore our results may not be applicable to women or to the general population. Finally, subjects were excluded from the study if they had

a myocardial infarction in the past 6 months or were unable to walk one block; therefore our findings may not be generalizable to those with a recent coronary event or disability.

An additional potential limitation is the use of single-item measures for both overall health and QOL. However, since our study aimed to compare the broad concepts of overall health and QOL between subjects with and without CKD, we believe single-item measures were appropriate. Multiple-item measures may be more precise for specific treatment effects, but single-item measures are valid for overall comparisons between study populations [33]. A single-item measure of health has been shown to be predictive of mortality in elderly patients [34]. In addition, studies have shown single-item measures of health-related QOL to correlate positively and significantly with multiple-item instruments in persons with chronic disease [24,33,35].

In conclusion, we found CKD to be independently associated with self-reported overall health, and modestly associated with QOL in a cohort of persons with coronary artery disease. However, moderate CKD was not associated with depressive symptoms, or perceived stress. These findings suggest that although overall health is diminished in subjects with moderate kidney disease, mental health may remain unchanged, resulting in only a modest reduction in overall QOL. Longitudinal studies of renal function with overall health, mental health, and QOL outcomes will help us to understand their relation over time.

Acknowledgments

The Heart and Soul Study was funded by grants from the Department of Veterans Affairs (Epidemiology Merit Review Program), the Robert Wood Johnson Foundation (Generalist Physician Faculty Scholars Program), the American Federation for Aging Research (Paul Beeson Faculty Scholars in Aging Research Program), the Ischemia Research and Education Foundation, and the University of California, San Francisco (Hellman Family Award). None of the funding sources had any role in the collection of data, interpretation of results, or preparation of the manuscript.

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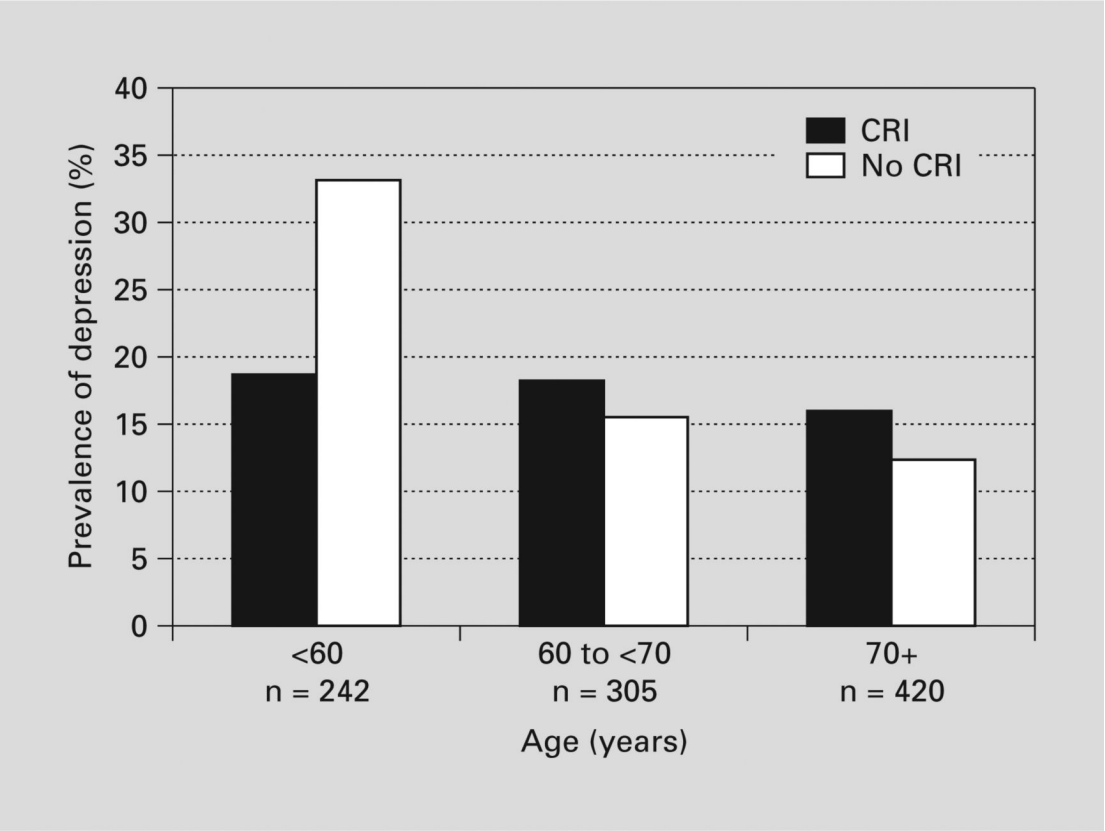

Fig. 1.
Prevalence of depressive symptoms in subjects with and without CKD in subjects <60, 60 to <70, and 70+ years old.

Table 1

Characteristics of participants with and without CKD (creatinine clearance <60 ml/min)

	CKD (%) n = 236	No CKD (%) n = 731	p value
Demographic			
Age, years	72 ± 11	65 ± 10	<0.001
Male	200 (85)	603 (83)	0.45
White	150 (64)	437 (60)	0.31
Married	101 (43)	313 (43)	1.00
Income USD >20,000	122 (52)	380 (52)	0.94
High school graduate	203 (86)	644 (88)	0.40
Comorbidities and measurements			
Creatinine clearance, ml/min	46 ± 11	92 ± 22	<0.001
Hemoglobin, g/l	14.1 ± 1.3	13.3 ± 1.5	<0.001
Hypertension	184 (78)	497 (68)	0.003
Diabetes mellitus	71 (30)	174 (24)	0.06
Heart failure	57 (24)	108 (15)	0.001
Angina	144 (61)	441 (60)	0.81
Albumin, g/l	3.9 ± 0.3	3.8 ± 0.4	<0.001
Smoking, current	48 (20)	139 (19)	0.67
Alcohol, regular use	59 (25)	216 (30)	0.18
BMI, kg/m^2	27 ± 5	29 ± 5	<0.001
Prior myocardial infarction	147 (62)	372 (51)	0.003
Prior stroke	53 (22)	87 (12)	<0.001
Prior revascularization	97 (41)	255 (35)	0.09

Table 2

Associations of CKD with worse overall health, worse QOL, depressive symptoms, and stress

	CKD (creatinine clearance <60 ml/min)	
	OR (95% CI)[a]	p value
Depressive symptoms (≥ 10 on PHQ)		
Age-adjusted	1.10 (0.73–1.64)	0.65
Adjusted[b]	0.86 (0.56–1.31)	0.48
Stressed (≥ 9 on PSS)		
Age-adjusted	0.86 (0.54–1.37)	0.53
Adjusted[b]	0.75 (0.46–1.22)	0.24
Worse QOL		
Age-adjusted	1.51 (1.15–1.98)	0.003
Adjusted[b]	1.31 (0.99–1.75)	0.06
Worse overall health		
Age-adjusted	1.95 (1.47–2.58)	<0.001
Adjusted[b]	1.65 (1.21–2.24)	0.001

[a] Calculated using logistic regression for depressive symptoms or stress and ordered logit regression for worsening QOL or overall health.

[b] Adjusted for age, sex, race, marital status, income, education, anemia, hypertension, diabetes, heart failure, angina, prior MI, prior stroke, prior revascularization, hypoalbuminuria, smoking status, alcohol use, BMI ($p < 0.01$).

Table 3

Age-adjusted and adjusted mean levels of creatinine clearance by level of self-reported QOL or health status

	Creatinine clearance, ml/min			
	age-adjusted mean (95% CI)	p value	adjusted[a] mean (95% CI)	p value
Quality of life				
Poor/fair	77.3 (74.4–80.1)	0.002	79.2 (76.3–82.0)	0.22
Good	80.1 (78.3–81.8)		80.3 (78.6–82.0)	
Very good	82.9 (80.8–84.9)		81.4 (79.4–83.4)	
Excellent	85.6 (82.3–89.0)		82.6 (79.1–86.0)	
Health status				
Poor/fair	77.2 (74.7–79.6)	<0.001	78.7 (76.3–81.1)	0.03
Good	80.9 (79.3–82.6)		80.7 (79.1–82.2)	
Very good	84.7 (82.3–87.1)		82.6 (80.2–85.0)	
Excellent	88.4 (84.5–92.3)		84.6 (80.6–88.5)	

[a] Adjusted for age, sex, race, marital status, income, education, anemia, hypertension, diabetes, heart failure, angina, prior MI, prior stroke, prior revascularization, hypoalbuminuria, smoking status, alcohol use, BMI ($p < 0.01$).