

# Association Among SF36 Quality of Life Measures and Nutrition, Hospitalization, and Mortality in Hemodialysis

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**Abstract.** Patients on maintenance hemodialysis (MHD) often show substantial reductions in quality of life (QoL). The SF36 (Short Form with 36 questions), a well-documented, self-administered QoL scoring system that includes eight independent scales and two main dimensions, has been widely used and validated. In 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 C-reactive protein 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 be-

tween SF36 scores and the BMI and NIR body fat percentage. Hypoalbuminemic, anemic, and obese patients on MHD had a worse QoL. 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 to 3.98;  $P = 0.02$ ). Of the eight components and two dimensions of the SF36, the Mental Health dimension and the SF36 total score had the strongest predictive value for mortality. Thus, 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.

Patients on maintenance hemodialysis (MHD) experience decreased quality of life (QoL) (1,2) and significantly greater rates of malnutrition, inflammation, hospitalization, and mortality compared with the normal population (3–5). QoL 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 on MHD (1,6). However, the association between this somewhat subjective outcome and other more objective measures, such as mortality and hospitalization, has not been well studied in these individuals.

Moreover, protein-energy malnutrition and inflammation are common complications in patients on MHD. Although the so-called malnutrition-inflammation complex syndrome (7,8) has been correlated with both hospitalization and mortality

rates, there are no data as to whether this syndrome is associated with adverse QoL.

The Short Form health survey with 36 questions (SF36) is a well-documented scoring system that has been widely used and validated as a QoL assessment tool for the general population as well as patients on MHD (9,10). It is used both as a stand-alone measure of QoL and as a core component of several major assessment tools, including the Kidney Disease Quality of Life survey instrument (11,12).

In this study, we used the SF36 to evaluate the QoL status in patients on MHD and examined the cross-sectional associations between this instrument and other pertinent clinical and laboratory values, including nutritional status and inflammatory measures. In addition, after the SF36 measurements were completed, the patients were monitored for 12 mo, and the propensity value of SF36 and its components to predict prospective hospitalization and mortality was explored.

## Materials and Methods

### Patients

The outpatient chronic dialysis program at the University of California Renal Center, San Francisco General Hospital, treated 92 adult patients on MHD at the time of the study. Inclusion criteria were those outpatients who had been undergoing MHD for at least 3 mo and who were  $\geq 18$  yr. Two patients were hospitalized in other centers at the

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time of the study, and two others had received dialysis for <3 mo. Out of 88 eligible patients on MHD, 65 individuals (35 men and 30 women) agreed to enroll in the study. The study was approved by the institutional review board, and written, informed consent was obtained from all participants. At the time of the study, patients' ages ranged from 22 to 87 yr (54.5 ± 15.8 yr), and the vintage (duration of chronic intermittent dialysis therapy) varied from 4 mo to 12 yr (41 ± 32 mo). Body mass index (BMI) was defined as the ratio of weight to height squared.

**SF36 QoL Scoring System**

The SF36, a short-form QoL 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 QoL (9,10).

Figure 1 shows the structure of SF36 scoring system. It consists of 36 questions, 35 of which are compressed 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 wk and the extent to which that pain interfered with normal 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 wk; (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, each 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 (9,10).

The scales of SF36 are summarized into two dimensions. The first five scales make up the "physical health" dimension, and the last five form the "mental health" dimension. The scales vitality and general health are parts of both dimensions (Figure 1). Hence, each dimension includes three specific and two overlapping scales (10). 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 (10,13). The scores of the two dimensions and the total SF36 score are based on mathematical averaging of the scale components.

To perform the SF36 measurements in our patients, we reformatted the questionnaire into a more user-friendly style without modifying the content of the original questions or their answers. We also translated the SF36 into Spanish and Chinese (Mandarin) for our non-English-speaking patients. Each translation was reviewed by two independent health-care providers who were proficient in both English and one of these other two languages, and the accuracy of the translations was certified. All participating patients were able to answer the SF36 questions independently within 7 to 25 min while undergoing hemodialysis treatment. Seven patients left several questions unanswered or gave more than one answer; they completed and corrected the inappropriately answered questions after their SF36 forms were handed back to them during the same or next dialysis session. No patient complained with regard to the clarity, relevance, or other aspects of the SF36 questions or its format.

Using Microsoft Excel 97, version 9.0 (Microsoft, Redmond, WA), we designed a program based on well-defined SF36 guidelines to perform automatic scoring of the scales, dimensions, and the total SF36 results. Our reformatted SF36 questionnaire (English version) and the programmed Excel sheet to calculate the results of SF36 analysis along with related instructions as to how perform the questionnaire and its scoring are posted on the internet as an appendix to this article ([www.nephrology.rei.edu/qol.htm](http://www.nephrology.rei.edu/qol.htm)).

**Subjective Global Assessment**

The subjective global assessment (SGA) of nutritional status, as it is commonly used in nephrology, is a semiquantitative scoring system based on the history and physical examination (14,15). The history consists of five components: weight loss during the preceding 6 mo, gastrointestinal symptoms, food intake, functional capacity, and comorbidities. Each of these features is scored separately as A, B, or C, reflecting well-nourished to severely malnourished categories. The physical examination includes two components: loss of subcutaneous fat and muscle wasting. The presence of edema or ascites is the third component of the original SGA physical exam, which is usually not used for patients undergoing dialysis. These two components are classified from 0 to 3, representing normal to severely abnormal. The

ITEMS	SCALES	Dimensions
3. Vigorous activities	Scale 1: Physical Functioning (PF)	Dimension A: PHYSICAL HEALTH
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		
14. Accomplished less		
15. Limited in kind		
16. Had difficulty	Scale 3: Bodily Pain (BP)	
21. Pain-magnitude		
22. Pain-interfere	Scale 4: General Health (GH)	Dimension B: MENTAL HEALTH
1. General health rating		
36. Excellent		
34. As healthy as anyone		
33. Sick easier		
35. Health worse	Scale 5: Vitality (VT)	
23. Pep/life		
27. Energy		
29. Worn out		
31. Tired	Scale 6: Social Functioning (SF)	
32. Social-extent		
20. Social-time	Scale 7: Role-Emotional (RE)	
17. Cut down time		
18. Accomplished less		
19. Not careful	Scale 8: Mental Health (MH)	
24. Nervous		
25. Down in dumps		
26. Peaceful		
28. Blue/sad		
30. Happy		
2. Change in reported health		

Figure 1. The SF36 quality of life (QoL) scoring system and its scales and dimensions. Note that the vitality and general health scales are overlapping components of both the 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.

data are weighted subjectively, and the patients are then classified in terms of three major SGA scores: A, well-nourished state; B, mild to moderate malnutrition; and C, severe malnutrition. In this study, numerical scores 1, 2, and 3 replaced A, B, and C, respectively. Details on the methods for SGA evaluation in patients undergoing dialysis are available on the Web site of the *American Journal of Kidney Diseases* ([http://www.ajkdjournal.org/abs31\\_2/ScoreSheet.htm](http://www.ajkdjournal.org/abs31_2/ScoreSheet.htm)) as the appendix to a recently published manuscript by one of the present authors (K.K.-Z.) (15).

### Near-Infrared Interactance

To evaluate the percentage of body fat and lean body mass, the near-infrared (NIR) interactance (16) was performed at the same time as the anthropometric measurements. A commercial NIR interactance sensor (portable Futrex 5000, Gaithersburg, MD) was used. NIR measurements were performed by placing a Futrex sensor on the nonaccess upper arm for several seconds, after entering the required data (gender, weight, height, and body frame size) from each patient, stipulating that the physical activity levels were uniform for all patients. It has been shown that NIR measurements of body fat correlate significantly with SGA and other nutritional measures in patients on MHD (16,17).

### Hospitalization

The hospitalization data were studied by assessing the frequency of hospitalization and its total duration in days, as defined recently by the United States Renal Data System report (18). Hospitalization data during the 12-mo period after the completion of the above measurements were obtained on all 65 patients on MHD. Hospitalization was defined as any hospital admission that included at least one overnight stay in the hospital (7). The admission day was counted as one full hospitalization day, but the discharge day was not. Therefore, the minimum duration of hospitalization per admission was 1 d. No exclusion criterion was used. Hence, hospital admissions for a variety of disorders were counted. However, because the vast majority of dialysis access related hospitalizations did not require overnight admission, essentially only those access-related hospitalizations were included that were associated with other comorbid conditions such as infection or cardiovascular events. For those few patients who were hospitalized at the start of the cohort, that hospitalization was not counted. For those patients who were in a hospital at the end of the 1-yr cohort, all hospitalization days during this last admission were counted. For those patients who died and those who left the cohort during the prospective follow-up, the hospitalization rates during the survival time were standardized by use of the factor 12/survival-time (in months) (7). The annual hospitalization days were the sum of all hospitalization days of a given patient during the 12-mo prospective cohort, as defined above. The annual hospitalization frequency was the total number of hospital admissions during the same period, irrespective of the length of each admission.

Moreover, the number of days at risk from the start of the study until the first hospitalization event for each individual per year was assessed. Accordingly, the risk time for each individual is defined as the days from study entry until the first hospitalization, a censoring event, or a study anniversary day occurs. A patient's risk period is truncated 3 d before transplant, to avoid attributing the transplant-related hospitalization to the observed days to event. This approach has been previously used by the United States Renal Data System in calculating the standardized hospitalization ratio (19).

### Laboratory Evaluation

The laboratory values, except for postdialysis serum urea nitrogen, which was used to calculate the urea reduction ratio, were measured

immediately before the initiation of dialysis treatment. The single pool  $Kt/V$  was used to represent the weekly dialysis dose, and the protein equivalent of total nitrogen appearance was calculated to estimate the daily protein intake (20). Serum C-reactive protein (CRP) was obtained to indicate the presence of an inflammatory state and was measured by the immunoturbidimetric method (Hitachi 747). The lower limit sensitivity of CRP assay was 6.9 ng/ml. Therefore, for patients whose serum CRP was reported to be <6.9 ng/ml, an arbitrary average of 3.4 ng/ml was used for statistical analyses. All laboratory measurements, including the CRP, were performed by Spectra Laboratories (Fremont, CA) by use of automated methods.

### Statistical Analyses

Hospitalization data were used as continuous outcome variables and the mortality as a dichotomized outcome. To determine the significance and strength of associations, we used Pearson's correlation coefficient  $r$  for analyses of associations between continuous variables. The  $t$  test (two-tailed) was used for group mean comparisons between male and female as well as between surviving and deceased patients. Multivariate regression analysis was performed to obtain partial (adjusted) correlations controlled for gender, age, race, and renal disease (case-mix adjustment). To calculate the relative risks of first hospitalization and death in the prospective cohort, we obtained hazard ratios and their 95% confidence intervals using Cox proportional hazard models, after controlling for the above-mentioned demographic variables. Plots of  $\log[-\log(\text{survival rate})]$  against  $\log(\text{survival time})$  were performed to establish the validity of the proportionality assumption (21). Each multivariate model included one outcome (dependent) variable and five predicting (independent) variables, *i.e.*, age, gender, race, underlying kidney disease, and the variable under study for that particular model ( $X$ ). Hence, the general multivariate model for Cox regression is

$$\lambda(t) = \lambda_0(t)[\exp(b_1\text{age} + b_2\text{sex} + b_3\text{race} + b_4\text{disease} + b_5X)],$$

where  $\lambda$  is the estimated hazard,  $t$  is time to event or censorship,  $b_1$  through  $b_5$  are coefficients of the model terms, and  $X$  is the predicting variable, including the SF36 result, its scales or dimensions, or other variables (SGA, BMI, NIR body fat,  $Kt/V$ , protein equivalent of total nitrogen appearance, or a pertinent laboratory measurement). Therefore, the association between each predicting variable and the outcomes (first hospitalization or death) was studied via separate multivariate models but with uniform case-mix adjustment for each model. Any 95% confidence interval that did not span 1.0 was considered to be statistically significant. Descriptive and multivariate statistics were carried out with the statistical software Stata, version 5.0 (Stata Corporation, College Station, TX), and the results were verified by use of a second statistical software, Statistica for Windows, Release 5.1 (Statsoft, Inc., Tulsa, OK). Fiducial limits are given as mean  $\pm$  SD.  $P < 0.05$  was considered to be statistically significant,  $P$  between 0.05 and 0.10 was considered marginal given the small sample size, and  $P > 0.10$  was NS.

### Results

Table 1 shows the demographic, clinical, and laboratory data. The women were, on average, 11 yr older than the men were, and this difference was statistically significant. The SF36 total score was slightly higher in men ( $58.2 \pm 17.1$ ) compared with that in women ( $50.6 \pm 17.1$ ), but this difference was not statistically significant ( $P = 0.08$ ). There were no statistically significant differences between the two genders in terms of

Table 1. Characteristics of 65 patients on maintenance hemodialysis according to gender<sup>a</sup>

	All Patients (n = 65)	Men (n = 35)	Women (n = 30)	P
SF36, total score (0 to 100)	54.7 ± 17.4	58.2 ± 17.1	50.6 ± 17.1	0.08
SF36, physical health (0 to 100)	48.0 ± 18.8	51.5 ± 19.4	44.0 ± 17.5	0.11
SF36, mental health (0 to 100)	55.7 ± 18.4	57.9 ± 17.4	53.9 ± 19.4	0.31
Annual hospitalization days	13.1 ± 26.3	15.1 ± 27.9	10.8 ± 24.7	0.52
Annual hospitalization frequency	1.83 ± 2.99	2.25 ± 3.65	1.33 ± 1.90	0.21
Age (yr)	54.5 ± 15.8	49.1 ± 15.7	60.8 ± 13.5	0.01
Dialysis months	41.1 ± 32.4	41.1 ± 30.4	41.0 ± 35.1	0.99
SGA (1 to 3)	1.86 ± 0.73	1.77 ± 0.73	1.97 ± 0.72	0.28
Near infrared measured body fat (%)	28.5 ± 8.3	24.3 ± 7.3	33.4 ± 6.6	<0.01
BMI (kg/m <sup>2</sup> )	25.5 ± 6.5	25.2 ± 6.1	25.9 ± 6.9	0.62
Serum				
albumin (g/dl)	3.79 ± 0.47	3.83 ± 0.55	3.74 ± 0.36	0.45
creatinine (mg/dl)	10.7 ± 3.2	12.0 ± 3.2	9.3 ± 2.5	0.01
cholesterol (mg/dl)	161.8 ± 31.0	156.9 ± 28.0	167.53 ± 33.78	0.17
hemoglobin (g/dl)	11.0 ± 1.6	11.3 ± 1.7	10.6 ± 1.4	0.06
ferritin (ng/ml)	799 ± 470	778 ± 468	823 ± 480	0.70
transferrin (mg/dl)	161.9 ± 37.2	168.9 ± 45.3	153.6 ± 22.7	0.09
iron saturation (%)	33.9 ± 11.8	36.2 ± 13.1	31.1 ± 9.5	0.08
intact PTH (ng/ml)	276.9 ± 234.6	253.9 ± 221.6	303.7 ± 250.0	0.39
C-reactive protein (ng/ml)	12.9 ± 15.6	12.3 ± 17.4	13.5 ± 13.4	0.75
Kt/V	1.38 ± 0.28	1.30 ± 0.23	1.48 ± 0.30	0.01
PNA (g/kg/d)	1.09 ± 0.26	1.09 ± 0.27	1.10 ± 0.25	0.92

<sup>a</sup> SGA, subjective global assessment; BMI, body mass index; PNA, protein equivalent of total nitrogen appearance, also known as PCR.

physical health or mental health dimensions. Women had significantly higher body fat ( $33.4 \pm 6.6\%$ ) compared with men ( $24.3 \pm 7.3\%$ ), but the BMI of both genders were essentially equal. The predialysis serum creatinine concentration was significantly higher in men ( $12.0 \pm 3.2$  mg/dl) compared with that in women ( $9.3 \pm 2.5$  mg/dl), which is probably due to a greater muscle mass and possibly to a higher meat intake in the men. Kt/V was significantly higher among women. Hemoglobin, serum transferrin, and the iron saturation ratio were slightly higher in men than in women, but the statistical significance of these differences were marginal ( $0.10 > P > 0.05$ ). No other statistically significant differences among two genders were observed.

Table 2 shows the raw (bivariate) and case-mix-adjusted (multivariate) correlation coefficients between the SF36 score, including its two main dimensions and prospective hospitalization data, as well as relevant demographic, clinical, and laboratory values. There were statistically significant correlations between the SF36 measurements (including its two dimensions) and the prospective annual hospitalization days and frequency of hospitalization ( $r = -0.28$  to  $-0.40$ ), denoting that patients with a lower QoL score experienced higher hospitalizations over the subsequent 12 mo period of time to the SF36 scoring. Significant inverse correlations between BMI and SF36 scores were observed, indicating that more obese patients with higher BMI values had lower QoL score (adjusted  $r = -0.31$ ,  $P = 0.02$ ). A similar trend was observed for body

fat percentage measured by NIR technology, although the correlation coefficients were slightly lower and the significance of the association disappeared with case-mix adjustment. The semiquantitative nutritional index SGA did not show any statistically significant correlation with the SF36 scores, but serum albumin did. Patients with higher serum albumin concentrations experienced greater QoL and physical and mental health scores. Among other laboratory values, only serum hemoglobin correlated significantly with the SF36 score, denoting that anemic patients had a worse perceived QoL. Serum CRP showed a weak, inverse correlation with SF36 ( $r = -0.22$ ,  $P = 0.08$ ), which became statistically insignificant after case-mix adjustment.

An additional analysis of hospitalization data was performed by studying the number of days from the start of the study until the first hospital admission (19). Thirty-five patients were hospitalized at least once, and 30 patients were not hospitalized at all during the 12-mo follow-up. The number of days to the first hospital admission varied between 13 and 352 d. When the Cox proportional hazard analysis was used on the basis of the time to first hospitalization, the relative risk (RR) of hospitalization for each 10 unit decrease in total SF36 score was 1.27 (95% confidence interval [CI] 1.01 to 1.59,  $P = 0.041$ ). Among the two major dimensions of the SF36, the physical health dimension score was also statistically significant, and the RR of first hospitalization for each 10-unit decrease in its score was 1.23 (95% CI, 1.01 to 1.51;  $P = 0.048$ ). A similar

**Table 2.** Comparison of raw and adjusted correlation coefficients *r* for the SF36 and its two major subcategories (physical health and mental health) against hospitalization data and pertinent clinical, laboratory, and demographic variables. Case-mix adjusted correlation coefficients (controlled for age, race, gender, and underlying renal disease) are indicated in parentheses.

	SF36 Total Score	SF36 Dimension A: Physical Health	SF36 Dimension B: Mental Health
Annual hospitalization days	−0.33 <sup>b</sup> (−0.34 <sup>b</sup> )	−0.28 <sup>a</sup> (−0.28 <sup>a</sup> )	−0.36 <sup>b</sup> (−0.36 <sup>b</sup> )
Annual hospitalization frequency	−0.36 <sup>b</sup> (−0.40 <sup>b</sup> )	−0.36 <sup>b</sup> (−0.40 <sup>b</sup> )	−0.36 <sup>b</sup> (−0.38 <sup>b</sup> )
SGA	−0.22 <sup>c</sup> (−0.16)	−0.18 (−0.10)	−0.16 (−0.12)
Near infrared body fat percentage	−0.29 <sup>a</sup> (−0.20)	−0.30 <sup>a</sup> (−0.23 <sup>c</sup> )	−0.26 <sup>a</sup> (−0.23 <sup>c</sup> )
BMI	−0.26 <sup>a</sup> (−0.31 <sup>a</sup> )	−0.29 <sup>a</sup> (−0.35 <sup>b</sup> )	−0.26 <sup>a</sup> (−0.31 <sup>a</sup> )
Serum			
albumin	0.32 <sup>b</sup> (0.30 <sup>a</sup> )	0.30 <sup>a</sup> (0.29 <sup>a</sup> )	0.27 <sup>a</sup> (0.25 <sup>a</sup> )
creatinine	0.04 (0.16)	0.03 (0.16)	0.00 (0.12)
cholesterol	0.07 (0.08)	0.07 (0.09)	0.10 (0.07)
intact PTH	−0.16 (−0.17)	−0.09 (−0.09)	−0.18 (−0.20)
hemoglobin	0.32 <sup>b</sup> (0.28 <sup>a</sup> )	0.30 <sup>a</sup> (0.27 <sup>a</sup> )	0.29 <sup>a</sup> (0.26 <sup>a</sup> )
perritin	−0.07 (−0.11)	−0.10 (−0.15)	−0.07 (−0.08)
transferrin	0.02 (0.08)	0.04 (0.15)	0.04 (0.07)
transferrin saturation	0.03 (0.06)	0.03 (0.05)	0.04 (0.01)
C-reactive protein	−0.22 <sup>c</sup> (−0.18)	−0.16 (−0.11)	−0.19 (−0.15)
<i>Kt/V</i>	−0.08 (−0.04)	−0.06 (−0.07)	−0.06 (−0.02)
PNA	−0.04 (−0.02)	−0.04 (−0.02)	−0.01 (−0.02)
Dialysis months	−0.10 (0.12)	−0.10 (−0.13)	−0.02 (−0.03)
Age (yr)	−0.20 (−0.15)	−0.20 (0.15)	−0.08 (−0.05)

<sup>a</sup> *P* between 0.05 and 0.01; <sup>b</sup> *P* < 0.01; <sup>c</sup> *P* between 0.10 and 0.05.

analysis for the mental health dimension was not statistically significant (RR, 1.20; 95% CI, 0.98 to 1.47; *P* = 0.76). Among other pertinent clinical and laboratory values, the SGA, serum albumin, and hemoglobin concentrations were the only other measures with statistically significant RR of first hospitalization.

During the 12-mo follow-up period, seven patients died (average time to death was 7.3 ± 3.0 mo) and five patients left the cohort, including two patients who underwent renal transplantation, two patients who were transferred to another location, and one patient who switched to peritoneal dialysis. Table 3 compares the characteristics of the deceased and surviving patients at the start of the cohort. The SF36 total score was significantly higher in surviving patients (56.3 ± 17.4) compared with those who died subsequently (41.4 ± 11.0). Among eight scales of SF36, bodily pain, SF, and RE had similar significant differences between surviving and expired patients. Among the two major dimensions of the SF36, the mental health dimension score was significantly higher in surviving patients (57 ± 18.1) when compared with that of deceased patients (38.2 ± 9.9), and this difference was statistically significant (*P* = 0.006). The physical health dimension score among surviving and deceased patients showed a similar trend, but the difference was not significantly different (*P* = 0.13). Surviving patients had significantly higher serum albumin and cholesterol levels, lower serum CRP concentrations, and more well-nourished SGA scores compared with the deceased patients.

Tables 4 and 5 describe the hazard ratios and their corresponding 95% CI of death by use of Cox proportional hazard models on the basis of the initial values at the start of the prospective cohort and the time to death. The model controls for age, sex, race, and underlying renal disease to estimate relative risks of death. In Table 4, only those values with statistically significant relative risks (*P* < 0.10) are listed, whereas in Table 5 the RR of death for SF36 and all its eight scales and two dimensions have been calculated for comparison. The SF36 total score showed a strong association with prospective mortality (Table 4). The relative risk of death for each 10-unit decrease in the SF36 score was 2.07 (95% CI, 1.08 to 3.98; *P* = 0.02), which denotes that patients with a lower QoL score had a significantly higher risk of death during the subsequent 12 mo. Among the nonlaboratory variables, only the SGA was significantly associated with dialysis mortality, exhibiting a relative risk of death of 8.68 for each unit of deterioration in SGA scale (95% CI, 1.85 to 40.61; *P* = 0.006). With regard to laboratory values, predialysis serum albumin was the strongest correlate with mortality (hazard ratio of 7.92 for each 1 g/dl decrease; 95% CI, 2.04 to 30.73; *P* = 0.003), and serum cholesterol had a similar correlative value for death (hazard ratio of 2.69 for every 10 mg/dl decrease; 95% CI, 1.48 to 4.89; *P* = 0.001). Serum CRP and creatinine were not quite significantly associated with annual mortality (Table 4). None of the other clinical, laboratory, and demographic variables

Table 3. Characteristics of 65 patients on maintenance hemodialysis according to survival

	Surviving Patients (n = 58)	Deceased Patients (n = 7)	t test P
SF36 total score	56.3 ± 17.4	41.4 ± 11.0	0.031 <sup>a</sup>
physical health	49.2 ± 19.0	37.8 ± 14.6	0.129
physical functioning	53.9 ± 27.7	55.0 ± 31.1	0.921
role-physical	39.7 ± 42.2	32.1 ± 42.6	0.658
bodily pain	57.7 ± 23.3	34.3 ± 16.4	0.012 <sup>a</sup>
general health	45.2 ± 22.7	30.6 ± 14.2	0.102
mental health	57.0 ± 18.1	38.2 ± 9.9	0.006 <sup>a</sup>
vitality	49.8 ± 18.4	37.1 ± 22.1	0.094
social functioning	64.4 ± 26.5	37.5 ± 10.2	0.010 <sup>a</sup>
role-emotional	63.8 ± 41.1	28.6 ± 40.5	0.036 <sup>a</sup>
mental health	66.1 ± 19.3	57.1 ± 17.8	0.248
SGA (1 to 3)	1.78 ± 0.702	2.57 ± 0.53	0.005 <sup>a</sup>
Near-infrared body fat (%)	28.9 ± 8.2	25.2 ± 9.0	0.266
BMI (kg/m <sup>2</sup> )	25.7 ± 6.8	23.8 ± 2.7	0.469
Serum			
albumin (g/dl)	3.86 ± 0.37	3.23 ± 0.81	0.001 <sup>a</sup>
cholesterol (mg/dl)	166.3 ± 28.5	124.4 ± 26.1	0.001 <sup>a</sup>
creatinine (mg/dl)	11.0 ± 3.0	8.9 ± 4.3	0.104
hemoglobin (g/dl)	11.0 ± 1.6	10.6 ± 1.8	0.571
ferritin (ng/ml)	839 ± 459	767 ± 456	0.469
transferrin (mg/dl)	160.4 ± 22.7	174.1 ± 98.2	0.359
transferrin saturation (%)	34.2 ± 11.4	31.3 ± 15.0	0.542
intact PTH (ng/ml)	286.9 ± 238.5	194.0 ± 193.9	0.326
C-reactive protein (ng/ml)	11.6 ± 14.1	23.5 ± 23.6	0.054
Kt/V	1.39 ± 0.29	1.31 ± 0.14	0.456
PNA (g/kg/d)	1.10 ± 0.2696	1.0171 ± 0.1293	0.420
Age (yr)	54.3 ± 15.5	55.9 ± 18.7	0.810
Dialysis months	40.3 ± 30.3	47.3 ± 49.1	0.594

<sup>a</sup> P < 0.05.

showed a statistically significant association with mortality on the basis of Cox proportional hazard modeling.

Table 5 compares the components of the SF36 in terms of their value in predicting mortality. Among the eight scale components of SF 36, bodily pain, SF, and RE had significant

hazard ratios of death. Similar to its relationship to hospitalization, the mental health dimension of the SF36, compared with the physical health dimension, showed a strong hazard ratio of 2.46 for each 10-unit decrease in its score (95% CI, 1.26 to 4.80; P < 0.01).

Table 4. Relative risk of death according to the Cox proportional-hazards model for SF36 and selected variables with P < 0.10 (adjusted for age, gender, race, and underlying renal disease)<sup>a</sup>

Variable (Increment and Direction)	Relative Risk of Death (95% Confidence Interval)	P
SF36 total score (every 10-unit decrease)	2.07 (1.08 to 3.98)	0.024
SGA (every one-unit increase)	8.68 (1.85 to 40.61)	0.006
Serum		
albumin (every 1 gm/dl decrease)	7.92 (2.04 to 30.73)	0.003
cholesterol (every 10 mg/dl decrease)	2.69 (1.48 to 4.89)	0.001
creatinine (every 1 mg/dl decrease)	1.25 (0.97 to 1.61)	0.083
C-reactive protein (every 10 ng/ml increase)	1.39 (0.98 to 1.97)	0.062

<sup>a</sup> The magnitude of increments and direction of change are described in parentheses.

Table 5. Cox regression-calculated hazard ratios of death for SF36 and its components and subcategories<sup>a</sup>

Scales and Summary Measures	Odds Ratio of Death	95% Confidence Interval	P	Pseudo R <sup>2</sup>	χ <sup>2</sup>
SF36 total score	2.07	1.08 to 3.98	0.02	0.1340	7.64
physical health	1.44	0.88 to 2.36	0.14	0.0671	3.83
physical functioning	0.98	0.70 to 1.33	0.84	0.0261	1.49
role-physical	1.05	0.86 to 1.27	0.63	0.0295	1.68
bodily pain	1.78	1.09 to 2.90	0.02	0.1545	8.81
general health	1.34	0.87 to 2.07	0.18	0.0619	3.53
mental health	2.46	1.26 to 4.80	<0.01	0.1984	11.32
vitality	1.47	0.94 to 2.30	0.09	0.0776	4.43
social functioning	1.50	1.05 to 2.14	0.02	0.1357	7.74
role emotional	1.30	1.02 to 1.65	0.03	0.1313	7.49
mental health	1.38	0.88 to 2.17	0.16	0.0612	3.49

<sup>a</sup> Odd ratios are based on 10-unit decrements in all QoL scores.

## Discussion

In this study, the score of the SF36, a self-administered questionnaire used to assess QoL, had significant correlations with serum albumin and hemoglobin and a strong association with prospective hospitalization and mortality in patients on MHD. The SF36 and its mental health dimension were found not only to reflect the simultaneous clinical condition of these patients but also to be significantly associated with subsequent 12-mo morbidity and mortality.

Monitoring a patient's functional status and the subjective state of well-being, together known as QoL measurements, is of particular importance in patients with end-stage renal disease (ESRD), because the physical debility experienced by patients with uremia can be insidious and have grave consequences (1,6,9). 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 QoL questionnaires in the dialysis population (9–12). The SF36 is one of the most commonly used instruments for QoL evaluation in patients undergoing maintenance dialysis and includes eight independent scales, each of which measures physical and mental aspects of functioning to varying degree (9,10). But the true utility and applicability of SF36 for patients with ESRD have not been fully elucidated.

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 (11). Diaz-Buxo *et al.* (9) recently used the SF36 to compare the QoL in patients undergoing maintenance hemodialysis and chronic peritoneal dialysis and found that perception of QoL among these two groups was similar before adjustment but that patients undergoing peritoneal dialysis scored higher for mental processes after adjustments. Laws *et al.* (22) used the SGA

to assess nutritional status in 69 patients on MHD and found that more severe degrees of malnutrition were associated with poorer QoL. Lowrie *et al.* (23) examined the relationship between SF36 and laboratory values and found that the SF36 score was significantly correlated with serum albumin, creatinine, and hemoglobin. Ohri-Vachaspati and Sehgal (24) showed that inadequate protein nutrition, as reflected by low serum albumin level and low protein catabolic rate, are independently associated with poor QoL. The results of our study are consistent with such findings. In our study, although we did not observe a strong correlation between the semiquantitative SGA and the SF36, we found that hypoalbuminemic patients had lower QoL scores even after adjustment for demographic characteristics. Because the predialysis serum CRP showed a weak correlation with SF36, 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 (7,8), an entity that may be associated with a worse QoL.

In this study, we found that the SF36 had a significant positive correlation with both the BMI and the percentage of body fat, as measured by NIR technology, which indicates that overweight outpatients undergoing MHD perceive a worse QoL when compared with less-obese individuals. Although this may be regarded as a contradiction to the assumed association between a poor nutritional state and lower SF36 score, the state of obesity should not necessarily be considered as being well-nourished. Han *et al.* (25) used SF36 to assess the QoL in >4000 healthy individuals and found that large waist circumferences and high BMI are more likely to be associated with impaired quality of life and disability affecting basic activities of daily living. Goller *et al.* (26) found that, in a group of patients undergoing chronic peritoneal dialysis, where a higher BMI is more frequently present than among patients on MHD, overweight patients had lower SF36 scores and were more impaired in physical functioning. If the association between obesity and poorer QoL in patients with ESRD can be

further verified, then the SF36 may be one of the only reliable tools to detect higher risk patients with poor clinical condition and outcomes among those patients who are usually considered as being “not malnourished” by the nutritional assessment tools such as the SGA. If a low SF36 score, an indicator of poor outcomes, has a significant negative correlation with the BMI and body fat, it is of interest, because the BMI has been shown to be associated with better outcomes in patients with ESRD (3,5). The explanation for this puzzling finding is unclear. One possibility is that the low QoL is a stronger predictor of poor outcome in patients on MHD than some of the nutrition indicators. Another alternative is that the QoL may be a better tool to distinguish among different subsets of BMI and to identify those obese patients on MHD that are at higher risk. However, because of the small sample size, subset analyses was not possible in our study.

Similar to our findings with regard to morbidity and mortality, two prospective longitudinal studies of functionally impaired elderly population found that the self-reported QoL score was independently predictive of mortality (27,28). McClellan *et al.* (29) reported that functional status and quality of life were strong independent risk factors for subsequent mortality in new dialysis patients. Ifudu *et al.* (30) showed that poor functional status measured by the Karnofsky score is associated with mortality. DeOreo (31) recently reported that an SF36 associated physical health dimension score below the median value was twice as likely to be associated with mortality and 1.5 times as likely with hospitalization. Lowrie *et al.* (32) found a similar association between both the physical and mental health dimensions of the SF36 and dialysis mortality.

In this study, we did not find any significant association between the physical health dimension of SF36 and mortality but showed that the mental health dimension displayed a stronger association with mortality among patients on MHD. Hence, it appears that patient’s reported perception of well-being and mental state, no matter how subjective it sounds, is indeed a strong correlate for subsequent outcome such as mortality. Kimmel *et al.* (33,34) showed that a depressed mental state among patients on MHD is associated with increased mortality. The mechanism for the causality between low QoL, especially low mental health dimension, and increased hospitalization and mortality remains unclear. It is possible that medically related deterioration among some patients leads to greater depressive symptoms before death. These findings become particularly pertinent when considered in the light that a depressed mental state is a common disorder in the older population and is not uncommon in the ESRD population (33) and that the mean age of the patients on MHD in the United States continues to increase (18,19). Such findings may suggest the need for more focused interventions in patients on MHD, because a poor self-reported QoL and its mental health dimension may indicate “a window of opportunity” during which therapy might enhance patient survival (33,35).

In this study, the SF36 was found to correlate weakly with the SGA and serum CRP concentration, although the correlation with serum albumin was strong. The SGA, although found to be a significant predictor of mortality in our study, is a

semiquantitative measure with only three levels (15) and, hence, this may account for the weak or absent statistical correlations observed between the SGA and continuous variables in our study. The serum CRP assay used in this study was only fully quantitative for values  $>6.9$  ng/ml. This limited the statistical power, because many patients were reported to have a CRP value  $<6.9$  ng/ml. Nevertheless, the CRP level was found to be higher among patients who died ( $23.5 \pm 23.6$  ng/ml) when compared with surviving patients ( $11.6 \pm 14.1$  ng/ml) at a *P* value that was marginal (*P* = 0.054). Moreover, the serum CRP showed a trend to predict mortality, because every 10 ng/ml increase was associated with a relative risk of death of 1.39 with a marginal *P* value of 0.062 (Table 5). Therefore, it is possible that the results would have been statistically significant if the sample size had been larger and a fully quantitative CRP assay had been used, because a number of recent studies underscore the strong relationship between serum CRP and other inflammatory measures and the increased incidence of morbidity and mortality in patients with ESRD (36).

The results of this study must be qualified by the small sample size. Hence, a more extended multivariate analysis to include all variables together in one large multivariate model was impossible because of drastic reduction of the statistical power that would ensue. Nevertheless, case-mix adjustment was done separately to compare the affect of each variable after controlling for age, gender, race, and underlying disease. Another possible limitation of the study is the relatively short duration of follow-up of 12 mo. Moreover, some patients who were sicker did not participate in this study because of their severe illnesses. This may introduce a possible selection bias, because only 70% of the eligible patients agreed to participate in the study; hence, the external validity and generalization of the results of the study may be somewhat limited. However, inclusion of sicker, more severely malnourished patients with inflammation might have led to a stronger association between the SF36 scores and nutritional and inflammatory measures. These points are indicative of bias toward null, which implies that our reported correlations are indeed conservative and that even stronger association might be expected if sicker patients were included.

During recent years, more efforts have been dedicated in exploring the potentials of patient self-reported QoL questionnaires in high-risk populations (10,13). 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 (9). Exploring the potentials of self-administered QoL questionnaires in patients with ESRD has been underscored by the contemporary emphasis on dialysis outcome research (37). Patients’ subjectively perceived QoL 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, which 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 MHD, serial annual assessments of the QoL that use this simple tool might



help to identify high-risk patients who may need intensified attention and risk modification interventions.

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 QoL 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 non-ESRD populations under diverse observational and interventional studies. More studies are required to verify the value of the SF36 measurements in predicting the clinical condition of patients with ESRD and their outcomes.

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