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Health related quality of life in patients with chronic kidney disease

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Abstract. Monitoring a patient's functional status and the subjective state of well being as it related to health condition, together known as health related quality of life (HRQOL) measurements, is of particular importance in patients with chronic kidney disease (CKD) including those with end stage renal disease (ESRD). The concept of quality of life in dialysis has evolved since the inception of renal replacement therapy from simple survival to enjoying a certain level of well being. The measurement of dialysis outcomes have paralleled the improvement in the delivery of renal replacement therapy progressing from level of functioning, symptom checklists, multi dimensional well being, and moving perhaps to more patient centered quality of life. HRQOL domains have been strongly associated with objective patient outcomes. The self reported physical functioning and mental well being correlate with serum albumin and body composition measures. The ability of those on hemodialysis to self administer questionnaires is a barrier to the widespread use of multidimensional HRQOL assessment in clinical practice. However, new technologies using computer adaptive testing and item response theory may allow those questionnaires to be quickly and more efficiently administered by clinic staff. The finding of different HRQOL scores among CKD patients of different racial and ethnic backgrounds supports the need to individualize the concept of HRQOL, so that we can assess the crucial aspects of life in our patients and integrate these domains into a comprehensive plan of care. These recent findings underline the critical need to measure HRQOL and to expand the boundaries of our multidimensional tools with technology and a more patient centered concept of quality of life.

Key words: End stage renal disease (ESRD), Health related quality of life (HRQOL), Hemodialysis, Hospitalization, Kidney disease quality of life (KDQOL), Mortality, Short form 36 (SF36)

Introduction

The physical debility experienced by patients with uremia can be insidious and have grave consequences. Hence, monitoring a patient's functional status and the subjective state of well being as it is related to health condition, together known as health related quality of life (HRQOL) measurements, is of particular importance in patients with chronic kidney disease (CKD) including those with end stage renal disease (ESRD) [1–4]. HRQOL measurements are based on a patient's "subjective" sense of well being and are commonly used as an important clinical measure for beneficial extent of medical treatments for patients undergoing maintenance hemodialysis (MHD), chronic peritoneal dialysis (CPD) or other types of renal replacement therapy such as kidney transplantation [4–6]. Furthermore, patient reports of HRQOL are recognized as providing important information about the impact of CKD or ESRD and its management on daily life in these patients [2, 6]. In recent years, more attention has been drawn toward reexamining the overall role and potential application of patient self reported states of well being and functioning by use of self administered HRQOL

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questionnaires in the dialysis population. HRQOL assessments may be used in patient care to screen for and prioritize problems, to improve communication between health care workers and patients, and to evaluate response to treatment. The concept of quality of life in dialysis has evolved since the inception of renal replacement therapy from simple survival to enjoying a certain level of well being. The purpose of this review is threefold. First, to outline the measurement of dialysis outcomes which have paralleled the improvement in the delivery of renal replacement therapy progressing from level of functioning, symptom checklists, multidimensional well being, and moving perhaps to more patient centered quality of life. Second, to review recent findings showing that self reported physical functioning and mental well being correlate with serum albumin, body composition measures, hospitalization, and patient survival. The finding of different HRQOL scores among CKD patients of different racial and ethnic backgrounds supports the need to individualize the concept of HRQOL, so that we can assess the crucial aspects of life in our patients and integrate these domains into a comprehensive plan of care. Third, we will suggest that these recent findings underline the critical need to measure HRQOL and to expand the boundaries of our multidimensional tools with technology and a more patient centered concept of quality of life.

Evolution of HRQOL measurement

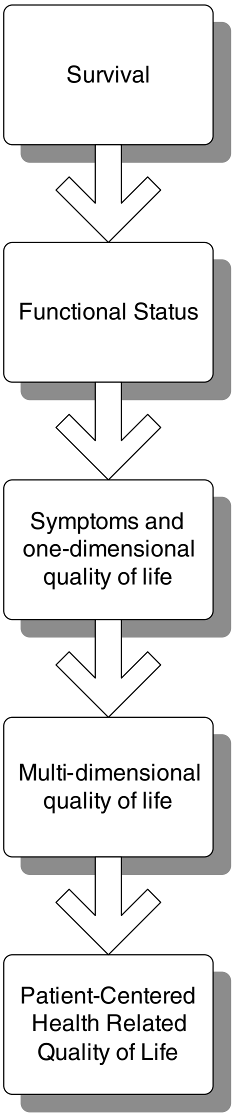

Figure 1. Evolving definition of successful therapy of chronic kidney disease.

In patients with kidney failure in developing countries, just having access to enough dialysis to survive remains the only outcome of significance. However, treatment of kidney failure in the industrialized nations has evolved over time as shown in Figure 1, so that patients have not only an expectation to survive, but they expect to achieve a certain level of well being [7, 8]. The assessment of physical functioning was an early outcome among clinical investigators [9, 10]. Next, investigators explored patient self report of symptoms, comorbidity checklists, and one dimensional HRQOL scales such as instruments measuring only bodily pain or social function [11–13]. More recently, patients have been assessed with multi-dimensional HRQOL assessments [14–17]. "Generic" multidimensional HRQOL measures are designed to provide information about function and well being that allows for comparison of individuals regardless of their specific condition. In contrast, "disease targeted" multidimensional HRQOL questionnaires collect information that is targeted towards the characteristics common to a subgroup of a population [18–20]. The most comprehensive assessment of HRQOL includes an assessment of both generic and disease targeted content [21]. In the future, it may be that patients demonstrate their own preferences for the domains of HRQOL that are important to them and weight the relative importance of these domains to their sense of well being. In addition to mental and physical domains assessed by most multidimensional HRQOL instruments, some have conceptualized that quality of life is a highly individual construct that should reflect the expectations and achievements of the individual.

Functioning

Over several decades, the subjective description of patient functioning has become an accepted tool in clinical research. Earlier studies, using tools such as the Karnofsky Performance Status Scale relied on observation of the patient by others, and focused on physical function [22]. The Karnofsky Performance Status (KPS) Scale was developed in the 1940s to measure the functional status of patients undergoing cancer chemotherapy. It is an ordinal scale ranging from a score of 100 (''Normal, no complaints'') to 50 (''Requires considerable assistance and frequent medical care'') to 0 (''Dead''). Table 1 shows all of the KPS categories. KPS has been in use for half a century and has been applied to many ESRD populations [23–26], and therefore allows wide comparison. However, it has several limitations. First, it focuses exclusively on physical functioning and on role limitations imposed by physical health; it does not inquire about other areas of experience, such as mental health, sleep or pain. Second, although some investigators have asked patients to assign scores to themselves, KPS was designed, and is generally used, as an observer-based tool. Several studies show relatively poor agreement between two observers assigning KPS scores. In one study using two nephrologists rating hemodialysis patients, the kappa statistic measuring agreement between the raters was 0.29 [9]. While self rated physical functioning has been a robust predictor of survival outcomes, self reported physical functioning has moderate reliability among the hemodialysis population compared to accelerometry that objectively measures movement [27, 28].

Symptom and comorbidity checklists

While functional status scores permit assessment of physical limitations, responses of patients to individual items may be of interest in clinical practice. Clinimetrics is concerned with the measurement of subjective symptoms for improved clinical care and research [29]. Patients undergoing renal replacement therapy have been shown to have physical symptoms such as fatigue, poor appetite, and poor sleep quality [30–33]. As Table 2 demonstrates, many of the first 1000 HEMO Study participants were also bothered by particular symptoms [2, 34]. The symptoms are ranked in descending order according to the proportion of subjects who reported being bothered at all by a symptom. Thus, the first symptoms listed are those bothering the largest proportion of subjects at least ''somewhat.'' The most common symptoms, bothering at least 60% of subjects, were dry skin, itchy skin, lack of strength, excessive thirst, fatigue and weakness,

Table 1. Karnofsky Performance Scale (KPS)

Karnofsky index	Definition
100	Normal, no complaints, no evidence of disease
90	Able to carry on normal activity; minor symptoms of disease
80	Normal activity with effort; some signs and symptoms of disease
70	Cares for self; unable to carry on normal activity or do active work
60	Requires occasional assistance but is able to care for most of own needs
50	Requires considerable assistance and frequent medical care
40	Disabled; requires special care and assistance
30	Severely disabled; hospitalization is indicated although death not imminent
20	Very sick; hospitalization necessary
10	Moribund; fatal processes progressing rapidly
0	Dead

feeling washed out or drained, dry mouth, muscle soreness, trouble sleeping, cramps during dialysis, and sleepiness during the day. In contrast, more than 60% were not at all bothered by faintness or dizziness, trouble getting your breath, swelling of ankles, loss of taste, chest pain, and clotting or other problems with access site.

While the scale scores allow for group comparisons, these patient responses to kidney disease specific items may also give providers improved familiarity with patient experience. The scores may guide clinicians when describing to patients what life is like on MHD. The kidney disease specific scales suggest that well dialyzed patients are not experiencing frequent chest pains, shortness of breath or edema. On the other hand, Table 2 demonstrates that patients with ESRD commonly have symptoms associated with skin, thirst, and fatigue. While patients may provide this information on a self assessment, they often will not voice these concerns to their physician unless prompted [35]. Disease specific measurement has the advantage of

Table 2. Severity of symptoms and problems among first 1000 participants in the HEMO Study (all results are%)

Symptoms	Not at all	Somewhat	Moderately	Very much	Extremely
Dry skin	21	27	16	23	13
Itchy skin	26	31	17	16	11
Lack of strength	27	32	20	15	6
Excessive thirst	28	25	16	19	12
Fatigue, weakness	29	33	19	14	5
Washed out or drained	29	35	18	13	6
Dry mouth	30	32	15	15	8
Soreness in your muscles	35	29	18	14	4
Trouble sleeping	37	27	12	13	10
Cramps during dialysis	38	35	14	9	5
Sleepiness during the day	38	35	16	9	3
Joint pain	41	24	15	14	6
Numbness in the hands or feet	42	27	13	12	7
Stiffening of joints	43	26	16	11	4
Low blood pressure	44	30	14	8	4
Ache in bones	44	26	15	11	4
High blood pressure	45	22	17	11	5
Blurred vision	47	27	11	8	8
Back pain	49	22	13	10	6
Headaches	50	27	14	6	3
Trouble with memory	50	29	13	6	2
Muscle spasms or twitching	52	23	15	8	3
Lack of appetite	53	23	12	8	3
Nausea or upset stomach	53	28	10	7	2
Hot or cold spells	54	24	13	7	3
Cramps after dialysis	56	28	8	6	2
Easy bruising	58	19	11	9	4
Shortness of breath	58	24	11	5	3
Trouble concentrating or thinking	58	24	11	5	2
Faintness or dizziness	62	23	10	4	2
Trouble getting your breath	65	21	8	4	2
Swelling of ankles	66	22	7	4	1
Loss of taste	67	18	9	4	2
Chest pain	70	19	8	2	1
Clotting or other problems with your access site	77	11	7	3	2

relating closely to areas of importance to clinicians [36]. These symptoms are often neglected although they have a major adverse effect on HRQOL. The quantitative measurement of these symptoms may improve the patient's health status by leading clinicians to treat the problems thereby improving compliance with therapy and commitment to maintain overall well being [37].

Multi-dimensional HRQOL assessment: SF36

The World Health Organization characterizes health as a state of mental, physical and social well being [38]. Consistent with this construct of health, the SF36, a short form HRQOL scoring system with 36 items, is a self administered questionnaire that was constructed to fill the gap between much more lengthy surveys and relatively coarse single-item measures of the HRQOL [4, 39, 40]. Figure 2 shows the structure of SF36 scoring system [4]. It consists of 36 questions, 35 of which form into eight multi-item scales: (1) physical functioning is a ten-question scale that captures abilities to deal with the physical requirement of life, such as attending to personal needs, walking, and flexibility; (2) role-physical is a four-item scale that evaluates the extent to which physical capabilities limit activity; (3) bodily pain is a two-item scale that evaluates the perceived amount of pain experienced during the previous 4 weeks and the extent to which that pain interfered with normal

ITEMS	SCALES	Dimensions	
3. Vigorous activities	Scale 1: Physical Functioning (PF)	Dimension A: PHYSICAL HELTH	
4. Moderate activities			
5. Lift, carry groceries			
6. Climb several flights			
7. Climb one flight			
8. Bend, kneel			
9. Walk mile			
10. Walk several blocks			
11. Walk one block			
12. Bathe, dress			
13. Cut down time	Scale 2: Role-Physical (RP)		
14. Accomplished less			
15. Limited in kind			
16. Had difficulty			
21. Pain-magnitude	Scale 3: Bodily Pain (BP)		
22. Pain-interfere			
1. General health rating	Scale 4: General Health (GH)		Dimension B: MENTAL HELTH
36. Excellent			
34. As healthy as anyone			
33. Sick easier			
35. Health worse			
23. Pep/life	Scale 5: Vitality (VT)		
27. Energy			
29. Worn out			
31. Tired			
32 Social-extent	Scale 6: Social Functioning		
20. Social-time			
17. Cut down time	Scale 7: Role-Emotional (RE)		
18. Accomplished less			
19. Not careful			
24. Nervous	Scale 8: Mental Health (MH)		
25. Down in dumps			
26. Peaceful			
28. Blue/sad			
30. Happy			
2. Change in reported health			

Figure 2. The SF36 quality of life (QoL) scoring system and its scales and dimensions. Note that *Vitality and General Health* scales are overlapping components of both Physical Health and Mental Health dimensions. Question #2, self-evaluation of change in health during the past year (Reported Health), does not belong to any score, dimension or the total SF36 score [4].

work activities; (4) general health is a five-item scale that evaluates general health in terms of personal perception; (5) vitality is a four-item scale that evaluates feelings of pep, energy, and fatigue; (6) social functioning (SF) is a two-item scale that evaluates the extent and amount of time, if any, that physical health or emotional problems interfered with family, friends, and other social interactions during the previous 4 weeks; (7) role emotional (RE) is a three-item scale that evaluates the extent, if any, to which emotional factors interfere with work or other activities; and (8) mental health is a five-item scale that evaluates feelings principally of anxiety and depression. Hence, in the SF36 scoring system, the scales are assessed quantitatively and independent of each other [4].

Each scale is on the basis of answers to two to ten multiple choice questions, and a score between 0 and 100 is then calculated on the basis of well-defined guidelines, with a higher score indicating a better state of health. The scales of SF36 are summarized into two dimensions or domains, also called "components" or "component summaries". The first four to five scales make up the "physical health" dimension (or physical summary component, (PCS)), and the last four to five form the "mental health"component (MHC) [4]. The scales vitality and general health can be parts of both dimensions (Figure 2). Hence, if the four-scale per dimension system is used, each dimension includes four mutually exclusive scales; and if the five-scale system is utilized, each dimension includes three specific and two overlapping scales 2. It should be noted that some of the specific (nonoverlapping) scales of the two summary components may still have correlations with each other. For instance, The Social Functioning scale, included in the MHC, is also significantly correlated with the PHC [41]. The SF36 also includes a question about self-evaluation of change in health during the past year (reported health) that does not belong to any score or dimension or the total SF36 score. The scores of the two dimensions and the total SF36 score are based on mathematical averaging of the scale components. Meyer and others have shown that repeated SF-36 responses from individual patients can be valuable tools in care of those with chronic kidney disease [15, 41].

Using the Microsoft Excel software program (Microsoft, Redmond, WA), we have designed a program based on well defined SF36 guidelines to perform automatic scoring of the scales, dimensions, and the total SF36 results 2. Our reformatted SF36 questionnaire (English version) and the programmed Excel sheet to calculate the results of SF36 analysis along with related instructions as how to perform the questionnaire and its scoring are posted on the internet under www.nephrology.rei.edu/qol.htm [4].

The SF36 is a well documented scoring system that has been widely used and validated as a HRQOL assessment tool for the general population as well as patients on MHD [15, 41]. It is used both as a stand-alone measure of HRQOL and as a core component of several major assessment tools, including the Kidney disease quality of life (KDQOL) survey instrument [2, 42–45]. The SF36 is one of the most commonly used instruments for HRQOL evaluation in patients with CKD with or without maintenance dialysis.

SF36 in patients with chronic kidney disease

Because of the increased use of the SF36, it has become possible to compare mean scale scores among groups of patients undergoing dialysis and between different populations of individuals. Several studies have reported that for the physical functioning, SF, and RE scales of the SF36, reliability estimates are the same or even slightly greater in patients undergoing dialysis compared with the nondialytic population [4, 14, 15, 41, 46]. Diaz-Buxo et al. [14] recently used the SF36 to compare the HRQOL in patients undergoing maintenance hemodialysis and chronic peritoneal dialysis and found that perception of HRQOL among these two groups was similar before adjustment but that patients undergoing peritoneal dialysis scored higher for mental processes after adjustments. Laws et al. [47] used the Subjective Globals Assessment to assess nutritional status in 69 patients on MHD and found that more severe degrees of malnutrition were associated with poorer HRQOL. Lowrie et al. [41] examined the relationship between SF36 and laboratory values and found that the SF36 score was significantly correlated with serum albumin, creatinine, and hemoglobin. Hypoalbuminemic MHD patients have lower HRQOL scores even after adjustment for demographic characteristics

[4]. In another recent study, the predialysis serum C-reactive protein (CRP) showed a weak correlation with SF36. Hence, it is possible that at least part of the correlation between albumin, a visceral protein and an acute phase reactant, and the SF36 may be due to the fact that serum albumin is a marker of malnutrition-inflammation complex syndrome (MICS) [4], an entity that may be associated with a worse HRQOL.

The KDQOL

The Kidney Disease Quality of Life (KDQOL^{TM}) assesses both generic and kidney disease-targeted HRQOL domains. The KDQOL family of survey instruments has been widely used in dialysis studies and has shown adequate reliability, validity, and responsiveness among diverse patient populations [2, 3, 16, 19, 48–51]. The internal consistency reliability and distribution of KDQOL scores have been previously described in the HEMO Study population [1, 2, 34]. The original KDQOL instrument included the SF36 as the generic core, supplemented with multi-item scales targeted at particular concerns of individuals with kidney disease and on dialysis: symptom/problems (34 items), effects of kidney disease on daily life (20 items), burden of kidney disease (4 items), cognitive function (6 items), work status (4 items), sexual function (4 items), quality of social interaction (4 items), and sleep (9 items). Also included are multi-item measures of social support (4 items), dialysis staff encouragement (6 items) and patient satisfaction (2 items), and a single-item overall rating of health [19]. A short form of the KDQOL, the KDQOL-SF, was derived that consisted of the SF36 plus a smaller set of 43 kidney disease-targeted items [3, 48, 51]. The KDQOL-SF has been used in HEMO and DOPPS studies [2, 3]. KDQOL-36 is an even briefer version of the KDQOL which includes the SF12 (short version of the SF36) as the generic core plus 24 (out of 43) kidney disease targeted items selected to constitute the three key kidney disease domains: burden of disease (4 items), symptoms (12 items), and effects of kidney disease (8 items) (See http: //gim.med.ucla.edu/kdqol and http: //www.nephrology.rei.edu/qol.htm). Use of the lean KDQOL-36 is recommended for large scale quality assurance evaluations in dialysis facilities to minimize patient burden during the annual assessment of patients and to improve compliance.

HRQOL as a predictor of mortality and hospitalization in ESRD patients

Several recent studies have shown that SF36 is a predictor of clinical outcome in dialysis patients[3, 4, 39, 41]. DeOreo et al. [39] showed that the SF36 provided a good screening tool for patients at high risk for death, hospitalization, poor attendance, and depression. Among the most recent studies, Kalantar-Zadeh et al. [4] examined 65 adult outpatients on MHD, the SF36 and its scales and dimensions, scored as a number between 0 and 100, and the nutritional and inflammatory state measured by subjective global assessment, near infrared (NIR) body fat, body mass index (BMI), and pertinent laboratory values, including hemoglobin, albumin, and CRP were assessed. Twelve month prospective hospitalization rates and mortality were used as the clinical outcomes. Multivariate (case-mix) adjusted correlation coefficients were statistically significant between SF36 scores and serum albumin and hemoglobin concentrations. There were significant inverse correlations between SF36 scores and the BMI and NIR body fat percentage. Hypoalbuminemic, anemic, and obese patients on MHD had a worse HRQOL. Prospective hospitalizations correlated significantly with the SF36 total score and its two main dimensions (r between −0.28 and −0.40). The Cox proportional regression relative risk of death for each 10 unit decrease in SF36 was 2.07 (95% CI, 1.08–3.98; $p = 0.02$). Of the eight components and two dimensions of the SF36, the MHD and the SF36 total score had the strongest predictive value for mortality. The authors concluded that in patients on MHD the SF36 appears to have significant associations with measures of nutritional status, anemia, and clinical outcomes, including prospective hospitalization and mortality. Even though obesity, unlike undernutrition, is not generally an indicator of poor outcome in MHD, the SF36 may detect obese patients on MHD at higher risk for morbidity and mortality [4].

The Dialysis Outcomes and Practice Patterns Study (DOPPS) investigators analyzed their data from an international, prospective, observational study of randomly selected MHD patients in the

USA (148 facilities), five European countries (101 facilities), and Japan (65 facilities) [3]. The total sample size was composed of 17,236 patients. Using the KDQOL, they determined scores for: (1) physical component summary (PCS), (2) mental component summary (MCS), and (3) kidney disease component summary (KDCS). Complete responses on HRQOL measures were obtained from 10,030 patients. Cox models were used to assess associations between HRQOL and the risk of death and hospitalization, adjusted for multiple sociodemographic variables, comorbidities, and laboratory factors. For patients in the lowest quintile of PCS, the adjusted relative risk (RR) of death was 93% higher (RR = 1.93, $p < 0.001$) and the risk of hospitalization was 56% higher (RR = 1.56, $p < 0.001$) than it was for patients in the highest quintile level. The adjusted RR values of mortality per 10-point lower HRQOL score were 1.13 for MCS, 1.25 for PCS, and 1.11 for KDCS. The corresponding adjusted values for RR for first hospitalization were 1.06 for MCS, 1.15 for PCS, and 1.07 for KDCS. Each RR differed significantly from 1 ($p < 0.001$). For 1 g/dl lower serum albumin concentration, the RR of death adjusted for PCS, MCS, and KDCS and the other covariates was 1.17 ($p < 0.01$). They concluded that lower scores for the three major components of HRQOL were strongly associated with higher risk of death and hospitalization in MHD patients, independent of a series of demographic and comorbid factors. A 10 point lower PCS score was associated with higher elevation in the adjusted mortality risk, as was a 1 g/dl lower serum albumin level [3].

Finally, Lowrie et al. [41] recently examined the data collected from 13,952 prevalent dialysis patients served by Fresenius Medical Care North America. Functioning and well being were measured via the SF-36 Summary scale scores, PCS, and MCS. Also collected was information about hospitalizations and patient mortality. PCS and MCS were consistent statistical predictors of hospitalizations and mortality rates even after adjustment for clinically relevant factors. They concluded that because PCS and MCS are associated with hospitalization and mortality, administering this self report measure may serve as a valuable supplement to clinical measures traditionally relied on to predict patient outcomes. Moreover, such information may be unavailable through any other single mechanism [41].

Hence, it is imperative to examine all aspects of possible associations between such health survey questionnaires as the SF36 and clinically relevant indices such as nutritional state, inflammation and anemia and to explore the potentials of such scoring tools in predicting relevant clinical outcomes. The tool has to be a well-established and adequately validated one, both inclusive and user-friendly, with optimal capability of serving as an interviewer independent, self administered questionnaire given the increasing time constraint involving health care personnel in charge of patients with ESRD. The SF36 may be a means to that end. Compared with those HRQOL tools that are tailored for patients undergoing dialysis, the SF36 has the advantage of being nonspecific, hence enabling the investigators to conveniently compare the health state of the patients with ESRD with nonESRD populations under diverse observational and interventional studies.

HRQOL measures in the HEMO study

The HEMO Study conceived HRQOL as a mental, physical and social construct, but also used kidney disease specific questions to examine the impact of kidney failure and its treatment on the lives of those supported by hemodialysis [1, 2, 34]. The HEMO Investigators examined existing instruments at the time of study initiations and adopted a survey that included both validated general instruments; the Index of Well Being and SF-36, as well as kidney disease targeted scales included in the KDQOL-LF. Additional items about the physical symptoms of patients on hemodialysis were included at the end of the survey. Because the KDQOL contains domains not measured in generic instruments, it was thought that those scales may be more sensitive to dialysis interventions and more representative of patient experience [19].

The HEMO study demonstrated that using these HRQOL instruments among the hemodialysis population demands resources to interviewer-administered surveys [34]. Previous studies of ESRD patients have included health status results from both self administration and interview-administration, but neglect to report the number of patients interviewed or adjust for mode of administration [3, 4, 39, 41]. Combining patient scores from different modes of administration may confound and make difficult the interpretation of scores. In addition, some authors have made comparisons between scores in different studies without accounting for mode of administration. For example, one study in ESRD reports SF-36 scores on self administered surveys from Italy, and compares these to previously published scores from patients in the United States and in England [51]. Since the scores from the United States reflected a mixture of self administered and interviewer administered surveys [15], any differences between the countries could reflect differences associated with survey administration. Despite potential bias in reporting of sensitive information about the participants' health status introduced by interviews, interviewer administered surveys were necessary in HEMO to achieve a high rate of item completion and were performed for over 40% of patients in the HEMO study for reasons of physical debility and patient preference [34].

Studies that have only included self administered HRQOL, may miss many patients. As previously noted, patients on dialysis frequently have problems with vision and also difficulty with manual dexterity given that arm range is limited during hemodialysis [35]. Interviewers also offer a clear advantage for those respondents who have difficulty in reading and writing. Finally, there are many people for whom an oral interview is easier than self administration, such as those who lack good reading and writing skills, whose first language is not English, or have difficulty seeing [52]. Perhaps the use of computer adaptive technology with voice recognition will ameliorate the burden of survey administration among those undergoing hemodialysis and allow instantaneous scoring of the survey.

Since the HEMO Study was a predominantly African-American patient population and since African Americans had been previously shown to have better survival outcomes, the HEMO investigators examined the association of HRQOL scores with African American race compared to those of predominantly Caucasian race. In adjusted models, African Americans had higher scores in the index of well being and burden of kidney disease, but lower scores in cognitive function (all $p < 0.05$) [1]. For scales reflecting Symptoms and Effects of Kidney Disease, Sleep quality, and the PCS, the fall in HRQOL with increasing comorbidity was significantly greater in non-African Americans (all $p < 0.05$). After adjustment, there were no racial differences in scores on the MCS, social support, dialysis staff encouragement, or patient satisfaction. We hope to examine if these differences affected health care utilization, medical decision making, and patient survival. The DOPPS has observed that African Americans showed higher HRQOL scores for all three components (MCS, PCS, and KDCS) compared to whites. Since the DOPPS Study included 6151 participants, the investigators were also able to examine other ethinic groups showing that compared to whites, Asians had higher adjusted PCS scores, but did not differ for MCS or KDCS scores; Hispanic patients had significantly higher PCS scores and lower MCS and KDCS scores; and Native Americans showed significantly lower adjusted MCS scores [53]. These investigators were also limited in explaining the cause of these HRQOL differences among the hemodialysis population.

The HEMO Study examined changes in HRQOL as a secondary study outcome [2]. Specific hypotheses were that study interventions would affect physical functioning, vitality, SF36 physical and MCS scores, symptoms and problems associated with kidney disease, and sleep quality. At baseline and annually, subjects responded to both the index of well being and the KDQOL long form questionnaires. The interventions were assessed on the basis of their average effects over 3 years. At baseline, the SF36 physical component summary score was lower than in healthy populations, but the mental component score was nearly normal. Over 3-year follow up, physical health continued to decline; mental health and kidney disease targeted scores remained relatively stable. The high dose hemodialysis intervention was associated with significantly less pain (4.49 points, $p < 0.001$) and higher physical component scores (1.23 points $p = 0.007$), but these effects were small compared to the natural variability in scores. High flux membranes were not associated with statistically significant differences in HRQOL. In conclusion, the HEMO Study results demonstrate the marked burden of chronic kidney failure and MHD treatment on daily life. In this trial among patients undergoing three times a week MHD, the SF36 physical component summary score and pain scale showed significant but very small clinical effects favoring the higher dialysis dose. No clinically meaningful benefits of either the dose or flux interventions were observed for other indices of HRQOL

Patient centered measures of quality of life

While recent clinical trials in chronic kidney disease have employed a multidimensional concept of quality of life, a recent notion in quality of life research supports the principle that quality of life is a highly personal construct that should mirror the expectations and achievements of the individual. Most HRQOL instruments used in dialysis patients are multidimensional instruments that assess physical, mental, and social domains [16]. On the other hand, a global measure of quality of life would assess the patient's overall satisfaction with his/her life. One of the drawbacks of these multi dimensional instruments is that they may fail to provide a meaningful global score that accurately represents the patients' satisfaction with life [54]. For example, a double amputee may describe very poor lower extremity physical functioning, yet rate his/her overall quality of life as being quite good [26]. In this circumstance, the score on a multi dimensional instrument may be low as a result of very poor physical functioning, but, the patient may perceive his or her quality of life to be quite good. This suggests that the domains measured by global instruments may not adequately assess specific areas that are critical to the individual patient. Moreover, many widely used measures are not patient centered for several reasons. First, the individual did not participate in generating the original items. Second, the questionnaire may restrict patients' choices of answers. Third, multi dimensional HRQOL instruments use weighting systems to score the instrument that neglect to incorporate individual patient values [54]. These limitations can compromise the accuracy and usefulness of individual measures. In a protocol examining quality of life of patients with kidney failure, we have used the schedule of evaluation of individual quality of life- direct weighting (SEIQOL-DW) [55]. The SEIQOL-DW is a patient centered measure of quality of life which is administered as a semistructured interview. The SEIQOL assesses three aspects of quality of life. It enables respondents to: (1) name the life areas which are important to their quality of life; (2) rate their current level of functioning in each of these salient areas, and; (3) rate the relative importance of these areas. In our experience to date of 20 patients, the patient elicited domains are often not captured on the SF–36. Many patients have cited family, marriage, sexual function, religious beliefs and work as critical domains to their perceived quality of life. Perhaps a combination of HRQOL instruments that include patient preference based domains of quality of life will provide a better understanding of patient experiences on renal replacement therapy.

Conclusions

Several recent studies have shown that subjective measure of HRQOL is a predictor of hospitalization and mortality in CKD patients undergoing dialysis 2, 10, 11. More efforts have been dedicated in exploring the potentials of patient self reported HRQOL questionnaires in high risk populations. The task is even more essential when it pertains to patients with ESRD, whose life prolongation via renal replacement therapy has left them with a different and less well known life style. Exploring the potentials of HRQOL questionnaires in patients with ESRD has been underscored by the contemporary emphasis on dialysis outcome research. Patients' subjectively perceived HRQOL status may not only be a clinically and psychosocially meaningful outcome *per se* but a predictor of more objective outcomes such as prospective hospitalization and mortality. If the SF36 or KDQOL, which each takes a few minutes of patient's time to complete, is a strong indicator of patient outcome and is indeed a predictor of morbidity and mortality in CKD patients, serial annual assessments of the HRQOL that use this simple tool might help to identify high-risk patients who may need intensified attention and risk modification interventions.

Improvement in HRQOL in patients with ESRD is a major goal of the ESRD program in the US. Several interventions, including higher hematocrit, physical therapy, and nocturnal hemodialysis have been shown to improve HRQOL [5]. Thus, there is a need to measure HRQOL among patients supported by renal replacement therapy, including patients with advanced age and comorbidity, in whom self-administration may be more difficult. Indeed, the development of new technology to measure HRQOL will be critical to including the patients most at risk in our assessments of quality of life. Lastly, nephrologists should consider supplementing multidimensional HRQOL with patient centered instruments that may more completely characterize that individual's quality of life.

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References

1. Unruh M, Miskulin D, Yan G et al. Racial differences in health related quality of life among hemodialysis patients. Kidney Int 2004; 65: 1482–1491.
2. Unruh M, Benz R, Greene T et al. Effects of hemodialysis dose and membrane flux on health related quality of life in the HEMO Study. Kidney Int 2004; 66: 355–366.
3. Mapes DL, Lopes AA, Satayathum S et al. Health-related quality of life as a predictor of mortality and hospitalization: the Dialysis Outcomes and Practice Patterns Study (DOPPS). Kidney Int 2003; 64: 339–349.
4. Kalantar-Zadeh K, Kopple JD, Block G, Humphreys MH: Association among SF36 quality of life measures and nutrition, hospitalization, and mortality in hemodialysis. J Am Soc Nephrol 2001; 12: 2797–2806.
5. Kutner NG, Jassal SV. Quality of life and rehabilitation of elderly dialysis patients. Semin Dialysis 2002; 15: 107–112.
6. Kimmel PL, Emont SL, Newmann JM et al. ESRD patient quality of life: symptoms, spiritual beliefs, psychosocial factors, and ethnicity. Am. J. Kidney Dis. 2003; 42: 713–721.
7. Rettig RA, Sadler JH: Measuring and improving the health status of end stage renal disease patients. Health Care Financing Rev 1997; 18: 77–82.
8. Rettig RA, Sadler JH, Meyer KB et al. Assessing health and quality of life outcomes in dialysis: a report on an Institute of Medicine workshop. Am J Kidney Dis 1997; 30: 140–155.
9. Hutchinson TA, Boyd NF, Feinstein AR et al. Scientific problems in clinical scales, as demonstrated in the Karnofsky index of performance status. J Chron Dis 1979; 32: 661–666.
10. Ifudu O, Brezsnyak WF, Reydel C et al. Pathobiology and functional status of long-term hemodialysis patients. Am J Nephrol 1995; 15: 379–385.
11. Kutner NG, Devins GM. A comparison of the quality of life reported by elderly whites and elderly blacks on dialysis. Geriatr Nephrol Urol 1998; 8: 77–83.
12. Johnson JP, McCauley CR, Copley JB. The quality of life of hemodialysis and transplant patients. Kidney Int 1982; 22: 286–291.
13. Parfrey PS, Vavasour H, Bullock M et al. Symptoms in end stage renal disease: dialysis vs transplantation. Transplant Proc 1987; 19: 3407–3409.
14. Diaz-Buxo JA, Lowrie EG, Lew NL et al. Quality-of-life evaluation using Short Form 36: comparison in hemodialysis and peritoneal dialysis patients. Am J Kidney Dis 2000; 35: 293–300.
15. Meyer KB, Espindle DM, DeGiacomo JM et al. Monitoring dialysis patients' health status. Am J Kidney Dis 1994; 24: 267–279.
16. Kimmel PL. Just whose quality of life is it anyway? Controversies and consistencies in measurements of quality of life. Kidney Int 2000; 57: S113-S120.
17. Kimmel PL. Psychosocial factors in adult end stage renal disease patients treated with hemodialysis: correlates and outcomes. Am J Kidney Dis 2000; 35: S132–S140.
18. Laupacis A, Wong C, Churchill D, Group TCES. The use of generic and specific quality-of-life measures in hemodialysis patients treated with erythropoietin. Control Clin Trials 1991; 12: 168S–179S.
19. Hays RD, Kallich JD, Mapes DL et al. Development of the kidney disease quality of life (KDQOL) instrument. Qual Life Res 1994; 3: 329–338.
20. Wu AW, Fink NE, Cagney KA et al. Developing a health related quality-of-life measure for end stage renal disease: the CHOICE Health Experience Questionnaire. Am J Kidney Dis 2001; 37: 11–21.
21. Bass EB, Jenckes MW, Fink NE et al. Use of focus groups to identify concerns about dialysis. Choice Study. Med Decis Making 1999; 19: 287–295.
22. Karnofsky D, Burchenal J. The clinical evaluation of chemotherapeutic agents in cancer. In: Maclead C ed. Evaluation of Chemotherapeutic Agents, New York, Columbia: University Press, 1949; 191–205.
23. Ifudu O, Mayers J, Matthew J et al. Dismal rehabilitation in geriatric inner-city hemodialysis patients [see comments]. JAMA 1994; 271: 29–33.
24. McClellan WM, Anson C, Birkeli K, Tuttle E. Functional status and quality of life: predictors of early mortality among patients entering treatment for end stage renal disease. J Clin Epidemiol 1991; 44: 83–89.
25. Jones KR. Risk of hospitalization for chronic hemodialysis patients. Lancet 1992; 339: 183.
26. Kimmel PL, Peterson RA, Weihs KL et al. Aspects of quality of life in hemodialysis patients. J Am Soc Nephrol 1995; 6: 1418–1426.
27. Johansen KL, Chertow GM, Ng AV et al. Physical activity levels in patients on hemodialysis and healthy sedentary controls. Kidney Int 2000; 57: 2564–2570.
28. Johansen KL, Painter P, Kent-Braun JA, et al. Validation of questionnaires to estimate physical activity and functioning in end stage renal disease. Kidney Int 2001; 59: 1121–1127.

29. Feinstein AR. An additional basic science for clinical medicine: IV. The development of clinimetrics. Ann Intern Med 1983; 99: 843–848.
30. Parfrey PS, Vavasour H, Bullock M et al. Development of a health questionnaire specific for end stage renal disease. Nephron 1989; 52: 20–28.
31. Simmons RG, Abress L. Quality-of-life issues for end stage renal disease patients. Am J Kidney Dis 1990; 15: 201–208.
32. Simmons RG, Abress L, Anderson CR. Quality of life after kidney transplantation. A prospective, randomized comparison of cyclosporine and conventional immunosuppressive therapy. Transplantation 1988; 45: 415–421.
33. Holley JL, Nespor S, Rault R. Characterizing sleep disorders in chronic hemodialysis patients. ASAIO Trans 1991; 37: M456–457.
34. Unruh M, Yan G, Radeva M et al. Bias in assessment of health related quality of life in a hemodialysis population: a comparison of self administered and interviewer-administered surveys in the HEMO study. J Am Soc Nephrol 2003; 14: 2132–2141.
35. Kurtin PS, Davies AR, Meyer KB et al. Patient-based health status measures in outpatient dialysis. Early experiences in developing an outcomes assessment program. Med Care 1992; 30.
36. Parfrey PS, Vavasour HM, Henry S et al. Clinical features and severity of nonspecific symptoms in dialysis patients. Nephron 1988; 50: 121–128.
37. Kutner NG. Assessing end stage renal disease patients' functioning and well being: measurement approaches and implications for clinical practice. Am J Kidney Dis 1994; 24: 321–333.
38. World Health Organization. The First Ten Years of the World Health Organization. Geneva, World Health Organization, 1958.
39. DeOreo PB: Hemodialysis patient-assessed functional health status predicts continued survival, hospitalization, and dialysis-attendance compliance. Am J Kidney Dis 1997; 30: 204–212.
40. DeOreo PB. The use of patient-based instruments to measure, manage, and improve quality of care in dialysis facilities. Adv Renal Replace Ther. 2001; 8: 125–130.
41. Lowrie EG, Curtin RB, Lepain N, Schatell D. Medical outcomes study short form-36: a consistent and powerful predictor of morbidity and mortality in dialysis patients. Am J Kidney Dis 2003; 41: 1286–1292.
42. Van Manen JG, Korevaar JC, Dekker FW et al. Adjustment for comorbidity in studies on health status in ESRD patients: which comorbidity index to use? J Am Soc Nephrol. 2003; 14: 478–485.
43. Walters BA, Hays RD, Spritzer KL et al. Health-related quality of life, depressive symptoms, anemia, and malnutrition at hemodialysis initiation. Am J Kidney Dis. 2002; 40: 1185–1194.
44. Valderrabano F. Quality of life benefits of early anaemia treatment. Nephrol Dial Transpl 2000; 15(3): 23–28.
45. Kutner NG, Zhang R, McClellan WM. Patient-reported quality of life early in dialysis treatment: effects associated with usual exercise activity. Nephrol Nurs J 2000; 27: 357–367 (discussion 368, 424).
46. Kalantar-Zadeh K, Block G, McAllister CJ et al. Appetite and inflammation, nutrition, anemia and clinical outcome in hemodialysis patients. Am J Clin Nutr: 2004; 299–307.
47. Laws RA, Tapsell LC, Kelly J. Nutritional status and its relationship to quality of life in a sample of chronic hemodialysis patients. J Ren Nutr 2000; 10: 139–147.
48. Carmichael P, Popoola J, John I et al. Assessment of quality of life in a single centre dialysis population using the KDQOL-SF questionnaire. Qual Life Res 2000; 9: 195–205.
49. Hyodo T, Yamamoto S, Inoguchi Y et al. Individual application of the kidney disease quality of life (KDQOL) instrument to monitor the health status of dialysis patients. Nephron 2000; 86: 391–392.
50. Korevaar J, Merkus M, Jansen M et al. Validation of the KDQOL-SFTM: A dialysis-targeted health measure. Quality of Life Research 2002; 11: 437–447.
51. Mingardi G, Cornalba L, Cortinovis E et al. Health-related quality of life in dialysis patients. A report from an Italian study using the SF-36 Health Survey. DIA-QOL Group. Nephrol Dial Transpl 1999; 14: 1503–1510.
52. Fowler FJ. Data collection methods. In Spilker B ed. Quality of Life and Pharmacoeconomics in Clinical Trials, Philadelphia: Lippincott-Raven, 1996.
53. Lopes A, Brag-Gresham J, Satayathum S et al. Health-related quality of life and outcomes among hemodialysis patients of different ethnicities in the United States: The Dialysis Outcomes and Practice Patterns Study (DOPPS). Am J Kidney Dis 2003; 41: 605–615.
54. Addington-Hall J, Kalra L. Who should measure quality of life? Bnit Med J 2001; 322: 1417–1420.
55. Hickey AM, Bury G, O'Boyle CA et al. A new short form individual quality of life measure (SEIQoL-DW): application in a cohort of individuals with HIV/AIDS. Bnit Med J 1996; 313: 29–33.

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