

Quality of Life and Its Determinants of Hemodialysis Patients in Taiwan Measured With WHOQOL-BREF(TW)

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• **Background:** In 1991, the World Health Organization (WHO) initiated a cross-cultural project to develop a quality-of-life (QOL) questionnaire (WHOQOL); soon after this, the clinically applicable short form was developed and named WHOQOL-BREF, followed by a Taiwanese version (WHOQOL-BREF(TW)). **Methods:** We first administered the WHOQOL-BREF(TW) and symptom/problem scale to 376 patients with end-stage renal disease on regular hemodialysis therapy in Taiwan. Analysis with multiple stepwise regressions was conducted to study determinants of QOL domains and items. **Results:** The WHOQOL-BREF(TW) was reliable and valid from various validation studies. The 4 domains (physical, psychological, social relations, and environment) and global items (overall quality of life and general health) of the WHOQOL-BREF(TW) each differentiated symptoms/problems of hemodialysis patients from age-, sex-, and education-matched healthy referents. The 4 domains, except for environment and global items of the WHOQOL-BREF(TW), each differentiated erythropoietin dosage from age-, sex-, and education-matched healthy referents. After adjusting for age, sex, marriage, and education, the prominent associated factors of various QOL domains and items were age, area (Taipei or Keelung), hemoglobin level, normalized protein catabolic rate, and symptom/problem scale. **Conclusion:** The WHOQOL-BREF(TW) is reliable and valid for long-term study of hemodialysis patients, and hemodialysis had negative impacts on QOL, especially in patients with more severe disease with greater symptom/problem scores, lower hemoglobin levels, and lower normalized protein catabolic rates. *Am J Kidney Dis* 46:635-641.

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INDEX WORDS: End-stage renal disease (ESRD); hemodialysis (HD); quality of life; validation; World Health Organization Quality-of-Life Questionnaire (WHOQOL).

QUALITY OF LIFE (QOL) is being used increasingly as an important parameter of health and well-being. QOL per se is an important outcome representing a person's concerns. QOL also is an important indicator of other outcomes, such as mortality and hospitalization.¹ There are several reasons that QOL study is emerging in prevalent patients with end-stage renal disease (ESRD) undergoing hemodialysis (HD). The prevalence of patients with ESRD on HD therapy is still increasing.^{2,3} Although HD therapy prolongs life, there often is a significant diminution in QOL.² ESRD is a chronic disease associated with many comorbidities and complications.³ Not surprisingly, these comorbid conditions adversely influence many aspects of QOL in HD patients.⁴

In 1991, the World Health Organization (WHO) initiated a cross-cultural project to develop a QOL questionnaire (WHOQOL) for generic use and defined QOL as "individuals' perceptions of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns."⁵ Soon after this standard long form, the clinically applicable short form was developed and named WHOQOL-BREF.^{6,7} Although a variety of generic and disease-specific instruments, such as the 36-Item Short-

Form Health Survey, Kidney Disease Quality-of-Life questionnaire, and Kidney Disease Questionnaire, had been developed and applied to the assessment of QOL in patients with ESRD, cross-culture and cross-disease comparability were lacking.^{8,9} Therefore, the Taiwan version of the WHOQOL-BREF (WHOQOL-BREF(TW)) was developed for clinical use.¹⁰

The aim of our study is to first assess the reliability and validity of the WHOQOL-BREF(TW) in HD patients, compare scores of

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QOL measured by means of the WHOQOL-BREF(TW) between groups of HD patients and age-, sex-, and education-matched healthy referents, and identify major determinants of QOL in HD patients under a multiple regression model in which one may be able to quantify more detailed QOL changes independently attributed to a favorable outcome of HD.

METHODS

Subjects

In February 2002, we enrolled as many patients with ESRD who were undergoing regular HD at the dialysis centers of 13 regional hospitals or outpatient clinics in metropolitan Taipei and Keelung city as possible to participate in the study. In the end, 513 patients were enrolled. Patients with ESRD with a creatinine clearance less than 5 mL/min (<0.08 mL/s) or a creatinine concentration greater than 8.0 mg/dL (>707 μ mol/L) were given first priority for HD therapy. Other patients with ESRD were eligible to receive HD if their creatinine clearance was less than 15 mL/min (<0.25 mL/s) or creatinine concentration was greater than 6.0 mg/dL (>530 μ mol/L) and they had at least 1 of the following complications: congestive heart failure, pulmonary edema, pericarditis, a propensity for bleeding, mental status changes, seizures, peripheral neuropathy, persistent hyperkalemia, refractory nausea and vomiting, intractable metabolic acidosis, cachexia, or a blood urea nitrogen level greater than 100 mg/dL (>36 mmol/L). Voluntary informed consent was obtained from all invited patients.

To evaluate test-retest reliability, 20 patients in stable condition were selected and invited for retest. All these patients received a retest 4 to 8 weeks later. Patients with mental status changes, those admitted to a hospital during the preceding 3 months, or those who refused to participate in the survey ($\sim 25\%$ of those enrolled) were excluded. To compare QOL of HD patients with that of a group of healthy referents, we used the database from the 2001 National Health Interview Survey, which was conducted by the National Health Research Institute and Bureau of Health Promotion, Department of Health, in Taiwan.¹¹ In the National Health Interview Survey, 13,083 subjects completed the WHOQOL-BREF(TW) questionnaire. Of these subjects, 9,107 were healthy and had no known medical conditions. Two hundred eighty-three healthy subjects were age- (± 10 years), sex-, and education-matched and therefore considered similar to our HD patients.

Tools of Investigation

The WHOQOL-BREF(TW) consisted of 2 global items, G1 for overall QOL and G2 for general health, and 26 items in the physical, psychological, social relations, and environment domains.^{10,12} Specifically, there were 7, 6, 4, and 9 items in the physical, psychological, social relations, and environment domains, respectively. There were 2 items specific to Taiwan; Q27 and Q28 represented "being respected" and "eating food" as part of the social relations and environment domains, respectively. Application method, ref-

erence time point, and item scoring were performed as described for the original WHOQOL-BREF.⁹ Global QOL score was calculated as the arithmetic mean of G1 and G2. Item scores ranged from 1 to 5, and domain scores, from 4 to 20, both on a Likert scale. A descriptor study was performed to make the scale interval-like.¹³

The symptom/problem (S/P) scale was used to show clinical sensitivity. The S/P scale of the Kidney Disease Quality-of-Life Short Form questionnaire¹⁴ consisted of 15 items pertaining to various symptoms or dialysis problems, such as headache, myalgia, dyspnea, pruritus, and so on. The descriptor, "not at all annoyed" to "most severely annoyed," ranged from 1 to 5. S/P score was the mean of these 15 items and ranged from 1 to 5, with a higher score indicating a greater number of symptoms and problems. Therefore, S/P score indicated the severity of HD conditions to some extent. Kt/V and normalized protein catabolic rate (nPCR) were important clinical variables and used in QOL determinant analysis. Kt/V was calculated by using Daugirdas' second formula.¹⁵ nPCR was calculated by using equations of Depner.¹⁶

Validation Analysis

All data were analyzed using SAS (SAS Institute Inc, Cary, NC) and LISREL-SIMPLIS (Scientific Software International, Inc, Lincolnwood, IL)¹⁷ software, from which reliability and validity were assessed in 249 HD patients living in metropolitan Taipei.^{18,19} Reliability assessments included Cronbach's α ²⁰ and test-retest reliability. Validation assessments included content validity, criterion-related validity, concurrent validity, exploratory factor analysis, and confirmatory factor analysis of construct validity.^{20,21} The comparative fit index and non-normed fit index were calculated to test goodness of fit²⁰ for confirmatory factor analysis.

Comparison of HD Patients With Healthy Referents

HD patients were divided into 2 groups with different severity of HD condition ($S/P < 2.0$ and $S/P \geq 2.0$), and erythropoietin (EPO) injection amounts per week ($<2,000$ and $\geq 2,000$ IU/wk). Next, QOL scores of 4 domains and global measures (G1, G2, and global QOL) were compared between HD patients and age-, sex-, and education-matched healthy referents.

Analysis of QOL Determinants

A multiple linear regression model was constructed by using summary scores of each facet/item and domain as dependent variables. Age, sex, marriage, and education were adopted as independent variables and controlled in this regression model. Religion, employment status in recent 1 year, Taipei/Keelung area, duration of HD therapy, and 8 clinical variables, including presence of comorbidity, Kt/V, hemoglobin (Hgb) level, hematocrit, albumin level, nPCR, S/P score, and EPO injection amounts per week, were considered independent variables for stepwise regression analysis. The adopted selection and exclusion criterion was P less than 0.15.

Table 1. Comparisons of Frequencies of Demographic Characteristics Between Maintenance HD Patients and Age-, Sex-, and Education-Matched Healthy Referents

Demographic Variable	HD Patients (n = 376)	Healthy Referents (n = 283)
Age (%)		
<40 y	11	15
40 to <50 y	16	22
≥50 y	64	61
Male (%)	52	50
Education (%)		
Illiterate or primary	54	46
Middle high	16	19
High school	17	22
College or graduate	9	10
Married*	68	78
Orient religious	72	75
Employed within 1 y†	19	61
Smoking‡	14	31
Drinking‡	7	32
With comorbidity†	42	0
S/P score < 2.0† (%)	76	100
Personal income (NTD‡)		
<30,000	86	
30,000~60,000	9	
≥60,000	3	
Family income (NTD‡)		
<30,000	57	
30,000~60,000	23	
≥60,000	14	

Abbreviation: NTD, new Taiwan dollar.

**P* < 0.01.

†*P* < 0.001.

‡1 NTD = 0.031 US dollar.

RESULTS

Subject Characteristics and Descriptive Statistics

All 513 patients completed the questionnaire. After deleting respondents who answered less than 80% (23 items) of 28 items or with illogical clinical values, 376 subjects were included for final analysis. Demographical data for these patients were compared with those for 283 healthy referents and are listed in Table 1. HD patients had lower percentages of employment, smoking, and drinking habit than healthy referents. For clinical variables, HD patients in this study had average values as follows: calculated Kt/V, 1.66 ± 0.35 (SD); albumin, 3.85 ± 0.39 g/dL (38.5 ± 3.9 g/L); Hgb, 10.0 ± 1.4 g/dL (99.6 ± 13.8 g/L); hematocrit, 30.8% ± 4.3%; calcium, 4.78

± 0.48 mEq/dL (2.39 ± 0.24 mmol/dL); inorganic phosphorus, 1.64 ± 0.50 mg/dL (0.53 ± 0.16 mmol/L); EPO, 2,536 ± 3,456 IU/wk; and S/P score, 1.69 ± 0.65.

Validation Verification of the WHOQOL-BREF(TW) in HD Patients

Reliability and validity of the WHOQOL-BREF(TW) in HD patients were verified and compared with those in a sample of the general population of Taiwan.¹² As listed in Table 2, the WHOQOL-BREF(TW) was reliable and valid in these HD patients. Validation results were similar between our HD patients and the general population with the exception that test-retest reliability of the physical domain was only 0.48. The comparative fit index and non-normed fit index were 0.92 and 0.90 and reached criteria, respectively.

QOL Measures of HD Patients and Comparison With Healthy Referents

All mean scores of 4 domains, except for environment, were significantly lower than those

Table 2. Comparison of the Reliability and Validity of the WHOQOL-BREF (TW) Between Maintenance HD Patients and the General Population

Reliability and Validity	HD Patients (n = 249)	General Population (n = 1,068)
Reliability		
Cronbach's α of domains	0.70-0.80	0.68-0.80
Test-retest		
Items	—	0.41-0.79
Domains	0.48-0.82	0.76-0.80
Validity		
Content		
Item-corresponding domain	0.44-0.79	0.53-0.78
Between domains	0.41-0.71	0.51-0.64
Criterion-related		
Item-global QOL	0.12-0.49	0.29-0.53
Domain-G1	0.36-0.50	0.39-0.53
Domain-G2	0.36-0.53	0.38-0.58
Predictive (%)		
G1	28	33
G2	31	36
Global QOL	38	45
Construct		
Exploratory factor analysis (factors)	4	4
Confirmatory factor analysis: comparative fit index	0.92	0.90

Abbreviations: G1, overall QOL; G2, general health.

for age-, sex-, and education-matched healthy referents ($P < 0.001$). All mean scores of items in the physical, psychological, and social relations domains were lower than those of healthy referents ($P < 0.01$). In the environment domain, some were nearly the same, including “finance” and “information”; some QOL scores of HD patients were lower than those of healthy referents, including “safety” and “leisure” ($P < 0.05$); some were higher than those of healthy referents, including “physical environment,” “health and social care availability,” and “home environment” ($P < 0.01$). All QOL item scores in HD patients living in metropolitan Taipei were inferior to those in Keelung city, except for “negative feeling” from the psychological domain and “leisure” from the environment domain. In general, HD patients with more symptoms/problems or greater EPO injection amounts had lower QOL scores in all domains except for environment, as listed in Table 3. Findings also indicate that the WHOQOL-BREF(TW) may be useful in clinical assessment of subjective feelings.

Determinants of QOL

After controlling for age, sex, education, and marriage, Kt/V was not associated significantly with any QOL domains or items. Conversely, HD patients living in Keelung showed significantly higher scores in most QOL items than those in metropolitan Taipei. When HD patients had higher

S/P scores, their QOL scores were significantly worse in all except social relations domains and in all items in the physical domain, as well as many items of other domains ($P < 0.05$). Comorbidity with other diseases decreased QOL scores of “social support” and “being respected” in the social relations domain and “health care availability and quality” in the environment domain ($P < 0.05$). Increased Hgb level and lower EPO injection amounts seemed to have an independent positive effect on different QOL items. nPCR values showed significant associations with many items in the physical, psychological, and environment domains, indicating the potential for relating to QOL in HD patients. Employment significantly increased the scores of “health care availability and quality” and “transportation” in the environment domain ($P < 0.05$). When duration of HD increased, the scores of the social relations domain decreased and corresponded to decreased scores in items of “sexual activity,” “being respected,” and “home condition.”

DISCUSSION

In our verification analysis of the WHOQOL-BREF(TW), test-retest reliability of the physical domain was lower, indicating that subjective physical QOL probably was not so stable in a duration of 4 to 8 weeks. All indicators of validity, listed in Table 2, show that the instrument is suitable for HD patients. Approximately 25% of enrolled patients refused to be interviewed. Many

Table 3. Comparisons Between Healthy Referents and HD Patients Stratified by More Than 2 Symptoms/Problems (S/P \geq 2.0) and Different Injected EPO Doses

Variable	(a) Healthy Referents (n = 283)	Stratified by S/P			Stratified by EPO Injection Amount		Tukey (HSD) Test
		(b) S/P < 2.0 (n = 222)	(c) S/P \geq 2.0 (n = 61)	Tukey (HSD) Test	(d) EPO < 2,000 (n = 121)	(e) EPO \geq 2,000 (n = 120)	
Global QOL	3.29 \pm 0.64	3.24 \pm 0.82	3.03 \pm 0.82	a-c	3.22 \pm 0.79	3.16 \pm 0.85	
G1: overall QOL	3.52 \pm 0.72	3.05 \pm 0.91	2.59 \pm 0.90	a-b, a-c, b-c	3.03 \pm 0.93	2.92 \pm 0.92	a-d, a-e
G2: general health	3.40 \pm 0.58	3.14 \pm 0.72	2.81 \pm 0.76	a-b, a-c, b-c	3.13 \pm 0.74	3.04 \pm 0.76	a-d, a-e
Physical domain	15.01 \pm 2.10	13.86 \pm 2.47	11.04 \pm 3.13	a-b, a-c, b-c	13.64 \pm 2.81	12.86 \pm 2.94	a-d, a-e, d-e
Psychological domain	13.58 \pm 2.24	12.52 \pm 2.83	10.15 \pm 3.04	a-b, a-c, b-c	12.04 \pm 3.01	11.91 \pm 3.16	a-d, a-e
Social relations domain	14.07 \pm 1.96	13.27 \pm 2.62	12.34 \pm 2.56	a-b, a-c, b-c	13.49 \pm 2.56	12.85 \pm 2.68	a-d, a-e
Environment domain	13.05 \pm 2.00	13.68 \pm 2.22	12.15 \pm 2.27	a-b, a-c, b-c	13.54 \pm 2.12	13.23 \pm 2.49	

NOTE. Only significance levels of $P < 0.05$ under Tukey tests were listed for comparisons of different groups. Abbreviation: HSD, honestly significant difference.

Table 4. Regression Coefficients for Determinants From Multiple Linear Regressions After Adjustment for Age, Sex, Education, and Marriage Status in 376 HD Patients

	Area Taipei/ Keelung	S/P Scores	Comorbidity (yes/no)	EPO Dosage (1,000 IU/wk)	Hgb	Albumin	nPCR	HD Duration (y)	Employed (yes/no)
G1: overall QOL		-0.20*							
G2: general health		-0.44*			0.01*				
Global QOL		-0.31*			0.01*				
Physical	-1.36*	-2.19*							
Psychological	-0.51*	-1.71*							
Social relations	-1.93*							-0.13*	
Environment	-1.71*	-0.94*					1.26*		
Q3: pain	-0.23*	-0.80*	0.30*						
Q4: medication	-0.33*	-0.62*	0.30*			-0.03†			
Q10: energy	-0.29*	-0.49*				0.04*			
Q15: mobility	-0.75*	-0.59*		-0.04*					
Q16: sleep	-0.33*	-0.46*					0.51*		
Q17: activities of daily living	-0.57*	-0.38*					0.48*		
Q18: work	-0.79*	-0.45*		-0.02			0.40*		0.32†
Q5: positive feeling		-0.39*			0.01*†		0.57*		
Q6: spirit	-0.90*			-0.05*			0.70*		
Q7: concentration	-0.29*	-0.53*							
Q11: appearance	-0.53*					0.03†			
Q19: esteem		-0.41*							0.23†
Q26: negative feeling	-0.31*	-0.68*		-0.08*		-0.04*			
Q20: relations	-0.59*			-0.04*					
Q21: sex	-0.58*	-0.37*						-0.04*	
Q22: support	-0.52*		-0.20*						
Q27: respect	-0.61*		-0.36*		0.01*			-0.03*	
Q8: safety	-0.54*	-0.45*					0.47*		
Q9: physical environment	-0.48*				0.01*				
Q12: finance	-0.41*								0.30†
Q13: information	-0.95*	-0.05					0.51*		
Q14: leisure		-0.42*		-0.07*					
Q23: home	-0.32*							-0.02*	
Q24: health care availability			-0.16†	0.03*	0.01*				0.36*
Q25: transportation								-0.02†	0.28*
Q28: eating	-0.23*	-0.38*			0.01†				

*P < 0.05.

†P < 0.10.

of them like to rest during the dialysis session, although they were in a grossly stable condition. Thus, QOL scores in our sample could be an overestimation. Compared with healthy referents, QOL scores of all except the environment domains, and most items, were significantly lower in our HD patients. Lower S/P scores, adequate EPO injection amounts, or greater nPCR seemed to correlate with higher QOL scores, as shown in

Tables 3 and 4. Findings corroborate the clinical validity of the WHOQOL-BREF(TW) instruments, also found in patients with other diseases, such as epilepsy and acquired immunodeficiency syndrome.^{22,23}

The following determinants of QOL were reported in HD patients, including hematocrit, socioeconomic level, education level, dialysis schedule, and physical exercise as improving

factors and comorbidity, diabetes mellitus, failed transplant, female sex, depression, and malnutrition as aggravating factors.⁷ To our limited knowledge, we are the first to apply multiple regression models to control potential confounding for assessing individual effects of various determinants for many QOL aspects in HD patients. Such models were useful for regular monitoring of clinical outcomes of HD patients. In our models, Kt/V was not the significant determinant of WHOQOL-BREF(TW) measures, which seemed consistent with QOL measured by means of the 36-Item Short-Form Health Survey.²⁴ Kt/V was an indicator of dialysis dose and related to mortality of dialysis patients.^{25,26} However, dissociation between dialysis adequacy and Kt/V was noted recently.²⁷ Thus, relations among QOL, Kt/V, dialysis adequacy, and mortality remain to be clarified.

HD patients in metropolitan Taipei had lower QOL scores for most items than those living in Keelung city. Taipei is the capital of Taiwan. Patients in Taipei might have a higher standard of QOL and seemed subjectively more difficult to please. Thus, even after adjustment for age, sex, education, marriage status, and all other clinical indicators, there was a significant difference in QOL scores between HD subjects in the 2 cities. The average Kt/V of HD patients living in metropolitan Taipei was almost the same as for those living in Keelung city (1.69 ± 0.37 versus 1.65 ± 0.34 ; $P = 0.48$), which corroborated the hypothesis that such a difference might not result from different treatment dosages.

Both symptom/problem scores and comorbidity were reported to impact on QOL.²⁸ However, S/P scores were associated independently with most items and domains of QOL, whereas comorbidity showed less significant items. S/P inquires directly about concurrent subjective discomforts, but the presence of comorbidity was associated with only preexisting diseases or long-term illnesses. An alternative explanation might be that the presence of comorbid diseases made HD patients more accustomed to handling physical discomfort, as listed in Table 4.

In our multiple regression models, lower EPO injection amounts and greater Hgb level were associated with higher QOL scores in some items, as listed in Table 4. Both Hgb level and EPO dosage are variables related to the amount of red blood

cells or severity of anemia. These 2 variables were reported to impact on several items of QOL.²⁹⁻³³ We incorporated both EPO dosage and Hgb level into our model fitting, which showed independent impacts, but of inverse direction, on QOL items. Hgb level was an outcome indicator that may connect closely with QOL, whereas EPO dosage was only a process indicator. Greater EPO dose might simply reflect more severe anemia and thus indicate poor QOL. Results listed in Table 4 show that the best fitted models for different items did not include both variables, which corroborated these explanations.

Both albumin level and calculated nPCR are outcome indicators of nutrition.³⁴⁻³⁷ Thus, both shared the same direction of effect on QOL, but did not show up in the same fitted regression model for individual items in Table 4. nPCR seemed to be incorporated into more models of WHOQOL items than albumin level. Taken together with these 2 variables, we conclude that nutrition had more impact on physical and psychological QOL, but not QOL of social relations.

The longer patients received HD, the worse they felt subjectively about sexual life and the extent of being respected. Improving these aspects of social relations would be crucial to improve the QOL of patients with ESRD in the future because survival of dialysis patients has much improved in recent decades.

The current study leads us to 3 conclusions: (1) the WHOQOL-BREF(TW) is valid for HD patients; (2) HD has a negative impact on many QOL measures with various degrees, especially in patients with more severe disease with greater S/P scores; and (3) Hgb level, nPCR, and symptoms/problems of HD patients were prominent and clinically manageable determinants of QOL in HD patients.

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