

Quality of Life in Patients With Chronic Kidney Disease: Focus on End-Stage Renal Disease Treated With Hemodialysis

Paul L. Kimmel and Samir S. Patel

The proper measures for assessing quality of life (QOL) in patients with chronic kidney disease (CKD) remain unclear. QOL measures are subjective or objective, functional or satisfaction-based, and generic or disease-specific. Treatment of end-stage renal disease with transplantation and treatment of anemia with erythropoietin in patients with CKD have been associated with dramatic improvements of QOL. Other factors such as age, ethnic or national background, stage of CKD, modality of dialytic therapy, exercise interventions, sleep disturbances, pain, erectile dysfunction, patient satisfaction with care, depressive affect, symptom burden, and perception of intrusiveness of illness may be associated with differential perception of QOL. Recent studies showed an association between assessment of QOL and morbidity and mortality in end-stage renal disease patients, suggesting the measures do matter. Further studies are necessary in patients with early stages of CKD and in children. QOL measures should include validated psychosocial measures of depressive affect, perception of burden of illness, and social support. The challenge for the next decade will be to continue to devise interventions that meaningfully increase the QOL of patients with CKD at all stages.

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The proper measures for assessing quality of life (QOL) in patients with chronic kidney disease (CKD) remain unclear.¹⁻⁴ Issues related to the tools used to assess QOL, the meanings of the measures, implications of comparisons and longitudinal change, and practical considerations regarding measurement remain controversial. Dissent still exists regarding the place of subjective compared with objective measures of QOL in patients with CKD.^{2,4,5}

The first tools to assess QOL in the United States were designed to evaluate diverse aspects of quotidian life, including sense of well-being, and satisfaction with health, marriage, income, housing, health, and satisfaction with life.^{6,7} Concepts identified by these surveys ranged from satisfaction to dissatisfaction, and pleasure to misery (positive and negative affect). The sample was intended to be representative of

the 48 contiguous United States, and included surveys of almost 13,000 people in 1957, 1971, 1972, and 1978.⁷ Normative data were collected across age ranges so QOL measurements could be assessed in relation to life stages. These original QOL measurements have been superseded for physicians, health care professionals, and policy makers by health-related QOL (HRQOL) measures, designed to assess the experience of patients in primary care and specialty settings, and with acute and chronic illnesses.^{4,8}

The domains of QOL for patients have been outlined as physical functioning, psychologic aspects, and social and interpersonal relationships.^{3-5,8} Another categorization of QOL for end-stage renal disease (ESRD) patients outlines assessments of functional status, health status, well-being, and patient satisfaction.⁹ In addition, recent emphasis has been placed on global QOL measurements,⁴ and assessments of patient satisfaction.¹⁰⁻¹³ Each of these domains can be divided into subsidiary parameters. For instance, physical functioning includes the ability to ambulate and perform activities of daily life such as bathing, and the ability to remain free of, or to obtain relief from, troublesome symptoms. Psychologic

Division of Renal Diseases and Hypertension, Department of Medicine, George Washington University Medical Center, Washington, DC.

Address reprint requests to Paul L. Kimmel, MD, Division of Renal Diseases and Hypertension, Department of Medicine, George Washington University Medical Center, 2150 Pennsylvania Ave NW, Washington, DC 20007. E-mail: pkimmel@mfa.gwu.edu

aspects of QOL include depressive affect and anxiety, and cognitive function, among others. Social aspects of QOL include the effects of perceived, received, and transmitted social support; marital and familial interactions; interactions with medical and dialysis personnel; and socioeconomic concerns such as financial burdens of illness, disability, and unemployment; and ecologic characteristics such as residence within a particular neighborhood or state.^{2,13} Global aspects of HRQOL include perceptions of illness burden, happiness and life satisfaction, satisfaction with care, and responses to direct questions regarding overall assessments of QOL.^{2,4,13} The ability to enjoy leisure activities might be viewed in terms of physical function, psychologic function, social function, and perception of burden of illness and happiness and life satisfaction. Similarly, the assessment of sexuality overlaps some of these domains. Finally, patients and practitioners have expressed interest in spiritual aspects of coping with life with a chronic illness.^{11,12,14}

Domains of HRQOL can be assessed by using objective or subjective measures.^{2,3,5} HRQOL can be measured using generic tools, which facilitate comparison between patients with different chronic illnesses, and between patients and the general population.^{2,3,5} In contrast, interest has developed over the past decade in evaluating the QOL of patients with ESRD using tools designed specifically to capture the symptoms and consequences of uremia and its treatment with hemodialysis (HD), peritoneal dialysis (PD), and renal transplantation.^{2,4,15-17} An alternative approach espoused has focused on the use of validated psychosocial measures to allow the comprehensible description of individual patients and patient populations, and to facilitate comparison between patient groups (such as those with ESRD and those with conditions such as chronic obstructive pulmonary disease or rheumatoid arthritis).²

This review concentrates on the assessment of QOL in patients with ESRD treated with HD because they represent the preponderance of ESRD patients in the United States and because controversy regarding the measurement tools is most marked regarding this group. We review the tools used to assess QOL in ESRD patients. This report assesses some recent factors associated with QOL in ESRD patients, including data on modality of therapy. Consideration is given to the question of whether these measures and their evaluation matter, especially regarding clinically important outcomes. Finally, recent studies of ESRD patients' QOL assessed in large populations are reviewed. The effects of renal transplantation and treatment with erythropoietin in patients with ESRD have been well appreciated,^{3,4,16-20} and will not constitute a focus of this review. This report represents an update to a review published several years ago.²

In a landmark study, Johnson et al²¹ assessed QOL in a small group of ESRD patients treated with different modalities of renal replacement therapies (RRTs) (renal transplant recipients and patients treated with dialysis), concentrating on established psychologic constructs, measures of physical functioning, and rehabilitation. Patients with functioning renal transplants had better function than those treated with HD. Importantly, there was no difference in affect between

the 2 groups, and mean levels of perception of QOL in the patients were considered normal. Patients with failed transplants had the poorest perception of QOL. The group argued for the use of psychologic evaluations in patients treated for ESRD. Simmons et al²² confirmed that patients with ESRD typically had perceptions of QOL that were in the range of those of people in the general population, although the studies were small. Patients with a functioning renal transplant, however, had improved perceptions of QOL. Patients with failed renal transplants, in contrast, had significantly decreased perceptions of QOL. The group outlined a conceptual approach to the measurement of QOL, including assessments of physical well-being, emotional well-being, social well-being, and happiness with treatment. The tools used to assess physical function included a symptom checklist, an activities of daily life scale, an assessment of hospitalizations, and a subjective health evaluation scale.^{4,22} The scales used assessed depressive affect, self-esteem, independence, control over destiny, and included the Campbell index of well-being, as measures of emotional status. Social function measures included occupational status, satisfaction with life roles, and assessments related to perceptions of sexuality.^{4,22} These findings were confirmed shortly after in a large well-designed study by Evans et al.²³ They showed that QOL and functional status (using Karnofsky scores) were greater in patients with functioning renal transplants compared with ESRD patients treated with HD. Other QOL measures included assessments of life satisfaction, well-being, and affect. Successful transplantation conferred a QOL comparable with that of the general population. Since that time, numerous studies, including some quite large investigations, using diverse measures, have confirmed these findings consistently^{3,4,16,18,19,24,25} in contemporary ESRD populations, notwithstanding improvements in dialytic techniques and immunosuppression over the decades.

Some QOL Measures for ESRD Patients

A seemingly enormous number of scales have been used to assess QOL in patients.¹ Gill and Feinstein¹ advocated the use of more than 1 instrument in research studies of patient QOL to yield a diverse evaluation of patient status. In addition, they suggested the use of a simple instrument, perhaps a 1-sentence Likert scale, in which a patient is asked to evaluate his or her QOL, using those exact words.^{1,26} The measures used for assessing HRQOL in ESRD patients have been reviewed previously.^{2-4,8,16}

A widely used HRQOL measure, particularly in early studies of ESRD patients, is the Karnofsky Performance Status Scale (KPSS)^{2,8} to quantify an individual's level of functioning. Scores range from 100, categorizing normal function, to 0, for death. Marking statements designate status such as requiring assistance, needing institutional care, and needing hospitalization. The scale was conceived originally as an objective measure for cancer patients, but the KPSS has been used in many studies of acute and chronic medical illness.

Typically a nurse or physician scores the scale. We have, however, used it as a subjective scale, administered to patients to assess their own perception of functional level. For subjective studies we modified the scale to end at 40 (disabled; requires special care and assistance). We also used the KPSS to compare the assessments of patients by physicians and spouses.²⁷ Interestingly, physicians scored patients at a higher level than spouses. Such data suggest family members, perhaps because of the burden of care in a dyadic relationship, or because of better knowledge, rate patients at lower levels of functional capacity than their physicians. Such disparities may help explain different perspectives on patient outcome as the stage of ESRD progresses. The KPSS has been criticized for lack of reproducibility and poor interrater reliability,²⁸ yet we have found it quite useful. HD patients often score in the range of 70 to 80, consistent with a performance status between being able to perform normal activity with effort (score, 80), and maintaining the ability to care for oneself but being unable to carry on with normal activities or perform active work (score, 70).

Comorbidity scales improve the usefulness and the subjective dimension of functional assessments.^{2,8} Such measures are essential to account for variations in medical illness, particularly in survival studies. We have used a severity of illness score composed of the modified product of the patient's age and relative mortality risk for comorbid illness, developed by Plough et al.²⁹ The hemodialysis (HEMO) study used the Index of Coexistent Disease score.³⁰ Symptom scores have been used since early studies,²² and continue to be generated^{11,17,31-33}

The Sickness Impact Profile (SIP)^{2,8,34} was developed as a subjective, general, non-disease-specific measure to assess the effects of the illness perceived by the patient. A total of 136 statements regarding 12 activities are used in the scale. Subscales include Physical Dimension, Psychosocial Dimension, and overall scores. The Psychosocial Dimension includes mental health and social relation scores. Scores range from 0 to 100 on subscales and total scales. It had been used about as frequently as the KPSS in patients with ESRD,^{3,8} and has been used in European studies of patients with ESRD.^{3,4,8,9}

The SF-36 Health Survey is a generic HRQOL measure used in the Medical Outcomes Study.^{2,8,9,35} Thirty-six items evaluate functional status, well-being, and perceptions of health status in 8 scales, scored from 0 to 100. Higher scores are associated with improved perception of HRQOL. The US general population scores range from 61 to 84, and have been disseminated widely. The norms can be adjusted for age. A Physical Component Score (PCS) is a summary of Physical Functioning, Role Physical, Bodily Pain, and General Health scores. The transformed mean is 50, with a standard deviation of 10. The Mental Component Score (MCS) summarizes Vitality, Social Functioning, Role Emotional, and Mental Health subscales, with the same transformed means and SDs. SF-36 summary scores more than 50 are greater than average, whereas scores less than 50 are less than average (Table 1).

The SF-36 has several potential uses. This generic survey can provide descriptive information and can be used to com-

Table 1 SF-36 Scales

Physical Functioning
Role Physical
Bodily Pain
General Health Perception
Vitality
Social Functioning
Role Emotional
Mental Health

pare populations. It can be used in individual patients to assess health status. It has been used to assess the course of ESRD patients longitudinally.³⁶ It has been used widely in ESRD patients, including in the Netherlands Cooperative Study on the Adequacy of Dialysis.^{37,38} The SF-36 also has been used in ESRD patients to measure HRQOL during erythropoietin treatment.³⁹ Patients with ESRD treated with HD had lower SF-36 scores compared with patients with other chronic diseases.¹⁵

Early attempts to create specific scales for patients with renal disease focused on symptoms. The Kidney Disease Questionnaire⁴⁰ provided a kidney disease-specific set of evaluations in 5 areas: Physical Symptoms, Fatigue, Depression, Relationships with Others, and Frustration. It was designed specifically for HD. A companion Kidney Transplant Questionnaire has been used to assess HRQOL in ESRD patients who have undergone renal transplantation.⁴¹

The Kidney Disease Quality of Life (KDQOL) instrument (dialysis version)¹⁵ is a self-report measure specifically developed for use with patients with ESRD treated with HD. It has become an extremely popular and widely used measure of HRQOL for patients with ESRD treated with hemodialysis. It is based on the SF-36, as the major measure of functioning and well-being, and is composed of its generic domains and items designed to assess aspects of uremia and its treatment by hemodialysis. These include a symptom/problem scale, an effects of kidney disease on daily life scale, and an employment status evaluation. Items to assess cognitive function were derived from the SIP.³⁴ Tools to evaluate quality of social interaction, sexual function, sleep, social support, patients' perceptions of encouragement by staff and their evaluation of their health status, and patient satisfaction were included from other sources or were derived for the KDQOL.¹⁵ Scale scores can be transformed into linear 0- to 100-point scores. Higher scores indicate more favorable perceptions. A shorter form, the KDQOL-SF, was developed because of concerns regarding the number of items and difficulty in patient effort and administration of the original version. The scales can be divided into 4 dimensions: Physical health (physical functioning, work status, role limitations caused by physical health, general health perceptions, pain, energy), mental health (emotional well-being, quality of social interactions, burden of kidney disease, social support, role limitations caused by emotional problems), kidney-disease issues (cognitive function, symptoms/problems, effects of kidney disease on daily life, sexual function, and sleep), and patient evaluation of care (patient satisfaction and per-

ceptions of staff encouragement). Social functioning is related to both the domains of physical and mental health.¹⁵ There are few questions regarding global satisfaction, social support, or marital satisfaction and conflict. This instrument has been criticized because of the difficulty in administration and the length of time needed for completion.

The use of the KDQOL has increased remarkably over the past several years. The KDQOL was used as a HRQOL measure in the National Institute of Diabetes, Digestive, and Kidney Diseases (NIDDK)-supported HEMO study.⁴² The HEMO study reported on its assessment of a large group of dialysis patients.^{42,43} The mean PCS of the HEMO patients was lower than the national average, but the mean MCS was comparable with the national norm.

Life satisfaction scores also have been proposed as generic, subjective, global, nondisease-specific QOL measures.^{2,13} The Satisfaction With Life Scale (SWLS)⁴⁴ is a 5-item scale with a 1 to 7 satisfaction rating for each item, which we have used extensively.^{2,13,29,45-47} The items ask about ideal life, conditions of life, and satisfaction with present and past life. The scale exhibits good psychometric properties⁴⁴ and correlations with other subjective well-being scales. We have used the SWLS in our studies as a general global subjective QOL measure.^{29,45-47} The Index of Well-Being shares some characteristics of the SWLS.^{2,13}

Burden of illness constitutes the patients' perception of how the disease state interferes with, intrudes on, or disrupts his or her life.^{2,13} Patients with similar demographic and medical characteristics may experience markedly different perceptions of burden of the same illness. Such findings emphasize the dissociation of measures of illness intrusiveness from functional status assessments, and their possible association with measurements of general well-being, happiness, depression, and social support. Intrusiveness indices can assess the illness, its treatment, or overall perceptions. At least 2 instruments have been developed and used in ESRD patient studies to assess perceptions of illness intrusiveness. The KDQOL also has a subscale assessing the burden of kidney disease. The Illness Intrusiveness Rating Scale is a self-report index that rates the extent to which the illness interferes with 13 domains related to QOL.⁴⁸ It has good psychometric properties in ESRD patients.^{2,8,13} The Illness Effects Questionnaire (IEQ)^{2,13,29,49-51} assesses a patients' perception of how the illness interferes with, disrupts, or affects personal, physical, and social behavior. It is a subjective, generic, nondisease-specific instrument. The IEQ has excellent psychometric properties^{2,13,49,50} and we have used it extensively in our studies of patients with ESRD.^{2,10-13,29,45-47,51} Several groups have advocated the use of the IEQ as a QOL measure.^{2,13}

Depressive affect has been recognized increasingly as linked to many more traditional QOL measures.^{2,8,13,52-57} Measures of depressive affect and indices of depressive symptoms are included as items and scales in many QOL indices.^{2,8,13} The most commonly used assessment of depressive affect in HD patients is the Beck Depression Inventory (BDI).^{2,8,13,51-61} The Zung and Hamilton scales have been used in ESRD patients as well.⁵⁷ The BDI has somatic and

cognitive components, and provides cut-off values for the diagnosis of depression. Scores of 11 or greater are indicative of depression in the general population. We derived the Cognitive Depression Index,^{2,13,45-47,51,54,55} which presents questions from the BDI with the somatic items removed. This index delineates thoughts and feelings such as guilt, disappointment, and failure. The Cognitive Depression Index and the BDI, as expected, are correlated highly.^{45,54,55} Both depression indices correlate with the perception of illness effects (IEQ) in ESRD patients.^{45,51,54,55} Finkelstein's group showed high correlations of the BDI and the SF-36,⁵³ and we showed similar correlations of the BDI and the KDQOL.⁶² The Affect Balance Scale is another tool with good psychometric properties used to measure depressive affect in ESRD patients.^{2,8,13}

A single-question QOL scale, using the specific term, suggested by Gill and Feinstein¹ and Lara-Munoz and Feinstein,²⁶ has been used in several recent studies of dialysis patients by groups in Washington, DC (in conjunction with investigators in West Virginia and New York),^{4,11,12} and in New Haven, CT,⁶³ and in association with the Renal Research Institute. We showed a 1-question global QOL measure correlated with depression, number of symptoms, life satisfaction scores, perception of burden of illness, social support, and satisfaction with nephrologist scores, but not with age, level of albumin or hemoglobin, Kt/V, or Karnofsky score, showing its validity as a QOL measure.^{11,12}

Correlations, Interventions, and Outcomes

In this section, we describe some of the factors associated with QOL in patients with CKD. These summaries are not meant to be exhaustive. Rather they are meant to highlight nonmodifiable and modifiable factors that may be amenable to intervention. We discuss associations of age, ethnicity, socioeconomic status, modality of ESRD therapy, including renal transplantation, HD and PD, stage of disease, treatment with erythropoietin, and intensity of hemodialytic therapy with patients' perceptions of QOL. In addition, consideration is given to recent work on the relationship between exercise interventions, symptoms, disturbed sleep, pain, erectile dysfunction, patient satisfaction, depressive affect, perception of burden of illness, and spirituality with various QOL measures in selected studies, and we review recent studies that established links between patient assessments of QOL and morbidity and mortality.

As patient age increases, function-based HRQOL measures generally decrease.^{2-4,6,13,45} Functional status parameters have been shown by several investigators⁶⁴⁻⁶⁶ to predict survival when the variation in several demographic predictors is controlled. The Spanish Cooperative Renal Patients Quality of Life Study Group showed, in a group of 117 nondiabetic patients less than 65 years of age from several centers, that, as expected, age was correlated with poorer results in many SF-36 domains, even in a relatively young cohort of patients.⁶⁷ However, it should be noted that functional scores

often are not correlated with satisfaction scores, often are not subjective, and are insufficient for making judgments regarding continuation of dialytic therapy.^{2,13,45} Various QOL measures increase dramatically as age increases in the general population, such as satisfaction with housing, community, and neighborhood, and family and global life satisfaction.⁶ Satisfaction with health status is an exception, which decreases markedly along the course of life.⁶ We found SWLS correlated with greater age and worsened severity of illness. SWLS, however, did not correlate with Karnofsky scores, which correlate with age and comorbidity.⁴⁵ Therefore, global subjective satisfaction with life can be assessed in patients with ESRD and is related to subjective factors other than objective physical function as assessed by the medical staff on the KPSS. We found satisfaction with life is related significantly to better subjective levels of function, as assessed by the patient in a burden of illness scale.⁴⁵ Specifically, Karnofsky ratings, an objective functional measure of QOL, correlated with relatively few of the parameters of patient perception and satisfaction we assessed.^{2,11-13,45} In a study of 82 dialysis patients, age was associated with increased life satisfaction.⁶⁸ Kutner et al⁶⁹ noted similar associations in elderly black patients. Similar findings also have been noted in renal transplant recipients, in whom older patients have higher life satisfaction.⁷⁰ These findings show dissociation of feelings of satisfaction from functional measures in elderly ESRD patients.

It seems reasonable to summarize that although functional status of patients with CKD decreases with age, subjective QOL, particularly focusing on satisfaction with life, often remains high.^{2,3,13,45,71} Such considerations are of paramount importance in planning initiation and supervising decisions regarding withdrawal from RRT in the elderly, who constitute the fastest-growing portion of the ESRD population in the United States.

Recent studies have emphasized the longevity of children and adolescents who begin therapy for ESRD.⁷² In the United States, Australia, and New Zealand, the majority of young patients are treated with transplantation. Few studies on HRQOL have been performed in this population, and most tools cannot be completed by children.⁷³⁻⁷⁵ Long-term survivors have MCS comparable with that of the general population, but socialization and school progress can be impaired by comorbidities.^{73,74,76}

Several studies have suggested improved perception of HRQOL for black compared with white patients in the United States. Kutner and Devins,⁷⁷ using several subjective QOL measures in a group of 131 long-term survivors of dialysis therapy in Georgia, showed consistently higher scores for black compared with white patients. Lopes et al⁷⁸ found blacks had higher PCS, MCS, and Kidney Disease Summary scores compared with white patients. Bodily Pain, Vitality, General Health, Mental Health, Effects of Kidney Disease on Daily Life, Burden of Kidney Disease, Sexual Function, and Sleep Scores were better in black compared with white patients. Because these are subjective scores, the meaning of the differences is unclear. Hicks et al,⁷⁹ in a group of 1,392 dialysis patients from several regions across the

United States, showed black patients had better perception of overall health compared with white patients. In the HEMO study, blacks had higher Index of Well-Being scores and perceived less burden of kidney disease than white patients. There were no differences in scores on the MCS, social support, dialysis staff encouragement, or patient satisfaction scales between the 2 groups.⁴² The Dialysis Outcomes and Practice Patterns Study (DOPPS) showed clear differences between perceptions of domains of HRQOL between patients from Japan, Europe, and the United States.⁸⁰ These intriguing results, however, may be involved in mediating the paradoxical improved survival of black compared with white patients in the US ESRD program, and between US results and those of Europe and Japan.^{2,13}

Whether socioeconomic status (SES) is associated with disparities between ethnic populations in the United States is currently a matter of study, with implications for the ESRD program, and for patients with earlier-stage CKD. An interesting Brazilian study highlighted the association of SES and SF-36 scores in 118 incident dialysis patients, showing lower SES was related to poorer SF-36 scores and increasing functional decline over time.⁸¹

Transplantation provided the first evidence that QOL measurements could detect important differences in populations subsequent to powerful interventions.³ The SF-36, Kidney Transplant Questionnaire, Kidney Disease Questionnaire, KDQOL, and other instruments have been used extensively to evaluate the QOL of renal transplant recipients.^{3,19,82-84} Patients undergoing successful transplantation have an HRQOL greater than that of HD or PD patients, and comparable with that of the general population.^{3,16,18,19,21-23,84-90} The role of selection, however, must be considered in evaluating such dramatic results. Interestingly, differences have emerged regarding the type of immunosuppressive therapy used.^{16,83} Studies suggest improved HRQOL in patients treated with immunosuppressive regimens not using cyclosporine. Differences appear to be most marked regarding fatigue and perceptions of body appearance. Side effects of cyclosporine such as gingival hyperplasia and hair growth may be important factors affecting patients' perceptions of well-being when treated with a modality that they are told will result in improved QOL.^{16,83} Further well-designed studies are necessary to resolve such issues. The QOL in diabetic patients treated with kidney/pancreas transplantation may be enhanced by diabetic-specific concerns and affected by pancreatic transplant function.⁹¹

More emphasis needs to be given to the care and monitoring of patients with failed transplants, and those with progressive renal dysfunction with chronic allograft nephropathy. Assessments of donor and recipient QOL, depression, anxiety, and psychologic status will become important in the future.^{16,82,92} Psychotherapeutic intervention may be useful.^{16,93}

Although a question of great interest, few studies have compared the QOL of patients with ESRD treated with PD and HD. Problems in performance and interpretation of such studies include the small number of patients and selected samples of patients. Wolcott and Nissenson⁹⁴ found PD pa-

tients had better QOL and less perception of stress, but HD and PD patients did not differ in mean locus of control or self-esteem assessments. PD patients had better social and vocational status. Mittal et al⁹⁵ found the mean PCS score was lower in PD than HD patients, whereas MCS scores and the prevalence of depression (about one quarter of patients) were comparable in the 2 groups. The level of serum albumin was associated with PCS score.

Peritonitis may be an important determinant of QOL for PD patients.⁹⁶⁻¹⁰⁰ Subjective Global Assessment scores were associated with QOL scores (Physical Health, Mental Health, Kidney Disease Issues, and Patient Satisfaction) in a group of 88 British PD patients. QOL scores decreased over time (in particular, general health symptoms/problems, burden of kidney disease, emotional well-being, and patient satisfaction).¹⁰¹ In an interesting randomized controlled trial evaluating PD and HD patients, the assessment of QOL of participants was hampered by the inability to recruit a sizeable cohort.¹⁰² In a small study of 56 HD and 26 PD patients, no differences in depressive affect, life satisfaction, or sexual function could be shown between groups.⁶⁸ Harris et al¹⁰³ showed higher KDQOL scores in a group of elderly PD compared with HD patients at baseline, but the differences dissipated at 6 and 12 months. There was no difference in mean SF-36, EuroQol EQ 5-D, and 9 of 11 KDQOL scores at baseline in a cohort of 192 prevalent patients who had selected either HD or PD. Scores were stable over time in PD and HD patients.¹⁰⁴ These studies are hampered from providing meaningful conclusions because of small sample sizes.

Wasserfallen et al¹⁰⁵ surveyed 455 HD patients and 50 PD patients. Recruitment rates were more than 75%. The 2 groups were similar in age, sex, and duration of treatment for ESRD. QOL was similar in both groups, except for a perception of greater restriction of activities by the PD patients. Pain and discomfort and anxiety and depression had the most impact on QOL scores in HD and PD patients, respectively. In the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) study, a cohort of incident ESRD patients was enrolled between October 1995 and June 1998 at 81 dialysis units throughout the United States and prospectively followed-up.¹⁰⁶ A total of 698 HD and 230 PD patients completed the CHOICE Health Experience Questionnaire. A total of 585 patients had 1 year of follow-up evaluation. One hundred and one patients died; 55 patients had received a renal transplant and 88 patients were lost to follow-up evaluation. PD patients had better adjusted baseline HRQOL scores in the domains of Bodily Pain and Ability to Travel, fewer dietary restrictions, and fewer problems with sleep and dialysis access. SF-36 scores improved at 1 year in only a minority of patients. Some aspects of QOL related to renal disease improved, whereas others deteriorated. HD patients had greater improvements in Physical Functioning and General Health perception than PD patients. Changes in other domains varied between treatment modalities. HD patients had better perception of sleep quality. HRQOL assessments were similar at 1 year in PD and HD patients. PD patients were more likely to note improvement in body image. The number of differences at baseline and longitudinally between patients treated

with different modalities was small. Such data suggest patient/physician selection biases, including personality, and psychosocial and socioeconomic factors might have important effects on the perception of HRQOL and the factors associated with specific modalities of dialytic therapy, especially in incident patients. Differences between patient populations have been reviewed by Lew and Piraino.⁹⁶

Few studies have assessed HRQOL systematically in patients with chronic renal insufficiency. Harris et al¹⁰⁷ used the SIP to evaluate 360 patients with serum creatinine concentrations greater than 1.5 mg/dL. As expected, patients were less affected by illness than a comparable group of ESRD patients treated with dialysis. Socioeconomic factors correlated with increased disability, and medical comorbidities and hypoalbuminemia were associated with poorer SIP scores. Rocco et al¹⁰⁸ found worsened renal function (measured by glomerular filtration rate) was associated with decreased scores on the Quality of Well-Being instrument, which was related to socioeconomic status. Symptoms also were associated with differential glomerular filtration rate. Valderrabano's group studied HRQOL in patients with CKD, and found progressive deterioration over time.³ We studied 57 patients treated with dialysis for ESRD and 16 patients with chronic renal insufficiency (CRI) using the BDI and IEQ.⁵¹ Patients with CRI were recruited in an outpatient setting at the time they were being scheduled for vascular access for dialysis. Their mean creatinine concentration was 5.4 ± 3.4 mg/dL. Levels of perception of burden of illness, depressive affect, and role disruption were comparable with those of the ESRD patients. In a later study, we assessed 50 patients with CRI at various stages in the outpatient setting.¹⁰⁹ The mean stage of CKD was lower than that of the aforementioned study. Levels of depressive affect and perception of burden of illness were minimal. Satisfaction with life scores and depressive affect were similar among patients with early and late stage CKD. IEQ scores, BDI scores, and SWLS were intercorrelated. There were few correlations of psychosocial factors and estimated creatinine clearance in this small study. In a large Australian study, SF-36 scores were poorer for patients with renal insufficiency.¹¹⁰ Mental Health was impaired prominently in younger patients.

In the African-American Study of Kidney Disease (AASK) study of patients with CRI, presumed to be caused by hypertensive nephrosclerosis, the mean PCS scores were lower than the MCS scores. Many factors were associated with PCS scores (such as socioeconomic factors, body mass index, and comorbid medical conditions) whereas fewer factors predicted MCS scores. The mean PCS score for the cohort was less than that of the US general population, whereas the MCS score was higher. SF-36 scores, as expected, were higher than those of a comparison group of black hemodialysis patients.¹¹¹ The Chronic Renal Insufficiency Cohort will study QOL longitudinally in a large group of carefully characterized patients with CKD in the United States.¹¹²

A recent European study suggested early referral of patients with CRI to nephrologists, and particularly planning before the initiation of dialysis resulted in improved QOL in ESRD patients, as assessed by SF-36 MCS scores, physical

functioning, role physical, general health, role emotional, and mental health scores.¹¹³ In their review, Valderrabano et al³ suggested that better HRQOL in patients with early stages of CKD was associated with higher hematocrit level and socioeconomic status, whereas poorer perceptions were associated with the presence of comorbid illnesses and unemployment.

Perhaps the greatest utility of HRQOL measures was in assessing the response to erythropoietin therapy in patients with CKD,^{3,20,114-124} using tools as varied as the KPSS, KDQ, Index of Well-Being, SIP, and the SF-36. Therapy with erythropoietin improved role physical, vitality, and mental health SF-36 scores in a Spanish study of patients with chronic allograft nephropathy.¹²⁵

Manns et al¹²⁶ showed an association of SF-36 and KDQOL scores and Kt/V in 128 prevalent HD patients. Hamilton and Locking-Cusolito¹²⁷ reported an association of dose of dialysis and social and emotional well-being domains of the SF-36 and the KDQ in a small study of HD patients. The HEMO study assessed the effect of increasing dose of dialysis from eKt/V 1.05 to 1.45, and providing high-flux dialysis on QOL indices, using the Index of Well-Being and the KDQOL. There was no difference between groups in most of the QOL assessments over time. The mean decrease in the Physical Component Summary Score and the Bodily Pain scale was slower in the high-dose compared with the standard-dose group. High-flux patients had better perceptions of sleep. However, in all cases the effects were small.⁴³

Several studies have suggested that QOL is enhanced dramatically in patients with ESRD treated with quotidian dialysis.^{128,129} The generalizability of the studies are hampered by small sample sizes and highly selected populations. A multicenter randomized trial of quotidian dialysis is expected ultimately to determine whether increasing the intensity of dialysis by daily treatment will affect the QOL of HD patients meaningfully.

Several studies have suggested interventions to increase exercise are associated with improved QOL in patients with ESRD. Although this is not unexpected if the criterion is functional scores, some investigations have suggested effects on mood predominate.¹³⁰⁻¹³³

We found¹¹ an inverse relationship between patients' reported number of symptoms and the SWLS, the McGill QOL scale score, and the single-question QOL scale we used. Almost half the patients had troublesome symptoms during the 2 days before the interview. Patients with 2 or more symptoms had significantly lower QOL scores than patients with fewer than 2 symptoms. Symptoms were associated strongly with HRQOL measures in a study that included patients with advanced CKD about to start therapy for ESRD.¹³⁴ Parfrey et al¹⁷ identified sleep disturbance as a key symptom for HD patients. Rocco et al¹⁰⁸ found the common symptoms of patients with CRI were tiring easily, weakness, lack of energy, and difficulty sleeping.

It long has been held that there is a relationship between sleep disturbance and perception of QOL in ESRD patients.¹³⁵ Iliescu et al¹³⁶ showed that perception of disordered sleep measured by the Pittsburgh Sleep Quality Index corre-

lated with MCS and PCS scores. Patients with high levels of perceived sleep disturbance had a higher prevalence of depression. Parker et al¹³⁷ were unable to show a relationship between various QOL measures and most polysomnographic variables, however, there were correlations of the Health and Functioning scales with measures of sleepiness. Perhaps more importantly, subjective measures of sleep dysfunction were correlated with QOL measures. In contrast, Sanner et al¹³⁸ were able to show correlations of sleep-disordered breathing parameters and Physical Functioning, Social Functioning, Role Limitation, General Health, and Vitality scores in 33 HD patients.

We studied the association of perception of sleep disturbances and pain with QOL indicators such as depression and perception of burden of illness in 128 primarily urban, black, HD outpatients using the BDI, IEQ, single-sentence QOL scale, SWL, and Karnofsky scores. Sleep was evaluated using the Pittsburgh Sleep Questionnaire. We found, in preliminary studies, that parameters of sleep disturbances correlated with the single-question QOL, SWL, IEQ, and BDI scores, but not with demographic variables, treatment, or laboratory parameters.¹³⁹

Binik et al¹⁴⁰ highlighted the importance of pain as a symptom and its prevalence in HD patients more than 2 decades ago. Half of a Canadian HD patient cohort reported troublesome pain.¹⁴¹ Pain was associated with longer time since beginning RRT. In a study of 165 HD patients from West Virginia, Washington, DC, and suburban New York, we showed almost half had been bothered by pain as a symptom.¹¹ We studied the association of perception of sleep disturbances and pain with QOL indicators such as depression and perception of burden of illness in 128, primarily black, stable, HD outpatients in Washington, DC, using the BDI, IEQ, single-sentence QOL, and other QOL measures.¹³⁹ The majority of patients had pain on needle insertion during HD and on nondialysis days. The degree of pain on needle insertion and during HD did not correlate with demographic, treatment, laboratory, or QOL parameters. The degree of pain on nondialysis days, however, correlated with QOL parameters.¹³⁹

Several studies have linked erectile dysfunction to perception of HRQOL in men with ESRD. Rebollo et al¹⁴² found a relationship between age, SF-36 scores, and the presence of erectile dysfunction as measured by the International Index of Erectile Function 5 scale in a group of 199 renal transplant recipients. A Turkish study showed 70% of 148 hemodialysis patients had erectile dysfunction. Patients with erectile dysfunction generally had lower SF-36 subscale scores than patients without dysfunction. International Index of Erectile Function scores correlated with PCS and MCS scores.¹⁴³

We showed that patient satisfaction was associated with better behavioral compliance and higher serum albumin concentration in a largely black, urban hemodialysis population,¹⁰ suggesting that this parameter was linked with intermediary survival markers. Patient satisfaction correlated with SWLS and IEQ scores, suggesting it is a QOL measure. Patients' perceptions of satisfaction with the physicians and staff were not associated with the severity of patients' ill-

nesses. These data suggest patient perceptions of their nephrologists may be associated with factors associated with lower mortality rates. Therefore, physician interactions with ESRD patients may be an important aspect of their assessment of the quality of their treatment, and therefore their HRQOL, and may affect mortality. Although patient satisfaction was not associated with mortality in the international Dialysis Outcomes and Practice Patterns Study (DOPPS) survey, it is interesting to note differential patient satisfaction was associated with differential mortality in black patients, but not white patients, in the United States.⁷⁸ In the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) study, a cohort of incident ESRD patients was enrolled between 1995 and 1998 at dialysis units throughout the United States. Almost 90% returned questionnaires after a mean of 7 weeks of RRT. Patients treated with PD were more likely than HD patients to rate their care as excellent.¹⁴⁴

The Spanish Cooperative Renal Patients Quality of Life Study Group showed, in a group of nondiabetic patients less than 65 years of age, that anxiety and depressive symptoms were the most important predictors of HRQOL.¹⁴⁵ Walters et al¹⁴⁶ surveyed 422 incident HD patients in a multicenter sample, and found lower SF-36 scores than a comparison prevalent sample. Forty-five percent of the incident sample had an evaluation that suggested high levels of depressive affect. All SF-36 scores and 9 of the 12 KDQOL kidney disease targeted scales were lower in patients with high levels of depressive affect, compared with those with lower depression scores. These findings have implications for the potential association of depression and mortality in ESRD patients. High psychologic distress was associated with diminished QOL in dialysis and transplant patients over time.¹⁴⁷

In a study of HD patients from Washington, DC, West Virginia, and suburban New York, spiritual beliefs correlated with McGill QOL scale scores and SWLS, and the single-question QOL score.¹¹ We found significant correlations between patients' spirituality and religious involvement scores and greater satisfaction with life and higher QOL scores.¹² Higher spirituality scores correlated with lower perceptions of burden of illness scores. Higher religious involvement and spirituality scores correlated with lower levels of depressive affect. Higher spirituality scores correlated with increased perception of social support. These data suggest religious beliefs are associated with perception of QOL, and may be useful coping measures in HD patients.

The DOPPS is an international prospective observational survey of more than 17,000 hemodialysis patients from the United States, Europe, and Japan. Data regarding sociodemographic variables and laboratory and treatment parameters were collected at baseline between 1997 and 1999. The KDQOL-SF was used as the QOL measure. Only 58.2% of patients completed the QOL portion of the survey. Patients who completed the QOL screen were more likely to be healthier.⁸⁰ Physical functioning scores were highest for Japanese patients. MCS scores were higher in US compared with European patients. Japanese patients reported a higher burden of illness. These data point out the potential differential cultural and ethnic effects on perception of QOL, and the

critical dissociation of function-based measures from satisfaction-based parameters. The role of experimental demand in mediating these results remains unclear. Mortality risk was increased for patients who had lower PCS scores and higher Kidney Disease Component Summary scores.¹⁴⁸ In some analyses, there was increased mortality risk for patients with higher MCS scores. In Cox regression analyses, worsened PCS and MCS scores were associated significantly with increased risk for mortality and hospitalization. Worsened Kidney Disease Component Summary scores (symptoms/problems, effects of kidney disease on daily life, burden of kidney disease, work status, cognitive function, quality of social interaction, and sleep) were associated significantly and independently with increased risk for mortality and hospitalization. Lower perception of social support, dialysis staff encouragement, and decreased sexual function were associated with increased mortality risk but not with hospitalization. Interestingly, differential patient satisfaction was not associated with outcome in this study. Finally, the associations between KCDS scores and outcomes could be explained by variation in SF-36 scores. Lowrie et al¹⁴⁹ confirmed worsened PCS and MCS scores were associated with mortality and hospitalization in 13,952 prevalent patients in the Fresenius Medical Care North America database. Knight et al¹⁵⁰ confirmed worsened PCS and MCS scores were associated with mortality in 14,815 incident patients in the Fresenius database. Interestingly, the meaning of the MCS scores in this context is unclear.

Conclusions

The proper measures of QOL in patients with renal disease are unknown. Measures include subjective and objective tools, and generic and disease-specific scales. The past several years have witnessed an explosion in the number of studies and the populations of patients with CKD in which various aspects of HRQOL have been assessed. It is clear that the many QOL measures are intertwined. A challenge remains to make these domains clinically meaningful. The meaning of the MCS remains unclear. Satisfaction and emotional measures and the functional aspects of HRQOL must be assessed. Psychologic assessments hold the best promise for accomplishing this goal because it is clear psychologic distress, anxiety, and depressive affect have enormous impact on traditional HRQOL measures. Recent large studies have shown associations of measures of HRQOL and important outcomes, such as risk for hospitalization or death. Differences in perceived HRQOL may explain differences between survival in different ethnic and national groups. The role of satisfaction-based measures, including affect, sense of well-being, and happiness need to be investigated further. Studies of QOL are needed in patients with early stages of CKD and in children. The subjective experiences of burden of illness, depressive affect, satisfaction with life, and care undoubtedly are important, however, the challenge remains to assess these domains in a meaningful way at the level of the individual patient, and to devise effective interventions to enhance QOL and extend quantity of life.

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