Depression and anxiety associated with KDQOL in Japan according to a dialysis patient's length of time on dialysis

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Summary. For dialysis patients, screening for depression and anxiety helps to obtain an understanding of a dialysis patient's overall mental health. This relationship was investigated regarding such factors as the time on dialysis and depression, anxiety, and the influence on Quality of Life (QOL) of primary kidney disease. In addition, the time on dialysis, gender, age, depression, anxiety, and sleep quality were also compared. The Kidney Disease Quality of Life (KDQOL) short form Version1.3 Japanese version was administered to 2796 patients with maintenance hemodialysis therapy at 49 outpatient dialysis facilities in 2002-2003. Depression and anxiety were assessed using the Hospital Anxiety and Depression Scale. Quality of sleep with a strong relationship to QOL was assessed by using the Pittsburgh Sleep Quality Index. The dialysis period was classified into 2 groups. Next, the groups were examined using the Mann-Whitney U-test. In addition, a multivariate analysis was also performed. A negative correlation was seen between the length of time on dialysis and the score of KDQOL on the subscales for anxiety and depression. However, when the score for each subscales and the correlation with the time on dialysis were analyzed, no significant difference was observed. In a multivariate analysis, most scales were found to be related to depression in the dialysis patient of less than 15 years. No

significant difference was observed in the mean value of the time on dialysis and the QOL each score. Therefore, the psychotic symptoms, such as depression, anxiety, were found to be closely related to the QOL in dialysis patients.

Key words — dialysis, Kidney Disease Quality of Life, anxiety, depression, time on dialysis.

INTRODUCTION

The number of dialysis patients in Japan keeps increasing. Moreover, the patient mortality rate is.^{1,2)} It is thought that aging in the entire Japanese society associated with the development of highly developed Medical Technology may be responsible for these observations. However, so far very few investigations have been performed addressing the mental health of dialysis patients. Depression is the mental disease reported most frequently in association with dialysis patients, 3,4,5,6,7) and anxiety is reported at a similar rate.8) Neither the diagnosis nor treatment regarding a dialysis patient's depression and anxiety have yet been sufficiently performed in Japan. For dialysis patient, screening for depression and anxiety would help understands the dialysis patient's degree of mental health. Moreover, Quality of Life (QOL) is highly

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Abbreviations — QOL, Quality of Life; KDQOL, Kidney Disease Quality of Life; HD, hemodialysis; CES-D, Center for Epidemiological Studies Depression Screening Index; HADS, Hospital Anxiety and Depression Scale; PSQI, Pittsburgh Sleep Quality Index; SF-36, 36-item Short Form Health Survey; PSQIG, global PSQI scores; CGN, chronic glomerulonephritis; DOPPS, Dialysis Outcomes and Practice Patterns Study.

associated with depression and anxiety. It is thought that examining the QOL regarding any associations with depression and anxiety may thus be important.

This study investigated the relationship between the time on dialysis and depression and anxiety, and the influence of primary kidney disease, the duration of dialysis, gender and age on QOL, depression, anxiety, and sleep quality.

SUBJECTS AND METHODS

The Kidney Disease Quality of Life (KDQOL) short form (SF) Version 1.3 Japanese version⁹⁾ was administered to 2796 patients with maintenance hemodialysis (HD) therapy at 49 outpatient dialysis facilities belonging to the Niigata Dialysis Society, Japan in 2002-2003. As a standard screening for depression, the Beck Depression Inventory (BDI)¹⁰⁾ and the Center for Epidemiological Studies Depression Screening Index (CES-D)¹¹⁾ were used. In this study, depression and anxiety were assessed by using the Hospital Anxiety and Depression Scale (HADS). 12,13) The investigation obtained and investigated the cooperation of the medical treatment staff in each of the facilities. The patients answered the questionnaire after they returned to their home following dialysis. For the visually handicapped, a family member or medical worker read the questionnaire out loud and recoded the answers of the patients.

The HADS is a14-item self-report scale with separate seven-item subscales for anxiety and depression. It was specifically designed for use with the medically ill. The depressive subscale places emphasis on anhedonia and does not include somatic items, which may confound the assessment of depression in medical patients. It is a brief scale, which is quite acceptable to patients and has been extensively used in the medically ill.

The quality of sleep and its relationship to QOL was assessed using the Pittsburgh Sleep Quality Index (PSQI¹⁴), Japanese version). Moreover, the effects of the age, sex, and the marriage were assessed using the patient's social life background questionnaire.

The KDQOL-SF¹⁵) questionnaire is a multidimensional, reliable and validated instrument specifically designed for dialysis patients and has as its generic core the 36-item Short Form Health Survey (SF-36). ^{16,17}) The Japanese version was developed by Miura *et al.*¹⁸)

SF-36 was developed to assess 8 different aspects of health namely; physical functioning, physical role functioning, bodily pain, general health perceptions, mental health, emotional role functioning, social functioning, vitality. The SF-36 is one of the most

widely used quality of life instruments worldwide.

The specific kidney-disease-targeted items (11 dimensions) included symptom/problem, effects of kidney disease, burden of kidney disease, cognitive function, quality of social interaction, sexual function, sleep, social support, work status, patient satisfaction, and dialysis staff encouragement. The scores on each dimension range from 0 to 100, with higher scores reflecting better health-related QOL.

In the HADS, the items ware selected for each question that related to depressive symptoms and anxiety one week in the past. It consisted of seven items to measure anxiety and seven items to measure depression. Each item is scored from 0 to 3, with total scores ranging from 0 to 21 for the anxiety and depression subscales. Higher scores indicate greater anxiety and/or depression. The three score ranges are classified as: normal (0 to 7), moderate (8 to 10), and severe (11 to 21).

The PSQI consists of 19 self-rated questions and 5 questions. The 19 self-rated questions assess a wide variety of factors relating to sleep quality, including estimates of sleep duration and latency and of the frequency and severity of specific sleep-rated problems. These 19 items are grouped into 7 component scores, all of which are weighted equally on a 0-3 scales. The 7 component scores are then added to yield a global PSQI scores (PSQIG) are with a range 0-21; higher scores indicate worse sleep quality. The 7 components of the PSQI are sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction.

In two groups of dialysis patients who were classified based on the duration of dialysis, the difference between KDQOL and the HADS score was examined. In addition, each score of SF-36 and a kidney-disease-targeted-scale was assumed to be an induced variable, presence of depression, anxiety, the age, sex, PSQI score, and the marriage and cohabitation people's presence and an primary kidney disease (chronic glomerulonephritis (CGN) and diabetic kidney disease) were assumed to be an autonomous variable according to time on dialysis, and the multivariate analysis was done

The statistical analysis was carried out using the statistical package for SPSS Ver.11.0. The correlation between numerical parameters were made using Spearman's p correlation test. The time on dialysis was classified into 15 years or more' and less than 15 years two groups. Then groups were compared using the Mann-Whitney U-test. In addition, the multivariate analysis was done. A P values less than 0.05 was considered to be significant.

RESULTS

The demographic and baseline clinical characteristics of the study sample are shown in Table 1. Responses were received from 42 facilities including 1946 people (respondent rate is 74.3%) from among the 49 dialysis facilities which belong to Niigata Dialysis Society. The mean age was 61.0 ± 12.2 years old (mean value \pm standard deviation), and the average time on dialysis was 127.3 ± 95.8 months. The primary kidney diseases included CGN (32.3%), the diabetic kidney disease (6.9%), cystic kidney disease (2.7%), renal vascular syndrome (2.4%), and others/uncertainty (55.7%). The QOL measurement results are shown in Tables 2 and 3. First of all, the score that corresponds to SF-36 is shown in Table 2 among the KDQOL-SF. All of the scores were decreased in comparison to a national standard value. Specifically, physical role functioning and general health perceptions decreased to less than 50 points. Next, the score of Kidney disease targeted scales is shown in Table 3. Burden of kidney disease was at the 20 point level, and a low score work status was at 40 points. The mean score of the HADS is shown in Table 4. Anxiety was 5.3 ± 3.7 , and depression was 6.9 ± 4.3 . Severe depression reached 19.9% and severe anxiety was 8.3% in 11 points or more. The score of the long-term dialysis patient who has dialysis for 15 years or more are compared to those patients with less than 15 years in Table 5. The long-term dialysis patient didn't show significant high scores in KDQOL subscales. The correlation of the scores of each subscales with anxiety and depression were shown in Table 6. A negative correlation was observed, and anxiety was -0.136~-0.627 and depression was -0.165~ -0.633. However, when the score of each of the subscales and the correlation with time on dialysis were analyzed, no significant difference was seen.

The multivariate analysis with forced entry selection analyses respectively, with less than 15 years' of 15 years or more according to time on dialysis, and the results are shown in Tables 7 and 8. The dependent variable was assumed to be subscales of KDQOL-SF (19 items), and the independent variable was assumed to be 9 items (PSQIG, anxiety, depression, gender, age, and cohabitation person's presence and the marriages, CGN, and diabetes mellitus (DM)). Primary kidney disease were selected two diseases with a lot of numbers of cases (CGN: n=628 (32.3%), DM: n=135(6.9%)) to the independent variable. As a result, all scales except for the sexual function and dialysis staff encouragement were found to be related to depression in the dialysis patient of less than 15 years. Especially, PSQIG, depression, and anxiety were related to general health perceptions. In addition, depression and anxiety were found to be related to general health perceptions though long-term dialysis patient's of 15 years or more.

Table 1. Demographic and Clinical Characteristics (n=1946)

Demographic					
Age (year)	61.0±12.2				
Gender					
Male (n)	35.2 (684)				
Female (n)	56.6 (1102)				
Unknown (n)	8.2 (160)				
Duration of dialysis treatment (month)	127.3±95.8				
Clinical					
Primary kidney disease (n)					
Glomerulonephritis	32.3 (628)				
Diabetes mellitus	6.9 (135)				
Renal vascular, excluding vasculitis	2.4 (46)				
Cystic kidney disease	2.7 (53)				
Others/unknown	55.7 (1084)				

Values expressed as mean \pm standard deviations or percent.

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Table 2. SF-36 mean scores

Subscales	Our study	Japanese
Physical functioning	64.8±28.0	87.9±15.5
Role functioning / physical	48.1 ± 42.3	85.3 ± 29.0
Bodily pain	63.0 ± 26.9	76.2±22.7
General health perceptions	41.6±18.4	65.0 ± 19.6
Mental health	63.4±22.2	72.7 ± 19.2
Role functioning / emotional	50.3 ± 45.8	83.8±31.5
Social functioning	69.3 ± 26.9	86.2±19.4
Vitality	53.0±23.7	65.8±20.4

Values expressed as mean \pm standard deviations.

All of the scores were decreased in comparison to a national standard value.

Table 3. Kidney-disease-targeted items scales

Subscales	Our study				
Symptoms&problems	78.8±15.6				
Effects of kidney disease	69.7 ± 20.8				
Burden of kidney disease	27.4±20.9				
Work status	46.9±42.5				
Cognitive function	81.0±19.6				
Quality of social interaction	82.1±19.5				
Sexual function	67.0±34.1				
Sleep	63.1±18.5				
Social support	72.9±21.0				
Dialysis staff encouragement	77.1±21.1				
Patient satisfaction	75.9±20.2				

Values expressed as mean \pm standard deviations.

Table 4. Means and standard deviations (SD) of patients' HADS scores

Anxiety	5.3±3.7
Normal (n)	74.7 (1156)
Moderate (n)	17.0 (264)
Severe (n)	8.3 (129)
Depression	6.9±4.3
Normal (n)	58.2 (923)
Moderate (n)	21.9 (347)
Severe (n)	19.9 (315)

Values expressed as mean \pm standard deviations or percent.

The three score ranges are classified as: normal (0 to 7), moderate (8 to 10), and severe (11 to 21).

Table 5. PSQI ,KDQOL scores and HADS scores by duration of dialysis

Variable	duration of dialysis <15years	duration of dialysis 15years ≦	P value
PSQIG	7.08	6.19	0.01
KDQOL			
Physical functioning	66.17	64.9	0.42
Role functioning / physical	47.68	49.53	0.17
Bodily pain	63.83	61.82	0.42
General health perceptions	41.85	40.72	0.24
Mental health	62.45	64.23	0.7
Role functioning / emotional	49.29	51.67	0.18
Social functioning	70.14	68.25	0.13
Vitality	52.83	53.68	0.65
Symptoms&problems	78.27	80.19	0.12
Effects of kidney disease	69.02	70.28	0.34
Burden of kidney disease	28.32	26.16	0.99
Work status	46.05	50.51	0.16
Cognitive function	81.08	80.42	0.13
Quality of social interaction	82.02	82.57	0.31
Sexual function	82.02	71.73	0.87
Sleep	62.23	63.1	0.76
Social support	72.24	71.6	0.82
Dialysis staff encouragement	76.92	76.13	0.62
Patient satisfaction	75.66	73.53	0.18
HADS			
Anxiety	5.13	5.52	0.051
Depression	6.82	7.02	0.18

The score of the long-term dialysis patient who has dialysis for 15 years or more are compared to those patients with less than 15 years.

KDQOL, Kidney Disease Quality of Life; HADS, Hospital Anxiety and Depression Scale.

Abbreviations; PSQIG, global Pittsburgh Sleep Quality Index scores;

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Tabel 6. Correlation coefficients for HADS and KDQOL subscales

	НА	DS
Subscales	Anxiety	Depression
Physical functioning	-0.302	-0.42
Role functioning / physical	-0.332	-0.438
Bodily pain	-0.398	-0.438
General health perceptions	-0.44	-0.633
Mental health	-0.627	-0.633
Role functioning / emotional	-0.352	-0.445
Social functioning	-0.42	-0.5
Vitality	-0.449	-0.588
Symptoms&problems	- 0.501	-0.481
Effects of kidney disease	-0.417	-0.452
Burden of kidney disease	-0.47	-0.496
Work status	-0.136	-0.263
Cognitive function	-0.552	-0.603
Quality of social interaction	-0.587	-0.594
Sexual function	-0.219	-0.399
Sleep	-0.395	-0.399
Social support	-0.336	-0.353
Dialysis staff encouragement	-0.165	-0.165
Patient satisfaction	-0.302	-0.268

The correlation of the scores of each subscales with anxiety and depression were shown.

Values expressed as r (Pearson's correlation coefficient).

All P<0.001.

Table 7-1. Multivariate analysis of factors associated with SF-36 subscales of HD patients less than 15 years

	SF-36 Subscales								
Parameter	PF	RP	BP	GHP	MH	RE	SF	VT	
PSQIG	- 0.145		- 0.182	-0.177	-0.16		·	- 0.154	
Anxiety		-0.213	-0.232	-0.18	-0.292	-0.172	-0.164	-0.183	
Depression	-0.364	-0.251	-0.265	-0.335	-0.381	-0.316	-0.468	-0.404	
CGN					0.115	0.172	0.115	0.133	
DM									
Marrige									
Cohabiter									
Age	-0.345	-0.348	-0.206			-0.285	-0.208		
Gender					-0.111				
R2	0.338	0.338	0.35	0.351	0.51	0.395	0.448	0.453	

The multivariate analysis with forced entry selection analyses respectively, with less than 15 years according to time on dialysis, and the results are shown.

Associations shown were the only significant associations found.

The number in each cell refers to the regression coefficient β .

Abbreviations; PF, physical functioning; RP, physical role functioning; BP, bodily pain; GHP, general health perceptions; MH, mental health; RE, emotional role functioning; SF, social functioning; VT, vitality; PSQIG, global Pittsburgh Sleep Quality Index scores; CGN, chronic glomerulonephritis; DM; diabetes mellitus.

Table 7-2. Multivariate analysis of factors associated with Kidney-disease-targeted subscales of HD patients less than 15 years

	Kidney-disease-targeted Subsclales										
Parameter	Sy/probl	EKD	BKD	WS	CF	QSI	SE	Sleep	SS	Encour	Satisfact
PSQIG	-0.324	- 0.254	-0.183					- 0.61	-0.141		
Anxiety	-0.229	- 0.253	- 0.256		-0.332	-0.341					
Depression	-0.216	- 0.197	-0.181	-0.24	-0.309	- 0.332		-0.132	-0.373		-0.203
CGN			0.138								
DM			0.157			0.116					
Marrige	٠										
Cohabiter					-0.141				0.182		
Age	-0.132		-0.175	-0.327		0.124	- 0.308		0.239	0.329	0.286
Gender				- 0.165					0.116	0.252	
R2	0.425	0.371	0.318	0.236	0.421	0.459	0.362	0.558	0.377	0.193	0.198

The multivariate analysis with forced entry selection analyses respectively, with less than 15 years according to time on dialysis, and the results are shown.

Associations shown were the only significant associations found.

The number in each cell refers to the regression coefficient β .

Abbreviations; Sy/probl, symptom/problem; EKD, effects of kidney disease; BKD, burden of kidney disease; WS, work status; CF, cognitive function; QSI, quality of social interaction; SE, sexual function; SS, social support; Encour, dialysis staff encouragement; Satisfact, patient satisfaction; PSQIG, global Pittsburgh Sleep Quality Index scores; CGN, chronic glomerulonephritis; DM; diabetes mellitus.

Table 8-1. Multivariate analysis of factors associated with SF-36 subscales of HD patients more than 15 years

	SF-36 Subscales											
Parameter	PF	RP	BP	GHP	MH	RE	SF	VT				
PSQIG						~~~						
Anxiety				-0.282	-0.374		-0.278					
Depression		-0.376		-0.26	-0.268	-0.318	-0.292	-0.407				
CGN	0.212	0.271			0.208	0.262	0.191	0.223				
DM						-0.175						
Marrige												
Cohabiter												
Age	-0.289	-0.31				-0.281	-0.208					
Gender												
R2	0.316	0.464	0.141	0.316	0.47	0.472	0.329	0.355				

The multivariate analysis with forced entry selection analyses respectively, with more than 15 years or 15 years according to time on dialysis, and the results are shown.

Associations shown were the only significant associations found.

The number in each cell refers to the regression coefficient β .

Abbreviations; PF, physical functioning; RP, physical role functioning; BP, bodily pain; GHP, general health perceptions; MH, mental health; RE, emotional role functioning; SF, social functioning; VT, vitality; PSQIG, global Pittsburgh Sleep Quality Index scores; CGN, chronic glomerulonephritis; DM; diabetes mellitus.

Table 8-2. Multivariate analysis of factors associated with Kidney-disease-targeted subscales of HD patients more than 15 years

	Kidney-disease-							lales			
Parameter	Sy/probl	EKD	BKD	WS	CF	QSI	SE	Sleep	SS	Encour	Satisfact
PSQIG	-0.347				0.198	0.19		- 0.616			
Anxiety			-0.283			-0.3			-0.27		
Depression					-0.508	-0.356				-0.279)
CGN				0.235							
DM											
Marrige					-0.169						
Cohabiter						0.174					
Age				-0.364		0.218				0.429	0.249
Gender					-0.249						
R2	0.309	0.225	0.263	0.229	0.51	0.432	0.261	0.492	0.254	0.25	0.132

The multivariate analysis with forced entry selection analyses respectively, with more than 15 years or 15 years according to time on dialysis, and the results are shown.

Associations shown were the only significant associations found.

The number in each cell refers to the regression coefficient β .

Abbreviations; Sy/probl, symptom/problem; EKD, effects of kidney disease; BKD, burden of kidney disease; WS, work status; CF, cognitive function; QSI, quality of social interaction; SE, sexual function; SS, social support; Encour, dialysis staff encouragement; Satisfact, patient satisfaction; PSQIG, global Pittsburgh Sleep Quality Index scores; CGN, chronic glomerulonephritis; DM; diabetes mellitus.

DISCUSSION

Recently, a lot of research has been focused on outcome research worldwide. The movement to improve the QOL has also grown, and research to improve the QOL of dialysis patients has also increased in Japan. It is now widely accepted that the QOL measurement is important, because the goals of chronic disease therapy are not only to improve survival, but also to improve the patient's QOL. 19,20,21,22) KDQOLTM23) developed by Hays et al in 1994, it is now standard method for evaluating the QOL for the kidney disease patients, especially for dialysis patients, and many scientific studies have thus been performed. It is useful though the clinical examination results such as the urea nitrogen, the creatinine, electrolytes, and Hematocrit become indices of objective physical health degree for the dialysis patient. In addition, the QOL is useful as the index of the physical and mental health degree.

Many Japanese dialysis patients undergo long-term treatment. For this reason, we examined the QOL according to the dialysis period. In this study, long term dialysis patients were defined as those receiving treatment for more than 15 years. We also took into consideration the fact that erythropoietin was developed as a new treatment of the renal anemia in around 1990.

As the dialysis period becomes longer, many problems have consequently occurred. Such as complications related to aging and long term dialysis, and the physical functions of such patients decreased. Arzu Acaray et al reported to be a decrease in the QOL for long-term patients.²⁴⁾ However, no significant difference was found in the mean value of the dialysis period and the QOL score in our study. Namely, time on dialysis did not greatly influence the QOL. The mean age was 41.1 ± 13.7 years old in the study of Arzu Acaray et al, and this was twenty years younger than the mean age in our patients. In addition, the mean dialysis period was 57.7 \pm 47.8 months in their study, which was about 70 months shorter than our results. We hypothesized about some possible factors that could improve the QOL in long-term dialysis patients in Japan. Mittal et al reported that the QOL decrease during the first several months, but it is thereafter stabilizes.²⁵⁾ The QOL tends to stabilize in long term dialysis patients in Japan, and little change is seen in the QOL because most patients are elderly and have limited physical functions in their daily life. As the time on dialysis becomes longer, the higher the PSQI tends to be.

Moreover, the PSQI was related to QOL according to a multivariate analysis based on the time on dialysis by the group receiving dialysis for less than 15 years. Sleep disturbances are extremely common in dialysis patients according many studies.²⁶⁾ The frequency of sleep disturbance can be as high as 80% or more.^{27,28,29)} The average time on dialysis for the patients in Sabbatini³⁰'s study is 56.0 ± 52.4 months in the control group and 65.1 ± 55.1 months in the insomnia group. The time on dialysis of our patients is 50-60 months further longer than theirs. Sabbatini demonstrated a significantly higher risk of insomnia in patients with more time spent on dialysis. He said that this is probably due to the progressive appearance of symptoms and concurrent diseases commonly associated with chronic dialytic treatment; one example is the increased risk of insomnia in patients with higher levels of parathyroid hormone (PTH), renal osteodystrophy, often associated with bone pain and/or pruritus. Therefore, renal osteodystrophy is not likely the main factor for insomnia in our dialysis patients. Many dialysis patients take the sleeping pills. The quality of sleep might therefore be excellent to do the drug therapy like this. Generally, the aged people sleep only for a short time. Therefore they don't realize that quality of sleep is inferior for dialysis. It is possibility of influencing the investigation result is thought. In addition to this, many dialysis patients don't realize that quality of sleep is inferior for complication of uremia encephalopathy.31)

The Dialysis Outcomes and Practice Patterns Study (DOPPS) is a large, prospective, observational study of representative samples of HD patients in France. Germany, Italy, Japan, Spain, the United Kingdom, and the United States, started in 2000.32) In the DOPPS study, depressive symptoms were assessed by the short version of CES-D, using <10 CES-D score as the cut-off value. A significantly increased relative risk of all adverse outcomes associated with CES-D scores >10 (compared with lower CES-D scores) was observed, being higher for mortality, hospitalization, and withdrawal from dialysis. These results support the validity of CES-D to identify HD patients at higher risk of hospitalization, death, and withdrawal from dialysis. We used HADS to screen patients for depression. It was therefore difficult to simply compare it with the results of DOPPS using CES-D. However, when the group with a moderate depression (8-10 points) was included, the ratio of depression was 41.8%. In addition, depression and anxiety showed a negative correlation with the subscales of KDQOL-SF. We did not perform a follow-up study on such factors as mortality and the hospitalization history. We therefore could not determine whether the mortality and the hospitalization risk were high when the depression and anxiety scores according to HADS were high. However, we can establish the result that the psychotic symptoms of not only depression but also anxiety were closely related to QOL as a massive investigation of the dialysis patient as well as DOPPS.

Depression and anxiety have a strong relation with each other. In addition, dialysis patients have a high frequency of such symptoms. Therefore, it is thought that the QOL is better when depression and anxiety can both improve at the same time. In our study, the quality of sleep was suggested to have a large influence on the QOL. It seems that research on further PSQI and QOL is thus necessary. As a result, in order to improve the QOL of such patients it is considered important to screen such patients for depression and anxiety at the same time.

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