The Association of Mental Health over Time with Cardiac Outcomes in HEMO Study Patients

Ea Wha Kang,†† Francis Pike,* Sarah Ramer,* Khaled Abdel-Kader,* Larissa Myaskovsky,‡§ Mary Amanda Dew,‖ and Mark Unruh**

Summary

Background and objectives Poor mental health over time is significantly associated with cardiovascular morbidity and mortality in the general population, which is the leading cause of death in dialysis patients. Most studies of dialysis patients, however, have investigated the relationship between baseline mental health measurements and all-cause mortality and not mental health measured longitudinally throughout a study and cause-specific mortality.

Design, setting, participants, & measurements This study examined the association of changes in mental health over time with all-cause and cause-specific deaths and cardiac hospitalizations in the Hemodialysis study patients. Mental health was assessed at baseline and annually during the study with short form 36 mental health index scores. Poorer mental health was defined by a mental health index score≤60.

Results Patients with poorer mental health at baseline were more likely to have less than a high school education and be unmarried, have significantly higher index of coexistent disease scores, and report taking β-blockers and sleep medications. Low mental health scores over time were independently associated with a decrease in survival time from all-cause mortality by −0.06 (−0.10, −0.03; $P<0.001$), and they also significantly hastened time to first cardiac hospitalization by −0.08 (−0.13, −0.02; $P=0.01$) and composite of first cardiac hospitalization or cardiac death by −0.04 (−0.07, −0.02; $P<0.001$).

Conclusions This study found an independent association between poor mental health over time and all-cause mortality, cardiac hospitalization, and the composite of cardiac death or cardiac hospitalization in hemodialysis patients. The results underscore the importance of attention to mental health related to cardiac complications and even death in dialysis patients.

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*Renal-Electrolyte Division, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; †Department of Medicine, National Health Insurance Corporation Ilsan Hospital, Goyangshi, Gyeonggi-do, Korea; ‡Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; §Center for Health Equity Research and Promotion, Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, Pennsylvania; and ‖Department of Psychiatry, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania

Correspondence: Dr. Mark Unruh, University of Pittsburgh School of Medicine, 200 Lothrop Street, PUH C-1111, Pittsburgh, PA 15213. Email: unruh@pitt.edu

Introduction

Despite improvements in the medical treatment of ESRD, the level of health-related quality of life (HRQOL) is still much lower for these patients than for the general population (1). Furthermore, there has been little progress in improving HRQOL of dialysis patients over the past decade (2), although routine follow-up of HRQOL is mandated by the US Centers for Medical Services. Low HRQOL has been associated with increased rates of hospitalization and death in dialysis patients (3–9). Among the components of HRQOL, self-reported mental health has been linked with higher mortality in dialysis patients in several studies (4–6,10,11). Most of these studies have only investigated the relationship between mortality and mental health at baseline and not mental health over time, although deterioration in HRQOL over time has been observed in dialysis patients (12,13).

The relationship between mental health and cardiac or infectious mortality in dialysis patients is particularly important, because they are the leading causes of death in dialysis patients. It has been reported that markers of impaired cellular immunity (decreased natural killer cell cytotoxicity) and inflammation (elevated IL-6, TNF-α, and C-reactive protein) are associated with psychological stress and depression (14). These immunologic markers have been associated with other medical illnesses such as cardiac disease, cancer, stroke, HIV/AIDS, and ESRD, suggesting that immune dysregulation may be a fundamental feature to both mental illness and its medical comorbidities (15). Dialysis patients with cardiac disease have a higher case fatality rate than nondialysis patients with heart disease, and the mortality rates secondary to sepsis in dialysis patients are several hundred-fold higher compared with the general population (16,17). There has been no large-scale study evaluating the effects of mental health on cardiac or infectious mortality in prevalent dialysis patients.

The Hemodialysis (HEMO) Study, a prospective, randomized, multicenter large clinical trial of prevalent hemodialysis (HD) patients provides an optimal opportunity to examine this issue because of the high prevalence of cardiac disease, the prolonged follow-up,

and the careful adjudication of all deaths for determination of cause (18). We, therefore, undertook this analysis to investigate the relationship between baseline mental health, mental health over time, and all-cause and cause-specific deaths and cardiac hospitalizations in a large cohort of HD patients.

Materials and Methods

Study Patients

The HEMO Study was a prospective, randomized, multicenter clinical trial of 1846 prevalent maintenance HD patients designed to explore the effects of dialysis dose and membrane flux on morbidity and mortality. Patient eligibility criteria have been described previously (19). The HEMO Study had very little missing data, and the follow-up intervals were uniform. At randomization and annually during 3 years of follow-up, the HEMO Study patients responded to a survey including the index of well-being and the kidney disease quality of life long form (KDQOL-LF) questionnaire. Standardized assessments of coexisting conditions with the use of the index of coexisting disease (ICED) were performed at randomization and annually. The patients were followed for 0.9–6.6 years, with a mean follow-up time of 2.8±1.8 years. The median number of repeated measure is three, and the maximum number is seven; most participants had two or more repeated measures.

The institutional review boards at the 15 participating institutions approved the study protocol, and written informed consent was obtained from all study participants. Enrollment began in March of 1995 and ended in October of 2000. This secondary analysis was approved by the University of Pittsburgh Institutional Review Board.

HRQOL

KDQOL-LF (20) assesses generic HRQOL using the Medical Outcomes Study short form 36 (SF-36) questionnaire as well as kidney disease-targeted HRQOL domains, including sleep quality scores. We selected physical functioning, bodily pain, and vitality domains among eight domains of SF-36 to control the number of comparisons; also, these domains have known association of mental health with physical function, pain, and fatigue. HRQOL questionnaires were either self- or interviewer-administered. The range of scores for all scales is from 0 to 100, with higher scores indicating better HRQOL. The sleep questions (10 items) assess subjective sleep initiation and maintenance as well as daytime drowsiness.

Mental Health Assessment

Mental health was assessed using the five-item mental health subscale of the SF-36. The mental health index (MHI) is derived from items asking respondents how often during the past month they have felt nervous, down in the dumps, calm and peaceful, downhearted and blue, and happy. There are six possible responses to the questions: (*1*) none of the time, (*2*) a little of the time, (*3*) some of the time, (*4*) a good bit of the time, (*5*) most of the time, and (*6*) all the time. Responses are scored between one and six. The score for each individual, therefore, ranges between 5 and 30. This score is then transformed into a variable ranging from 0 to 100 using a standard linear transformation, and higher scores reflect better mental health (21).

We divided patients into two groups based on their MHI score: patients with poorer mental health (MHI score$\leq$60) and patients with better mental health (MHI score$>$60). We chose a score of 60 as the cutoff point for this division, because it was the upper limit of the lowest quartile of MHI scores in our study. Additionally, it had good sensitivity and specificity for diagnosing depression in general population and chronic medical illness patients (22–25). MHI has also been used for detecting depressive symptoms in dialysis patients (10,11), and it was well correlated with the Beck Depression Inventory in a study of dialysis patients (26).

Outcomes Assessment

Primary outcomes of the study were all-cause and cause-specific mortality in the HEMO Study. Secondary outcomes were first cardiac hospitalization and composite of first cardiac hospitalization or cardiac death. Classifications of hospitalizations for cardiac and other causes of death were first determined locally and then reviewed by an outcomes committee. Causes of cardiac death include ischemic heart disease, congestive heart failure, and arrhythmia.

Covariate Selection

Multiple confounding factors previously reported to be associated with mental health and outcomes in the general population and dialysis patients were considered as covariates (27–29). Demographic and clinical factors included in the analysis were age, sex, race, education, marital status, history of cardiovascular disease (CVD), history of coronary artery disease (CAD), body mass index, blood pressure, smoking status, comorbidities (including ICED scores and diabetic status), dialysis vintage, treatment arms, sleep quality, and medication use. Laboratory values included white blood count, hematocrit, serum ferritin, serum albumin, serum creatinine, serum bicarbonate, calcium, and phosphorous.

Statistical Analyses

We summarized baseline variables using means and standard deviations for continuous variables and percentages for categorical variables. We tested differences in summary statistics using the Mann–Whitney test for continuous variables and exact chi-squared tests for categorical variables. To determine the baseline relationships between the dichotomized mental health variable and the covariates, we used univariable and multivariable logistic regression models. We selected baseline variables with $P<0.20$ in univariable logistic regression for inclusion in multivariable logistic regression models, which we built employing a stepwise selection procedure after forcing in age, sex, race, diabetes status, body mass index, and treatment arm. We investigated the relationship between dichotomized mental health groups and cause-specific morbidity and mortality using unadjusted and adjusted Cox proportional hazards regression with the Efron adjustment for ties. To include the longitudinal MHI scores as a dichotomized or continuous covariate in the survival models for all-cause or cause-specific mortality models, we employed two different methods. We employed the nonparametric Cox time-dependent covariate model to assess the impact of the current value of the MHI score on the hazard. We also employed joint

modeling techniques that accounted for the fact that there may be some degree of association between the longitudinal and survival submodels and thus, improvement of the precision of the estimate defining the association of the longitudinal MHI scores on survival. In essence, we can think of the joint model as a technique to reduce the bias in the estimation process for the longitudinal and survival models simultaneously. The degree of association between the longitudinal mental health score and cause-specific morbidity and mortality is measured by the coefficient on the association parameter linking the submodels together. This degree is referred to as the mean survival estimate, and it is interpreted as the change in mean survival time per unit change in the log odds of mental health or unit change in MHI score for dichotomized and continuous MHI scores, respectively.

Results

Comparison between Patients with Poorer Mental Health and Patients with Better Mental Health

Table 1 details clinical characteristics of patients by mental health group. When the patients were divided into the two groups using the dichotomous definition for poorer versus better mental health, patients with poorer mental health were more likely to have less than a high school education, be unmarried, have a significantly higher ICED score, and report use of β-blocker or sleep medication. Patients with poorer mental health also reported a significantly lower baseline HRQOL in the domains of vitality, bodily pain, physical functioning, and sleep quality ($P<0.001$).

Factors Related to Poor Mental Health at Baseline

The unadjusted and adjusted odds ratios are reported in Table 2 along with their 95% confidence intervals (CIs) and corresponding P values. Multivariable logistic regression revealed that being married and dialysis vintage had significant protective effects on mental health. However, having less than a high school education and using sleep medication were independently associated with poor mental health. The associations of medical comorbidities and β-blocker use with mental health were marginally significant after adjustment for other covariates. There was no significant association between treatment arm and baseline mental health.

Association of Poor Mental Health at Baseline and Outcomes

The unadjusted and adjusted associations of poor mental health at baseline with variable outcomes are shown in Table 3. Poor mental health at baseline was associated with all-cause mortality (unadjusted hazard ratio=1.17, 95% CI=1.02–1.36) and composite of first cardiac hospitalization or cardiac death (unadjusted hazard ratio=1.18, 95% CI=1.02–1.36) in unadjusted analyses, but the strength of these relationships was attenuated in adjusted analysis.

Association of Longitudinal Changes in Mental Health on Survival

The estimates of association obtained from the joint modeling of dichotomized mental health and cause-specific morbidities are reported in Table 4 along with their 95% CIs and P values. The association is interpreted as the change in mean survival time per unit change in the log odds of mental health for dichotomized MHI scores. A low mental health score ($\leq$60) during follow-up was associated with decreased survival time by 5.8% from all causes ($P<0.001$) and decreased survival time by 5.1% from infectious causes (P=0.06). There was no significant effect of poor mental health over time on cardiac death. However, poor mental health over time significantly hastened time to first cardiac hospitalization by 7.6% (P=0.01) and the composite of first cardiac hospitalization or cardiac death by 4.1% ($P<0.001$).

Sensitivity Analysis

To overcome results that were not completely model-dependent, we conducted sensitivity analysis using a joint model with MHI scores as continuous variables. It showed comparable results as follows. A 10-unit increase in MHI reduced the hazard of all-cause death by 11.8% (P=0.001) and the risk of cardiac hospitalization by 7.9% (P=0.01). In addition, a 10-unit increase in MHI ameliorated the risk of composite outcome of first cardiac hospitalization or cardiac death by 9.3% ($P<0.0001$). It was interesting to note that, despite the numerous biases in using the time-varying Cox model, we found approximately the same trends of results in time-varying Cox regression analysis (data not shown). We also got the same trends of results when we analyzed with cutoff of 52, which was used in another study (11).

Discussion

This study of data from a large trial of prevalent HD patients showed that longitudinal changes in mental health were associated with all-cause mortality, cardiac hospitalization, and a composite of cardiac mortality or first cardiac hospitalization. Although these findings are in accordance with previously published research (4–6), this study is the first investigation to show that poor mental health over time was associated with higher risk of cardiac morbidity as well as all-cause mortality in prevalent HD patients.

Our findings extend the findings in the work by Boulware *et al.* (11), which showed that MHI scores used for screening for depressive affect predict survival and CVD deaths in incident HD patients when assessed in a time-varying analysis but not when assessed only at baseline. The work by Kimmel *et al.* (30) showed the importance of following the course of depressive affect, because there was no significant association between baseline depressive affect and mortality in prevalent dialysis patients. In contrast, when depressive affect was treated as a time-varying covariate based on periodic follow-up assessments, it was significantly associated with mortality. The significant association of poor mental health over time with cardiac morbidity is particularly meaningful, because this result was significant even after adjustment for demographic risk factors, previous CAD history, and comorbidities. Poor mental health, including depression, is associated with an increased risk of developing CAD and cardiac mortality in the general population (31,32). Additionally, recent literature has examined both transient and persistent models of depressive symptoms prospectively predicting CVD. Among elderly

Table 1. Comparison between patients with poorer mental health and patients with better mental health

Characteristic	Total (n=1798)	Mental Health		P Value
		Poorer (MHI Score≤60; n=548)	Better (MHI Score>60; n=1250)	
Age (years)	57.7±14.1	57.3±14.0	57.9±14.0	0.27
Male (%)	43.7	44.9	43.1	0.50
African-American (%)	63.6	62.8	64.0	0.63
Currently working (%)	9.5	7.5	10.3	0.07
Less than a high school education (%)	37.8	44.4	34.9	<0.001
Married (%)	37.7	33.8	39.4	0.03
Currently smoking (%)	17.4	19.8	16.4	0.10
Time on dialysis (years)	3.9±4.4	3.6±4.0	4.0±4.5	0.17
High Kt/V (%)	50.0	49.1	50.4	0.64
High flux (%)	49.9	50.0	49.9	1.00
Residual kidney function of >200 ml/d (%)	12.3	11.2	12.8	0.39
SBP (mmHg)	151.0±25.5	151.0±26.6	151.0±25.1	0.95
DBP (mmHg)	81.2±15.3	81.9±15.5	80.9±15.2	0.12
BMI (kg/m^2)	25.5±5.3	25.3±5.2	25.6±5.3	0.34
Diabetic (%)	44.8	46.2	44.2	0.47
ICED score (%)				0.01
0 or 1	35.4	31.6	37.1	
2	31.2	30.1	31.7	
3	33.4	38.3	31.2	
Past history of CVD (%)	19.6	21.4	18.9	0.25
Past history of cardiac disease				
CAD (%)	39.0	42.0	37.8	0.09
CHF (%)	39.5	41.6	38.6	0.23
arrhythmia (%)	30.9	33.6	29.7	0.11
Laboratory values				
WBC count (1000/mm^3)	6.9±2.4	6.9±2.2	6.9±2.4	0.27
albumin (g/dl)	3.6±0.4	3.6±0.4	3.6±0.4	0.07
creatinine (mg/dl)	10.3±3.0	10.4±3.0	10.3±3.0	0.84
hematocrit (%)	33.6±4.6	33.8±4.4	33.5±4.7	0.32
log ferritin (ng/ml)	5.3±1.2	5.4±1.1	5.3±1.2	0.47
bicarbonate (mEq/L)	21.4±3.6	21.1±3.6	21.5±3.6	0.07
phosphorus (mg/dl)	5.8±1.9	5.8±1.9	5.8±1.9	0.68
Ca × P product	53.7±17.4	53.9±17.1	53.6±17.5	0.79
log iPTH (pg/ml)	5.1±1.2	5.1±1.2	5.2±1.2	0.10
Medications used (%)				
ACE inhibitor	24.9	24.6	25.0	0.91
β-blocker	30.0	26.5	31.6	0.03
α-1 blocker	6.6	7.4	6.3	0.41
EPO	90.6	91.0	90.5	0.79
sleep medication	25.3	36.1	20.5	<0.001
HRQOL measures				
SF-36 MHI score	71.7±19.3	48.1±12.1	82.0±11.0	<0.001
SF-36 vitality	50.1±21.8	37.7±19.1	55.5±20.7	<0.001
SF-36 body pain	62.8±27.9	51.6±27.0	67.6±26.8	<0.001
SF-36 physical functioning	48.2±26.9	41.2±26.7	51.2±26.5	<0.001
SF-36 PCS score	35.7±10.1	34.4±9.9	36.3±10.2	<0.001
SF-36 MCS score	49.9±10.9	38.7±8.4	54.7±8.0	<0.001
KDQOL sleep quality score	58.8±22.6	47.3±21.7	63.8±21.2	<0.001
Interviewed (%)	39.8	40.2	39.6	0.83

Data were expressed as mean ± SD. MHI, mental health index; SBP, systolic BP; DBP, diastolic BP; BMI, body mass index; ICED, index of coexistent disease; CVD, cardiovascular disease; CAD, coronary artery disease; CHF, congestive heart failure; WBC, white blood cells; iPTH, intact parathyroid hormone; ACE, angiotensin-converting enzyme; EPO, erythropoietin; HRQOL, health-related quality of life; SF-36, short form 36; PCS, physical component summary; MCS, mental component summary; KDQOL, kidney disease quality of life.

Table 2. Unadjusted and adjusted predictors of poor mental health at baseline

Characteristic	Crude Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)	*P* Value[a]
Age (years)[b]	0.99 (0.99, 1.00)	0.99 (0.99, 1.00)	0.11
Male (%)[b]	1.08 (0.88, 1.32)	1.14 (0.91, 1.43)	0.24
African-American (%)[b]	0.95 (0.77, 1.17)	1.02 (0.81, 1.30)	0.87
Currently working (%)	0.70 (0.48, 1.03)	c	
Less than a high school education (%)	1.49 (1.22, 1.83)	1.50 (1.20, 1.88)	<0.001
Married (%)	0.79 (0.64, 0.97)	0.77 (0.61, 0.97)	0.03
Currently smoking (%)	1.25 (0.97, 1.62)	c	
Time on dialysis (years)	0.97 (0.95, 0.99)	0.97 (0.94, 1.00)	0.03
High flux (%)[b]	1.00 (0.82, 1.23)	1.01 (0.82, 1.25)	0.91
BMI[b]	0.98 (0.97, 1.01)	0.99 (0.97, 1.01)	0.40
Diabetic[b]	1.08 (0.88, 1.32)	1.03 (0.81, 1.30)	0.83
ICED score			0.05
2 versus ≤1	1.12 (0.87, 1.44)	1.14 (0.90, 1.50)	
3 versus ≤1	1.44 (1.13, 1.84)	1.39 (1.06, 1.82)	
Past history of CAD (%)	1.19 (0.97, 1.46)	c	
Laboratory values			
albumin	0.78 (0.59, 1.04)	c	
bicarbonate	0.97 (0.95, 1.00)	c	
Medications used			
β-blocker	0.78 (0.62, 0.98)	0.79 (0.62, 1.00)	0.05
sleep medication	2.19 (1.75, 2.74)	2.32 (1.84, 2.95)	<0.001

CI, confidence interval; BMI, body mass index; ICED, index of coexistent disease; CAD, coronary artery disease.
[a]*P* values are for adjusted model.
[b]Forced in age, sex, race, flux group, diabetic status, and BMI.
[c]Variables not significant at $P<0.20$ in a stepwise selection procedure.

Table 3. Association of baseline poor mental health with all-cause mortality, cause-specific mortality, and cardiac hospitalization in Cox proportional hazards models

	Baseline Poor Mental Health (MHI Score≤60)	
	Crude hazard ratio (95% CI)	Adjusted hazard ratio (95% CI)
All-cause mortality	1.17 (1.02, 1.36)[a]	1.13 (1.00, 1.32)
Cause-specific mortality		
cardiac death	1.26 (1.00, 1.60)	1.20 (0.92, 1.57)
IHD death	1.20 (0.91, 1.60)	1.10 (0.81, 1.50)
HF death	1.50 (0.73, 2.90)	1.51 (0.68, 3.32)
arrhythmic death	1.03 (0.59, 1.80)	0.99 (0.54, 1.81)
death from other heart diseases	0.70 (0.32, 1.54)	0.70 (0.30, 1.61)
infectious death	1.10 (0.80, 1.52)	0.97 (0.68, 1.38)
First cardiac hospitalization	1.11 (0.95, 1.30)	1.00 (0.84, 1.19)
First cardiac hospitalization or cardiac death	1.18 (1.02, 1.36)[a]	1.10 (0.90, 1.25)

Adjusted for age, sex, race, currently working, less than a high school education, married, currently smoking, time on dialysis, flux group, index of coexistent disease score, history of coronary artery disease, serum albumin, bicarbonate, β-blocker use, and sleep medication use. MHI, mental health index; CI, confidence interval; IHD, ischemic heart disease; HF, heart failure.
[a]$P<0.05$.

persons, a significant and substantial excess risk of death and stroke or myocardial infarction was associated with an increase in depressive symptoms over time but not baseline depressive symptoms (33). Persistent depression symptoms were also associated with left ventricular hypertrophy and diastolic dysfunction but not when the depression symptoms measured a single time at baseline in the prevalent HD patients (34). The mechanism underlying the more significant association of persistent depressive symptom with CVD compared with transient depression is unknown. Previously, a study suggested that persistent depressive symptoms even when they are subclinical in severity, assessed three times at yearly intervals, are strongly associated with heightened platelet activation in dementia caregivers (35). In contrast, transient depressive symptoms were not significantly associated with platelet activation.

Table 4. Adjusted time-varying effects of longitudinal changes in mental health on all-cause mortality, cause-specific mortality, and cardiac hospitalization in a joint model

	Mean Survival Estimate	Percent Change in Mean Survival	*P* Value
All-cause mortality	−0.06 (−0.10, −0.03)	−5.8	<0.001
Cause-specific mortality			
cardiac death	−0.04 (−0.09, 0.01)	−3.9	0.11
IHD death	−0.04 (−0.10, 0.01)	−4.4	0.13
HF death	−0.01 (−0.16, 0.13)	−1.4	0.85
arrhythmic death	0.02 (−0.12, 0.15)	1.6	0.81
death from other heart diseases	−0.03 (−0.17, 0.10)	−3.2	0.64
infectious death	−0.05 (−0.11, 0.001)	−5.1	0.06
First cardiac hospitalization	−0.08 (−0.13, −0.02)	−7.6	0.01
First cardiac hospitalization or cardiac death	−0.04 (−0.07, −0.02)	−4.1	<0.001

Adjusted for age, sex, race, currently working, less than a high school education, married, currently smoking, time on dialysis, flux group, index of coexistent disease score, history of coronary artery disease, serum albumin, bicarbonate, β-blocker use, and sleep medication use. IHD, ischemic heart disease; HF, heart failure.

We used MHI scores from the SF-36 to assess mental health rather than mental component summary (MCS) scores, which may underestimate the mental health problems in dialysis patients (36). Although physical component summary and MCS scores from the SF-36 are representative of physical and mental wellbeing separately and are associated with various clinical outcomes, MCS is known to be imperfect for diagnosing accurate mental health problems (37–39). The MHI, meanwhile, has been validated to detect mental health, such as mood and anxiety disorders, in the general population (24,40), and also, it has good specificity and sensitivity for the detection of depressive symptoms in chronic medical illness and dialysis patients (10,11,25,26,41). Patients with poor mental health had significantly lower KDQOL sleep quality scores, and sleep medication use was significantly associated with poor mental health in our study. These results are consistent with the results of prior studies that found that poor sleep quality in HD patients was associated with depression and lower MCS scores (42,43). In addition, sleep medication use might conceal underdiagnosed and undertreated depression. For example, HD patients in Japan with symptoms of depression have been treated with benzodiazepines rather than antidepressants, a practice associated with higher mortality (44). Before prescribing sleep medications to patients with poor sleep quality, nephrologists need to pay close attention to detect hidden mental health problems. The possibility that some symptoms of depression result from or are aggravated by sleep medication use should also be considered.

The present study has several strengths. The data come from a large multicenter trial with several years of follow-up, providing an ideal dataset with which to examine the association of longitudinal changes in mental health with morbidity and mortality in prevalent HD patients. In addition, the joint model that we used in our analysis is unique in its ability to reduce the bias encountered when dealing with missing data in that it allows us to obtain more precise estimates of survival. We should also consider certain limitations of this work. First, the HEMO Study did not formally assess depression and anxiety. In the United States, however, widespread use of the KDQOL means that it is usual practice to evaluate mental health using the MHI. Second, the inclusion of only prevalent dialysis patients in the HEMO Study may have led to selection bias, which could render our results not applicable to incident HD patients. Third, the HEMO Study did not have data of insurance status, which is an important factor affecting patients' mental health and outcomes. Fourth, patients with poor mental health might disproportionally drop out of studies and/or not complete questionnaires, although the HEMO Study had very little missing data.

In summary, we found a significant association between poor mental health over time and cardiac hospitalization in prevalent HD patients independent of other known risk factors, and we also found a significant association of poor mental health with all-cause mortality and a composite of cardiac death or cardiac hospitalization. Our results emphasize the link between mind and body in patients with chronic illness and underscore the importance of attention to mental health for preventing cardiac complications and even death in dialysis patients. In addition to examining novel factors such as tryptophan depletion, which may contribute to the mental health burden of ESRD, it is time to consider exploring effective strategies that could improve mental health problems in these patients. Presently, short questionnaires such as the MHI may be more easily implemented in actual practice than longer instruments, thus permitting earlier assessment and treatment of troubled patients.

Although very few studies have evaluated the safety and efficacy of antidepressants in the CKD patient population, in the most of studies, treatment reduced depressive symptoms, which are closely associated with quality of life, cognitive impairment, and sleep quality (45). The recent meta-analysis of selective serotonin reuptake inhibitors in patients with depression and coronary heart disease showed that selective serotonin reuptake inhibitor use was associated with a significant decrease in coronary heart disease readmission and mortality rates in the general

population (46). Future studies are needed to clarify the potential impact of pharmacotherapy and/or psychotherapy on ESRD patient survival and cardiac complication in those patients with poor mental health.

Disclosures

None.

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