Depression and All-Cause Mortality in Hemodialysis Patients

Li Fan^a Mark J. Sarnak^a Hocine Tighiouart^{c, d} David A. Drew^a Amy L. Kantor^a
Kristina V. Lou^a Kamran Shaffi^e Tammy M. Scott^b Daniel E. Weiner^a

^aDivision of Nephrology, Department of Medicine, ^bDepartment of Psychiatry, and ^cInstitute for Clinical Research and Health Policy Studies, Tufts Medical Center, and ^dTufts Clinical and Translational Science Institute, Tufts University, Boston, Mass., and ^eDivision of Nephrology, University of New Mexico, Albuquerque, N.Mex., USA

Key Words

All-cause mortality · Antidepressant medication · Depression · Hemodialysis

Abstract

Background: There are limited data regarding the relationship between depression and mortality in hemodialysis (HD) patients. **Methods:** Among 323 patients receiving maintenance HD, depression symptoms were assessed using the Center for Epidemiologic Studies Depression (CES-D) scale, with a score of ≥ 16 consistent with depression. Adjusted Cox proportional-hazards models with additional analyses incorporating antidepressant medication use were used to evaluate the association between depression and mortality. Baseline CES-D scores were used for the primary analyses, while secondary time-dependent analyses incorporated subsequent CES-D results. **Results:** The mean age was 62.9 ± 16.5 years, 46% of the subjects were women and 22% were African-American. The mean baseline CES-D score was 10.7 ± 8.3 , and 83 (26%) participants had CES-D scores ≥ 16 . During a median (25th, 75th) follow-up of 25 (13, 43) months, 154 participants died. After adjusting for age, sex, race, primary cause of kidney failure, dialysis vintage and access, baseline depression was associated with an increased risk of all-cause mortality (HR 1.51 and 95% CI 1.06–2.17). This attenuated with further adjustment for cardiovascular disease, smoking,

Kt/V, serum albumin, log C-reactive protein and use of antidepressants (HR 1.21 and 95% CI 0.82–1.80). When evaluating time-dependent CES-D, depression remained associated with increased mortality risk in the fully adjusted model (HR 1.44 and 95% CI 1.00–2.06). **Conclusions:** Greater symptoms of depression are associated with an increased risk of mortality in HD patients, particularly when accounting for the most proximate assessment. This relationship was attenuated with adjustment for comorbid conditions, suggesting a complex relationship between clinical characteristics and depression symptoms. Future studies should evaluate whether treatment for depression impacts mortality among HD patients.

© 2014 S. Karger AG, Basel

Introduction

Depression is common among people with chronic kidney disease (CKD), with an estimated prevalence of 21–27% in nondialysis CKD [1]. It is likely that the prevalence of depression is higher among patients receiving

An abstract based on the manuscript was presented at the 2013 American Society of Nephrology Kidney Week in Atlanta, Ga., USA.

hemodialysis (HD), with estimated rates ranging from 23 to 42% in the USA and Europe [1–3]. In the general population, depression is associated with an increased risk of mortality; a similar association has been noted among non-HD CKD patients [4–6].

Existing data on HD patients are limited, with many studies relying on the administrative diagnoses of depression and few including data on antidepressant medication use or sequential depression screening. Several have shown that patients with depression have a poorer quality of life, more functional impairment, greater comorbidity and psychopathologic states, lower treatment compliance and an increased risk of both hospitalization and mortality [3, 7–12]. Most of these studies rely on self-reported symptoms; among these, one study, which evaluated 98 HD patients, revealed an association between depression diagnosed by structured clinical interviews performed by physicians and mortality [2]. In the largest study to date, an analysis of HD patients in the Dialysis Outcomes and Practice Patients study ($n = 5,256$), physician-diagnosed or self-reported depression was associated with increased risks of both mortality and hospitalization [9]. In this particular study, depression was defined either by administrative diagnosis or answers to two self-response questions from the Kidney Disease and Quality of Life short form (KDQOL-SF).

Two studies [13, 14], both of which examined repeated measures of depression and showed an association between time varying but not baseline depression symptoms and mortality, differ importantly from the current study by using a more limited tool for evaluating depression and by evaluating an exclusively urban, African-American population. We evaluated the relationship between depression (assessed using a validated depression screening instrument at baseline and annually thereafter) and all-cause mortality in a large generalizable cohort of maintenance HD patients, exploring the role of time-dependent screening and the use of antidepressant medication. Given that HD patients with symptoms of depression have a higher occurrence of cognitive impairment [10], a lower adherence to dietary fluid restrictions, medication and dialysis treatments [15, 16] and an increased risk of hospitalization [17], we hypothesized that a greater burden of depression symptoms is associated with an increased risk of all-cause mortality in HD patients.

Methods

Participants and Data Collection

Patients receiving HD at 5 units of the Dialysis Clinic Inc. (DCI) and 1 hospital-based unit (St. Elizabeth's Medical Center) in the Boston, Mass., region were considered for the Cognition and Dialysis Study. Eligibility criteria included English fluency and sufficient visual and hearing acuity to be able to complete cognitive testing. Exclusion criteria were individuals with pre-existing advanced dementia based on provider testimony or medical record review, nonvascular access-related hospitalization within 1 month, delirium, receipt of maintenance HD for <1 month and single-pool (sp)Kt/V <1.0.

Demographic, clinical and laboratory characteristics were ascertained at the time of study enrollment. Demographic and clinical characteristics were obtained from the patients' reports, medical charts and the DCI and St. Elizabeth's Medical Center databases. Blood pressure was defined as mean predialysis blood pressure for the month prior to the baseline visit, and body mass index was calculated using predialysis weight. Laboratory tests including hematocrit, white blood cell count, serum albumin and spKt/V were obtained from the DCI or St. Elizabeth's electronic record. All DCI laboratory tests were measured in a central laboratory in Nashville, Tenn., USA. High-sensitivity C-reactive protein (CRP) was measured from frozen sera obtained at study enrollment. The use of antidepressant medication was obtained from the databases, and included selective serotonin reuptake inhibitors, tricyclic antidepressants, dopamine/norepinephrine reuptake inhibitors (bupropion), noradrenergic and serotonergic agonists (mirtazapine), serotonin/norepinephrine reuptake inhibitors (venlafaxine) and serotonin modulators (nefazodone and trazodone). The Tufts Medical Center/Tufts University Institutional Review Board approved the study and all participants signed informed consent and research authorization forms.

Depression Symptom Assessment

All participants were assessed using the Center for Epidemiological Studies Depression (CES-D) scale as part of a broader neurocognitive assessment. Neurocognitive testing was performed by trained research assistants, with testing observed by the study neuropsychologist at intervals of 3–6 months in order to maintain quality and interrater reliability. To limit participant fatigue, neurocognitive testing was completed during the first hour of HD.

The CES-D scale is a validated, self-report questionnaire comprising 20 questions, with higher scores indicating a greater burden of depression symptoms. In the general population, a CES-D score of ≥ 16 is considered to be consistent with major depression [18] while, in one analysis of HD patients, in whom somatic symptoms are more common, a threshold of 18 showed greater diagnostic accuracy [19]. Accordingly, in our primary analyses, we defined a high depression symptom burden as a CES-D score of ≥ 16 , while sensitivity analyses use a threshold CES-D score of ≥ 18 . We also explore the CES-D score as a continuous variable, reporting the association of each one standard deviation (SD) change (8.3 points) in CES-D score with the mortality.

Outcome

The primary outcome was all-cause mortality, which was obtained by monitoring the electronic medical records as well as communicating with each patient's dialysis unit. We defined the

survival time for each participant as the time from enrollment to death, transplantation or end of study follow-up (March 31, 2013), whichever occurred first.

Covariates

A priori selected covariates included demographic characteristics (age, race and sex), primary cause of kidney failure (diabetes vs. nondiabetes), time on dialysis, dialysis access (fistula vs. non-fistula), history of cardiovascular disease (CVD, either coronary artery disease, peripheral vascular disease, stroke or heart failure), smoking, spKt/V, serum albumin, CRP and baseline use of antidepressant medication.

Statistical Analyses

Participants were stratified according to a baseline CES-D score of ≥ 16 , and the baseline demographic and clinical characteristics of participants with or without depression symptoms were compared using the χ^2 test for categorical variables and the Student t test or Mann-Whitney U test for continuous variables, as appropriate.

Cox proportional hazards regression models were used to evaluate the association of CES-D score and all-cause mortality. Cox regression models a priori were adjusted according to the following potential confounders: Model 1: age, sex and race, Model 2: model 1 plus primary cause of kidney failure, dialysis access and period on dialysis, Model 3: model 2 plus history of CVD and smoking status and Model 4: model 3 plus spKt/V, serum albumin, log-transformed CRP and baseline antidepressant medication use. Variables that were not included a priori or that were not significant in the univariate analyses (e.g. blood pressure) were not included in the sequentially adjusted models. In secondary analyses conducted to account for changes in CES-D score over time, Cox models incorporated annually measured time-dependent CES-D scores, carrying the last score forward between each successive visit. We also explored (a priori) the interaction between baseline CES-D score and antidepressant medication use, as antidepressant medications could modify the CES-D score and its relationship with mortality. All analyses were performed using the SAS (version 9.3, SAS Institute, Cary, N.C., USA) and R package (version 2.15.1).

Results

Baseline Characteristics

Of the 323 participants, mean age was 62.9 ± 16.5 years, 46% were female, 22% were African-American, 33% had diabetes as a primary cause of kidney failure, 61% had a history of CVD and 61% had a history of smoking (9% of these were current smokers). Median (25th, 75th) period on dialysis was 14.1 (6.8, 33.8) months and 65% of the patients used a fistula as vascular access (table 1).

For each participant, a median of 2 (25th–75th percentile, 1–3) CES-D assessments occurred. Mean CES-D score at baseline, and then the 2nd and 3rd visits was 10.7 ± 8.3 ($n = 323$), 10.9 ± 8.7 ($n = 196$) and 12.3 ± 9.6 ($n =$

121), respectively. At baseline, 83 (26%) participants had CES-D scores of ≥ 16 and 42.7% were treated with an antidepressant medication. Of the patients for whom antidepressant medication had been prescribed, 90 (65.2%) had a baseline CES-D score of <16 while 48 (34.8%) had a score of ≥ 16 ($p = 0.002$). Participants with a higher CES-D score at baseline were more likely to have diabetes as the primary cause of kidney failure, a history of smoking, lower serum albumin and spKt/V and to be on antidepressant medication (table 1).

Depression Symptoms and All-Cause Mortality

During a median (25th, 75th) follow-up of 25 (13, 43) months, 154 participants died. Among participants with a baseline CES-D score of <16 , there were 17.7 deaths per 100 patient-years whereas for individuals with a baseline CES-D score of ≥ 16 , there were 23.3 deaths per 100 patient-years. After adjusting for age, sex and race, depression was associated with an increased risk of all-cause mortality (HR 1.50 and 95% CI 1.05–2.14); this association remained significant after further adjustment for the primary cause of kidney failure, dialysis access and period on dialysis (HR 1.51 and 95% CI 1.06–2.17). After further adjustment for a history of CVD and smoking, this relationship was attenuated (HR 1.39 and 95% CI 0.96–2.00); in models that also included serum albumin, CRP and antidepressant medications, the relationship was no longer significant (HR 1.21 and 95% CI 0.82–1.80; table 2). Results were similar when a baseline CES-D threshold of ≥ 18 and a continuous term for CES-D were used (table 2).

The association of CES-D score with all-cause mortality was robust when the CES-D score was treated as a time-dependent variable (table 3). Participants with a CES-D score of ≥ 16 had a higher risk of all-cause mortality in a model adjusted for age, sex and race (HR 1.55 and 95% CI 1.10–2.17), with a similar effect size maintained in further-adjusted models. Results were similarly robust in time-dependent models when using a CES-D threshold of 18, in analyses examining CES-D score as a continuous variable and when cardiovascular versus noncardiovascular causes of death were examined (data not shown).

Antidepressant Medication Use, Depression and All-Cause Mortality

There was no significant interaction between baseline CES-D score and the use of antidepressant medication (p values for interaction in models 1–4 were 0.74, 0.80, 0.52 and 0.80, respectively). Figure 1 shows the associa-

Table 1. Baseline characteristics of participants

Variable	Total (n = 323)	CES-D score <16 (n = 240; 74%)	CES-D score ≥16 (n = 83; 26%)	p value
CES-D score	10.7±8.3	6.8±4.3	22.2±5.8	<0.001
Age, years	62.9±16.5	63.2±16.5	62.0±16.6	0.60
Female	150 (46.4)	112 (46.7)	38 (45.8)	0.89
African-American	71 (22.0)	52 (21.7)	19 (22.9)	0.82
Primary cause of ESRD				0.03
Diabetes	107 (33.1)	77 (32.1)	30 (36.1)	
Hypertension	59 (18.3)	48 (20.0)	11 (13.3)	
Glomerular disease	55 (17.0)	47 (19.6)	8 (9.6)	
Other	52 (16.1)	38 (15.8)	14 (16.9)	
Unknown	50 (15.5)	30 (12.5)	20 (24.1)	
History of CVD	198 (61.3)	141 (58.8)	57 (68.7)	0.11
Smoking status				0.04
Current	29 (9.1)	17 (7.1)	12 (14.6)	
Past	167 (52.2)	121 (50.8)	46 (56.1)	
Never	124 (38.8)	100 (42.0)	24 (29.3)	
Vascular access				0.24
Fistula	211 (65.3)	158 (65.8)	53 (63.9)	
Graft	18 (5.6)	16 (6.7)	2 (2.4)	
Catheter	94 (29.1)	66 (27.5)	28 (33.7)	
Dialysis vintage, months	14.1 (6.8, 33.8)	13.6 (6.9, 35.4)	15.3 (6.4, 30.7)	0.73
Systolic BP, mm Hg	141.3±20.8	141.3±20.4	141.3±21.8	0.98
Diastolic BP, mm Hg	73.3±12.1	73.3±11.9	73.2±12.6	0.93
BMI	28.4±7.0	28.1±6.9	29.2±7.3	0.22
Hematocrit, %	35.5±3.5	35.6±3.5	35.1±3.5	0.25
Albumin, g/dl	3.8±0.4	3.8±0.4	3.7±0.4	0.03
WBC count, µl	7.4±2.3	7.4±2.4	7.5±2.3	0.64
CRP, mg/l	5.3 (2.2, 11.5)	4.9 (1.9, 9.8)	6.5 (2.6, 18.5)	0.05
spKt/V	1.51±0.24	1.53±0.25	1.46±0.21	0.02
Antidepressant use	138 (42.7)	90 (37.5)	48 (57.8)	0.001

Data are presented as mean ± SD, number (%) or median (25th, 75th). Conversion factors for units: albumin in g/dl to g/l, ×10; phosphorus in mg/dl to mmol/l, ×0.3229. BMI = Body mass index; BP = blood pressure; ESRD = end-stage renal disease; WBC = white blood cell.

Table 2. Association between baseline CES-D score and all-cause mortality

		Model 1		Model 2		Model 3		Model 4	
		HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
CES-D score ≥16	23.3 vs. 17.7	1.50 (1.05–2.14)	0.03	1.51 (1.06–2.17)	0.02	1.39 (0.96–2.00)	0.08	1.21 (0.82–1.80)	0.34
CES-D score ≥18	24.1 vs. 17.9	1.67 (1.13–2.48)	0.01	1.68 (1.13–2.50)	0.01	1.46 (0.97–2.18)	0.07	1.27 (0.82–1.98)	0.29
CES-D score (per 1 SD higher)	overall 19.0	1.25 (1.05–1.48)	0.01	1.26 (1.06–1.50)	0.008	1.20 (1.01–1.42)	0.04	1.13 (0.94–1.35)	0.21

Each SD for CES-D score is 8.3. Model 1 is adjusted for age, sex and race. Model 2: Model 1 + primary cause of kidney failure, dialysis access and dialysis vintage. Model 3: Model 2 + history of CVD and smoking status. Model 4: Model 3 + spKt/V, serum albumin, log CRP and baseline use of antidepressant medication.

Table 3. Association between time-dependent CES-D score and all-cause mortality

	Events per 100 patient-years	Model 1		Model 2		Model 3		Model 4	
		HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
CES-D score ≥ 16	23.3 vs. 17.7	1.55 (1.10–2.17)	0.01	1.54 (1.09–2.16)	0.01	1.47 (1.04–2.08)	0.03	1.44 (1.00–2.06)	0.05
CES-D score ≥ 18	24.1 vs. 17.9	1.49 (1.02–2.17)	0.04	1.48 (1.01–2.16)	0.05	1.40 (0.95–2.05)	0.09	1.36 (0.91–2.03)	0.14
CES-D score (per 1 SD higher)	overall 19.0	1.24 (1.06–1.44)	0.006	1.25 (1.07–1.46)	0.004	1.23 (1.05–1.43)	0.008	1.21 (1.04–1.42)	0.02

Each SD for CES-D score is 8.3. Model 1 is adjusted for age, sex and race. Model 2: Model 1 + primary cause of kidney failure, dialysis access and dialysis vintage. Model 3: Model 2 + history of CVD and smoking status. Model 4: Model 3 + spKt/V, serum albumin, log CRP and baseline use of antidepressant medication.

Fig. 1. Association of CES-D score ≥ 16 and antidepressant medication (meds) prescription with all-cause mortality. Error bars show the 95% CI. Model 1: adjusted for age, sex and race. Model 2: model 1 plus primary cause of kidney failure, dialysis access and dialysis vintage. Model 3: model 2 plus history of cardiovascular disease and smoking status. Model 4: model 3 plus spKt/V, serum albumin and log CRP.

tion of depression defined by a CES-D threshold of ≥ 16 , the use of baseline antidepressant medication and all-cause mortality. Depressed individuals who were prescribed antidepressants had a significantly higher risk of all-cause mortality in all models compared to those with a CES-D score < 16 not receiving antidepressants. Similar results were found using a CES-D score threshold of ≥ 18 (online suppl. fig. 1; for all online suppl. material, see www.karger.com/doi/10.1159/000363539).

Discussion

We demonstrate here that a greater depression symptom burden is associated with an increased risk of all-cause mortality in patients on maintenance HD. This as-

sociation was attenuated following multivariable adjustment for CVD and for markers of inflammation and nutrition, all factors that may be on the causal pathway linking depression and mortality, although in models incorporating the most proximate measure of the CES-D until study completion, depression remained independently associated with mortality (even after adjustment). We also noted that there was no interaction between baseline depression and the use of antidepressant medication, although individuals receiving medication who had a high CES-D score were found to be at the highest risk.

Given the effects on quality of life and medical outcomes, depression screening has been proposed by the Centers for Medicare and Medicaid Services in the USA as a quality indicator [20] while the guideline of the Kidney Disease Outcomes Quality Initiative for CVD in di-

alysis patients suggests evaluating patients' psychological states at least biannually with a specific focus on the presence of depressive symptoms [21]. Despite this, as was recently reviewed by Hedayati et al. [22], screening and treatment for depression likely remain insufficient within the dialysis population [8, 17].

Studies have previously demonstrated a relationship between depression and mortality [4]; in many of these, however, this relationship is attenuated after multivariable adjustment, and so possibly reflects mediating factors. In the nondialysis CKD population, a recent meta-analysis of 83,381 individuals in 22 cohort studies showed that depression was associated with a 59% higher risk of all-cause mortality [6]. In individuals treated with HD, a meta-analysis of 41,941 participants in 25 studies similarly demonstrated that a higher burden of depression symptoms was associated with an increased risk of mortality [23]. These two meta-analyses had similar limitations, with heterogeneous depression-ascertainment methods, variable times between ascertainment and outcomes, reliance on a single assessment and an absence of data on the use of medication. Only a few studies contained evaluated repeated assessments of depression symptoms. Boulware et al. [14] performed a post hoc analysis of the CHOICE (Choices for Healthy Outcomes in Caring for End-Stage Renal Disease) study. Using responses to questions on the short form 36 (SF-36), they assessed symptoms 4 times at 6-month intervals and noted that, among 917 incident dialysis patients, persistent symptoms of depression were associated with a greater risk of all-cause and cardiovascular mortality. This association was not significant when defining depression using only the baseline assessment. Similar results were reported in an analysis of 295 chronic HD patients, such that depression symptoms (varying over time) assessed using the Beck Depression Inventory and the Cognitive Depression Index, but not depression symptoms at baseline, were associated with an increased risk of mortality [13].

Our primary results demonstrate that greater depression symptoms at baseline are associated with an increased risk of all-cause mortality in patients on maintenance HD, but this association was attenuated with further adjustment for comorbidity. There are several potential interpretations of this finding. First, depression itself may increase mortality. HD patients with depression symptoms have a higher occurrence of cognitive impairment and a higher risk of hospitalization, a poorer quality of life and a lower adherence to dietary and fluid restrictions and dialysis treatment [2, 3, 7–12], all of which may contribute to an increased risk of mortality.

Second, greater depression symptoms may reflect an existing comorbidity burden and therefore confound the relationship between comorbid conditions and mortality. The converse can also be true, with depression resulting in more severe comorbidity, such as malnutrition due to anorexia, with these comorbidities confounding the relationship between depression and mortality. For example, in our analyses, a history of CVD substantially attenuated the relationship between CES-D score and outcomes, but determining which may be causal and which may be a confounder was not possible in a study with an observational design. In the exploratory analyses, we noted that there was no statistically significant interaction between baseline CES-D score and the use of antidepressant medication, but individuals with a higher CES-D score and who were on medication had the highest risk of mortality. One explanation for this result is indication bias, whereby HD patients with more severe depression symptoms are more likely to be treated with antidepressant medication.

There are several strengths to our study. First, the relationship between depression symptoms and outcomes was evaluated using both the baseline and time-dependent CES-D results. Second, we were able to incorporate data on the use of medications that target depression. Third, we had detailed ascertainment of other mortality risk factors and outcomes and were able to account for these in the multivariable analyses. This study also has several limitations including the absence of gold standard for the ascertainment of depression. It is important to note that the CES-D is a widely used instrument for depression screening and has been validated in the HD population [19]. Second, we did not capture longitudinal use of antidepressant medication or dosages. In addition, we were unable to account for indication bias, i.e. that individuals with more symptoms of depression are more likely to receive antidepressant medications. Third, we had relatively few events when examining subgroups based on the constellation of medications and symptoms. Finally, given the observational nature of the cohort and the heterogeneity of depression symptoms, it is possible that both residual confounding and unmeasured confounding occurred.

In conclusion, the symptoms of depression were associated with an increased risk of mortality in maintenance HD patients, but this relationship was attenuated by adjustment for comorbid conditions, suggesting a complex relationship between depression and clinical conditions. Further studies are needed to evaluate whether the treatment of depression with medication, cognitive behavioral therapy [24] or other techniques can impact morbidity and mortality among patients on HD.

Acknowledgements

This study was funded through the following grants: R21 DK068310 and R01 DK078204 (M.J.S.), UL1 TR000073 NIH CTSA, K24 DK078204, American Society of Nephrology Research

Fellowship Grant (D.A.D.). We would like to acknowledge the tremendous assistance of Dialysis Clinic, Inc. and, in particular, the staff and patients at the 5 DCI units in the Boston area and St. Elizabeth's Dialysis Unit, whose generous cooperation made this study possible.

References

- 1 Palmer S, Vecchio M, Craig JC, et al: Prevalence of depression in chronic kidney disease: systematic review and meta-analysis of observational studies. *Kidney Int* 2013;84:179–191.
- 2 Hedayati SS, Bosworth HB, Briley LP, et al: Death or hospitalization of patients on chronic hemodialysis is associated with a physician-based diagnosis of depression. *Kidney Int* 2008;74:930–936.
- 3 Riezebos RK, Nauta KJ, Honig A, Dekker FW, Siegert CE: The association of depressive symptoms with survival in a Dutch cohort of patients with end-stage renal disease. *Nephrol Dial Transplant* 2010;25:231–236.
- 4 Mykletun A, Bjerkeset O, Overland S, et al: Levels of anxiety and depression as predictors of mortality: the HUNT study. *Br J Psychiatry* 2009;195:118–125.
- 5 Patten SB, Williams JV, Lavorato D, et al: Mortality associated with major depression in a Canadian community cohort. *Can J Psychiatry* 2011;56:658–666.
- 6 Palmer SC, Vecchio M, Craig JC, et al: Association between depression and death in people with CKD: a meta-analysis of cohort studies. *Am J Kidney Dis* 2013;62:493–505.
- 7 Tsay SL, Healstead M: Self-care self-efficacy, depression, and quality of life among patients receiving hemodialysis in Taiwan. *Int J Nurs Stud* 2002;39:245–251.
- 8 Watnick S, Kirwin P, Mahnensmith R, Concato J: The prevalence and treatment of depression among patients starting dialysis. *Am J Kidney Dis* 2003;41:105–110.
- 9 Lopes AA, Bragg J, Young E, et al: Depression as a predictor of mortality and hospitalization among hemodialysis patients in the United States and Europe. *Kidney Int* 2002;62:199–207.
- 10 Agganis BT, Weiner DE, Giang LM, et al: Depression and cognitive function in maintenance hemodialysis patients. *Am J Kidney Dis* 2010;56:704–712.
- 11 Chilcot J, Davenport A, Wellsted D, Firth J, Farrington K: An association between depressive symptoms and survival in incident dialysis patients. *Nephrol Dial Transplant* 2011;26:1628–1634.
- 12 Lacson E Jr, Li NC, Guerra-Dean S, et al: Depressive symptoms associate with high mortality risk and dialysis withdrawal in incident hemodialysis patients. *Nephrol Dial Transplant* 2012;27:2921–2928.
- 13 Kimmel PL, Peterson RA, Weihs KL, et al: Multiple measurements of depression predict mortality in a longitudinal study of chronic hemodialysis outpatients. *Kidney Int* 2000;57:2093–2098.
- 14 Boulware LE, Liu Y, Fink NE, et al: Temporal relation among depression symptoms, cardiovascular disease events, and mortality in end-stage renal disease: contribution of reverse causality. *Clin J Am Soc Nephrol* 2006;1:496–504.
- 15 DiMatteo MR, Lepper HS, Croghan TW: Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med* 2000;160:2101–2107.
- 16 Cukor D, Rosenthal DS, Jindal RM, Brown CD, Kimmel PL: Depression is an important contributor to low medication adherence in hemodialyzed patients and transplant recipients. *Kidney Int* 2009;75:1223–1229.
- 17 Lopes AA, Albert JM, Young EW, et al: Screening for depression in hemodialysis patients: associations with diagnosis, treatment, and outcomes in the DOPPS. *Kidney Int* 2004;66:2047–2053.
- 18 Radloff LS: The CES-D scale: A self report depression scale for research in the general population. *Applied Psychological Measurements* 1977;1:385–401.
- 19 Hedayati SS, Bosworth HB, Kuchibhatla M, Kimmel PL, Szczech LA: The predictive value of self-report scales compared with physician diagnosis of depression in hemodialysis patients. *Kidney Int* 2006;69:1662–1668.
- 20 Centers for Medicare & Medicaid Services (CMS): 2013 CMS Measures Inventory. <http://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/QualityMeasures/CMS-Measures-Inventory.html>
- 21 K/DOQI clinical practice guidelines for cardiovascular disease in dialysis patients. *Am J Kidney Dis* 2005;45:S1–S153.
- 22 Hedayati SS, Yalamanchili V, Finkelstein FO: A practical approach to the treatment of depression in patients with chronic kidney disease and end-stage renal disease. *Kidney Int* 2012;81:247–255.
- 23 Farrokhi F, Abedi N, Beyene J, Kurdyak P, Jassal SV: Association between depression and mortality in patients receiving long-term dialysis: a systematic review and meta-analysis. *Am J Kidney Dis* 2014;63:623–635.
- 24 Cukor D, Ver Halen N, Asher DR, et al: Psychosocial intervention improves depression, quality of life, and fluid adherence in hemodialysis. *J Am Soc Nephrol* 2014;25:196–206.