Nephrol Dial Transplant (2011) 26: 1058–1065
doi: 10.1093/ndt/gfq476
Advance Access publication 4 August 2010

Sleep disorders, depressive symptoms and health-related quality of life—a cross-sectional comparison between kidney transplant recipients and waitlisted patients on maintenance dialysis

Agnes Zsofia Kovacs[1,2], Miklos Zsolt Molnar[1,3], Lilla Szeifert[1], Csaba Ambrus[4], Marta Molnar-Varga[1,5], Andras Szentkiralyi[1], Istvan Mucsi[1,6] and Marta Novak[1,7]

[1]Institute of Behavioral Sciences, Semmelweis University, Budapest, Hungary, [2]Quintiles Hungary Ltd, Budapest, Hungary, [3]Department of Transplantation and Surgery, Faculty of Medicine, Semmelweis University, Budapest, Hungary, [4]Division of Nephrology, University Health Network, University of Toronto, Toronto, Ontario, Canada, [5]Department of Learning Difficulties and Intellectual Disabilities, Eotvos Lorand University, Budapest, Hungary, [6]1st Department of Internal Medicine, Semmelweis University, Budapest, Hungary and [7]Department of Psychiatry, University Health Network, University of Toronto, Toronto, Canada

Correspondence and offprint requests to: Istvan Mucsi; E-mail: istvan@nefros.net

Abstract

Background. Kidney transplantation is believed to improve health-related quality of life (HRQoL) of patients requiring renal replacement therapy (RRT). Recent studies suggested that the observed difference in HRQoL between kidney transplant recipients (Tx) vs patients treated with dialysis may reflect differences in patient characteristics. We tested if Tx patients have better HRQoL compared to waitlisted (WL) patients treated with dialysis after extensive adjustment for covariables.

Methods. Eight hundred and eighty-eight prevalent Tx patients followed at a single outpatient transplant clinic and 187 WL patients treated with maintenance dialysis in nine dialysis centres were enrolled in this observational cross-sectional study. Data about socio-demographic and clinical parameters, self-reported depressive symptoms and the most frequent sleep disorders assessed by self-reported questionnaires were collected at enrolment. HRQoL was assessed by the Kidney Disease Quality of Life Questionnaire.

Results. Patient characteristics were similar in the Tx vs WL groups: the proportion of males (58 vs 60%), mean ± SD age (49 ± 13 vs 49 ± 12) and proportion of diabetics (17 vs 18%), respectively, were all similar. Tx patients had significantly better HRQoL scores compared to the WL group both in generic (Physical function, General health perceptions, Energy/fatigue, Emotional well-being) and in kidney disease-specific domains (Symptoms/problems, Effect- and Burden of kidney disease and Sleep). In multivariate regression models adjusting for clinical and socio-demographic characteristics, sleep disorders and depressive symptoms, the modality of RRT (WL vs Tx) remained independently associated with three (General health perceptions, Effect- and Burden of kidney disease) out of the eight HRQoL dimensions analysed.

Conclusions. Kidney Tx recipients have significantly better HRQoL compared to WL dialysis patients in some, but not all, dimensions of quality of life after accounting for differences in patient characteristics. Utilizing multidimensional disease-specific questionnaires will allow better understanding of treatment, disease and patient-related factors potentially affecting quality of life in patients with chronic medical conditions.

Keywords: depression; dialysis; health-related quality of life; kidney transplantation; sleep disorders

Introduction

Patients with advanced chronic kidney disease (CKD) requiring renal replacement therapy (RRT) have impaired health-related quality of life (HRQoL) [1–4]. Socio-demographic (age, gender, education, income) and clinical parameters (duration of renal disease, comorbid conditions, haemoglobin (Hb), serum albumin, etc.) as well as psychological factors (personality characteristics, depression and anxiety, etc.) are reportedly associated with HRQoL [5–10]. Furthermore, sleep disorders, which are very common in patients with CKD, are also important predictors of poor HRQoL in this patient population [3,11–13].

Successful kidney transplantation (Tx) is the preferred RRT for many patients with advanced CKD since it offers longer survival and less morbidity than dialysis. It is also believed to improve quality of life [7,9,14–16]. Most studies comparing HRQoL between patients after Tx vs on maintenance dialysis, however, involved only limited number of participants and assessed only a few covariables. Furthermore, many studies compared Tx patients to unselected patients on dialysis with significantly different characteristics.Frequently, those differences were not appropriately accounted for as recently pointed out by several authors

[6,17–19]. In a recent study, in which Tx patients were compared to matched (age, gender and comorbidity) waitlisted (WL) dialysis patients, no difference in perceived health status (SF-36 scores) was found [19]. Finally, the potential association between psycho-social characteristics and sleep disorders vs HRQoL has largely been neglected; only a few recent studies considered those associations in their analyses [8,11,20,21]. Thus, considerable uncertainty remains as to the difference in quality of life of dialysis patients vs Tx patients when appropriately adjusted for covariates.

Many of the cited studies utilized the SF-36 questionnaire, a generic instrument. Since many of the factors associated with impaired HRQoL in patients with CKD are closely related to the kidney disease, disease-specific instruments may provide a better understanding about the potential differences of HRQoL across treatment modalities.

Based on the above considerations, we wanted to compare HRQoL between waitlisted patients requiring maintenance dialysis (WL) vs a large prevalent cohort of stable kidney transplant recipients (Tx) using the Kidney Disease Quality of Life-SF (KDQoL-SF) [22,23] questionnaire which includes the SF-36 instrument and 11 kidney disease-targeted sub-scales. We collected information about a large number of socio-demographic and clinical variables, assessed depressive symptoms and self-reported data about the presence of the most frequent sleep disorders [insomnia, restless legs syndrome (RLS) and obstructive sleep apnoea (OSA)]. This information was used to adjust for differences in these variables between the Tx and WL samples in multivariate analyses. We hypothesized that Tx patients will have better HRQoL compared to WL patients but this difference will be attenuated after adjustment for clinical variables, depressive symptoms and sleep disorders. We expected that the differences would be more consistent on the kidney disease-targeted sub-scales.

Materials and methods

Sample of patients and data collection

This prevalent cohort of stable kidney-transplanted patients (Tx) was selected by inviting all patients 18 years or older ($n = 1067$) who were regularly followed at a single kidney transplant outpatient clinic at the Department of Transplantation and Surgery at Semmelweis University, Budapest on 30 June 2002, to participate in our cross-sectional study (Transplantation and Quality of Life-Hungary Study, TransQoL-HU Study) [12,24–27]. All patients received renal transplant between 1977 and 2002. We also approached all WL dialysis patients ($n = 214$) (WL), who were listed with the above transplant centre on 30 June 2002, and had been receiving dialysis for at least 1 month in any of the nine dialysis centres in Budapest. Data were collected between August 2002 and February 2003. Patients who had had transplantation, an acute rejection or infection within 1 month of the data collection, had dementia (determined by their most responsible physician) or refused to participate were excluded.

Demographic information and details of medical history were collected at enrolment when information about age, sex, aetiology of CKD, the presence or absence of diabetes and other comorbidities were obtained. Other socio-demographic parameters also collected were level of education, employment status (full-time or part-time job) and perceived financial situation (good, fair or poor). Participants also completed a battery of validated questionnaires during the dialysis sessions or while waiting for their regular follow-up visit at the transplant centre.

Laboratory data were extracted from the patients' charts and from electronic laboratory databases of hospitals. The following laboratory parameters were tabulated: Hb, serum creatinine and albumin. Estimated glomerular filtration rate (eGFR) was calculated using the 4-variable Modification of Diet in Renal Disease Study equation [28].

Transplant- and dialysis-related data extracted from the medical records included the following information: medications (including current immunosuppressive treatment), single-pool Kt/V, 'vintage', i.e. time elapsed since the time of the transplantation or since starting dialysis treatment. Cumulative end-stage renal disease (ESRD) time (time elapsed since the initiation of the first treatment for ESRD) was also computed.

The study was approved by the Ethics Committee of the Semmelweis University. Before enrolment, the patients received detailed written and verbal information regarding the aims and protocol of the study and signed informed consent.

Assessment of HRQoL

HRQoL was assessed with the KDQoL-SF^{TM} questionnaire which includes the Medical Outcomes Study Short Form-36 generic core (SF-36) and several multi-item scales targeted at quality of life concerns with special relevance for patients with CKD [22]. Scores for each item are computed in order to gain a potential range from 0 to 100 within each dimension/domain, with higher scores indicating better HRQoL [29]. The generic core consists of eight multi-item measures of physical and mental health status, of which four are reported in the present analysis: 'Physical functioning', 'General health perceptions', 'Energy/fatigue' and 'Emotional well-being'. The kidney disease-targeted domains that were used in this analysis focus on health-related concerns of individuals with kidney disease: 'Symptoms/problems', 'Effects of kidney disease on daily life', 'Burden of kidney disease' and 'Sleep'. These kidney disease-targeted domains were selected since they were psychometrically sound both in the original validation studies and in the Hungarian version of the instrument.

The Hungarian version of the KDQoL has been prepared by the FACIT translation group which followed the FACIT translation methodology [30]. We have recently provided evidence that most of the sub-scales of the Hungarian KDQoL-SF^{TM} are psychometrically sound and reliable both in dialyzed and transplanted populations [23]. The internal consistency of the individual sub-scales and test–retest reliability was similar to the original tool and to other translations.

Assessment of depressive symptoms

In the present analysis, scores obtained with the Center for Epidemiologic Studies Depression (CES-D) questionnaire were used to describe the severity of depressive symptoms in the sample [31]. The Hungarian version of the CES-D scale had been prepared according to a recommended procedure and has been validated by our team in Hungarian haemodialysis and kidney-transplanted patients [32,33]. Internal consistency was excellent both in transplanted (Cronbach's alpha = 0.865) and dialysis (Cronbach's alpha = 0.894) patients. We found a very good fit between the original four-factor structure of the scale (Depressed Affect, Positive Affect, Somatic Component and Interpersonal) and the data obtained both from Hungarian haemodialysis and kidney-transplanted patients. Finally, the CES-D score showed a moderate–strong correlation with other self-reported measures of emotional well-being, suggesting that the Hungarian version is a reliable tool to measure depressive symptoms in different CKD populations.

Self-reported comorbidity and self-reported sleep problems

Information about the presence or absence of comorbid conditions was obtained from the patients, as described. Self-reported comorbidity score was calculated by summing up the number of comorbid conditions the patients reported. Earlier work of our group suggested that this score correlates with mortality and provides valuable information about the overall clinical condition of the patients [2,12,25,34,35].

Symptoms of RLS were identified by using the RLS questionnaire (RLSQ). This scale has been validated as a screening instrument for RLS in sleep clinics [36]. The questionnaire was used in a recent epidemiologic survey [37] and in our earlier work [12,26,34]. RLS was identi-

Table 1. Patients characteristics

	Transplanted patients (Tx) (n = 888)	Waitlisted patients (WL) (n = 187)	P-value*
Male — n (%)	515 (58)	112 (60)	0.7
Age (years) (mean ± SD)	49 ± 13	49 ± 12	0.8
Working part- or full-time job — n (%)	231 (26)	45 (24)	0.5
Self-reported financial situation — n (%)			
Good or very good	462 (52)	90 (48)	0.5
Balanced	311 (35)	65 (35)	
Poor or very poor	115 (13)	32 (17)	
Number of years in education — n (%)			
<12 years	408 (46)	86 (46)	0.9
High school or equivalent	293 (33)	64 (34)	
University diploma	187 (21)	37 (20)	
BMI (kg/m^2)	24.8 ± 5.2	25.0 ± 4.4	0.2
Diabetes — n (%)	151 (17)	34 (18)	0.8
Number of comorbid conditions (median; min–max)	2; 0–7	2; 0–6	0.9
Transplant or dialysis vintage (months) [median; (IQR)]	54; (64)	36; (46)	N/A
Cumulative ESRD time (months) [median; (IQR)]	81; (70)	36; (46)	<0.001
Serum albumin (g/L) (mean ± SD)	41.6 ± 3.3	40.8 ± 4.2	0.01
Haemoglobin (mean ± SD) (g/L)	132 ± 19	112 ± 5	<0.001
Kt/V or eGFR (mL/min/1.73 m^2) (mean ± SD)	49 ± 19	1.28 ± 0.26	N/A
CES-D score [median; (IQR)]	9 (11)	13 (15)	0.001
Insomnia (yes) — n (%)	71 (8)	28 (15)	0.002
RLS (yes) — n (%)	44 (5)	21 (11)	0.001
High risk of OSAS (yes) — n (%)	240 (27)	62 (33)	0.1

fied only if the patient met all the diagnostic criteria. If the questionnaire was not filled completely or the patient did not follow the instructions, the scale was not scored and the information was considered missing.

The Athens Insomnia Scale (AIS) was used to identify insomnia [38]. The AIS consists of eight items (score range 0–24, with higher scores indicating worse sleep). Subjects are asked to grade the severity of their specific sleep complaints (absent, mild, severe, very severe) only if the particular complaint occurred at least three times per week during the last month. A cut-off score of 10 was used to identify patients with clinically relevant insomnia [12,27].

The risk status for OSA was assessed by using the Berlin Sleep Apnoea Questionnaire [39]. This self-administered tool includes 10 questions regarding the most frequent symptoms and consequences of OSA. The instrument consists of three major domains: the first domain is associated with snoring behaviour and the presence of apnoea. The second domain relates to the consequences of the apnoea, and the third domain assesses hypertension or high body mass index (BMI) (>30 kg/m^2). An individual is considered to be at 'high risk' for OSA if two of the three main domains are positive. If at least two domains are negative, the patient is classified as 'low risk'. If the answers were incomplete or violated the instructions, the scale was not scored and the data were considered missing [24].

Statistical analysis

Statistical analysis was carried out using the SPSS 18 software. To compare continuous variables between the Tx vs WL groups, the Student's t-test or the Mann–Whitney U-test was used. Categorical variables were analysed with the chi-square test. To compare QoL scores between WL vs Tx groups, the Mann–Whitney U-test was used since the distribution of these variables deviated from normal. To assess the independent association between quality of life scores and RRT, multiple linear regression models were built. The skewed QoL scores were natural log-transformed. Independent variables were entered in blocks to assess the relative contribution of group variables to the overall model. RRT (WL or Tx) was the first block, followed by socio-demographic characteristics (age, gender, education and self-perceived financial situation) and clinical variables (Hb, serum albumin, comorbidity and cumulative ESRD vintage), reportedly associated with HRQoL in various patient populations, in one block. The presence of the most frequent self-reported sleep problems (insomnia, RLS and OSAS) was entered as the third block of independent variables followed by the CES-D score as the fourth block.

Results

Socio-demographic and basic clinical characteristics of the sample

Quality of life data were not available due to refusal or inappropriate completion of the questionnaires for 179 (17%) of the Tx and 27 (13%) of the WL patients (non-participants). The final sample analysed, therefore, consisted of 888 Tx and 187 WL patients. Participants and non-participants in both the Tx and the WL groups were similar in age, gender distribution, serum albumin and cumulative ESRD 'vintage', and also had similar eGFR or Kt/V, respectively (not shown). Non-participant Tx patients had longer transplant 'vintage' compared to participants [median (inter-quartile range — IQR) 66 (57) vs 54 (64) months for non-participants vs participants, respectively; $P < 0.001$]. All participants were Caucasians.

The basic characteristics of the Tx vs WL groups are shown in Table 1. Tx patients had significantly longer cumulative ESRD 'vintage', higher Hb and higher serum albumin compared to the WL group. Sleep disorders were more frequent among WL compared to Tx patients, except high risk of OSAS, as reported by our group [24,26,27] (Table 1). Similarly, as we have already reported, WL patients had higher CES-D scores compared to the Tx group, indicating more severe depressive symptomatology [33]. All other parameters assessed were similar in the two groups (Table 1). Detailed description of the study sample has been published in several publications [26,27,33].

HRQoL in WL vs Tx patients

Scores for selected domains of the KDQoL-SF questionnaire for the Tx vs WL groups, respectively, are shown

Table 2. Quality of life scores of WL vs Tx patients

General HRQoL domains (SF-36)	Waiting list (n = 187)		Tx (n = 888)		P-value	Effect size (Cohen's d)
	Median	IQR	Median	IQR		
Physical functioning	70	35	80	35	0.001	0.24
General health perceptions	35	30	50	40	<0.001	0.65
Emotional well-being	72	36	80	32	0.003	0.25
Energy/fatigue	60	35	70	35	<0.001	0.32
Kidney disease-targeted domains						
Symptoms/problems	82	23	89	18	<0.001	0.41
Burden of kidney disease	50	38	75	38	<0.001	0.90
Effects of kidney disease	69	28	87	25	<0.001	0.70
Sleep	65	30	75	28	<0.001	0.32

Table 3. Multivariate linear regression analysis of quality of life domains (Ln-transformed scores) to assess the association with RRT modality

	A: modality			B: A+ Block 2			C: B+ Block 3			D: C+ Block 4		
	Beta	P-value	Adjusted R square	Beta	P-value	Adjusted R square	Beta	P-value	Adjusted R square	Beta	P-value	Adjusted R square
physfctn	0.068	0.04	0.004	0.036	0.3	0.198	0.019	0.6	0.258	0.005	0.9	0.309
genhealth	**0.225**	<0.001	0.050	**0.195**	<0.001	0.175	**0.173**	<0.001	0.228	**0.158**	<0.001	0.290
energy	0.110	0.001	0.011	0.082	0.2	0.116	0.057	0.09	0.222	0.027	0.3	0.479
emotional	0.065	0.5	0.003	0.059	0.09	0.109	0.033	0.3	0,193	−0.001	0.9	0.510
sympt	**0.124**	<0.001	0.014	**0.092**	0.008	0.144	**0.067**	0.05	0.214	0.038	0.1	0.321
burden	**0.321**	<0.001	0.102	**0.263**	<0.001	0.180	**0.241**	<0.001	0.233	**0.219**	<0.001	0.364
effects	**0.230**	<0.001	0.052	**0.228**	<0.001	0.148	**0.200**	<0.001	0.222	**0.182**	<0.001	0.313
sleep	**0.117**	<0.001	0.013	**0.095**	0.008	0.092	0.042	0.2	0.361	0.024	0.4	0.455

Shown in the cells are the parameters of the independent variable: waiting list vs transplantation. Independent variables entered into the model: Block 1: modality; Block 2 (clinical and socio-demographic): age, gender, education, self-reported financial situation, serum albumin, haemoglobin, number of comorbid conditions, ESRD vintage; Block 3 (sleep disorders): self-reported restless legs syndrome, obstructive sleep apnoea, insomnia; Block 4: depressive symptoms (CES-D score).
Abbreviations: physfctn, physical function; genhealth, general health perceptions; energy, energy-fatigue; emotional, emotional well-being; sympt, symptoms/problems list; burden, burden of kidney disease; effects, effects of kidney disease; sleep, sleep.
Highlighted with bold when the association between HRQoL domain and RRT modality is statistically significant.

in Table 2. Median scores were significantly higher for the Tx vs WL groups for all individual sub-scales assessed. The difference between the Tx vs WL groups was substantial, more than 10 points for most of the domains. Numerically, the largest difference was seen for two of the kidney disease-targeted dimensions, namely 'burden' and 'effects' of kidney disease and for the 'general health perceptions' sub-scale. The effect size varied between 0.24 (for 'physical function') and 0.90 ('burden of kidney disease'). The effect sizes were small for the SF-36 domains, except for the 'general health perceptions' sub-scale, which was 0.65, and medium–big for the kidney disease-targeted domains, except for 'sleep', which was 0.32 (Table 2).

Multivariate analysis

To assess if renal replacement modality, i.e. dialysis vs transplant is significantly associated with the various HRQoL domains independent of socio-demographic and clinical variables, multiple linear regression models were built, where the logarithmically transformed HRQoL scores were the dependent variable. Variables which were significantly associated with HRQoL in bivariate analyses or had been reported to be associated with HRQoL by others were selected for the multivariable models. Independent variables were entered in blocks to assess the relative contribution of these blocks to the overall model (see 'Materials and methods'). The results of these analyses are shown in Table 3.

The first block of independent variables was RRT modality alone. In this set of analyses, modality was significantly associated with all the HRQoL domains assessed in accord with data shown in Table 2. The adjusted R square for these models, however, was quite small for most of the domains, indicating that modality alone explained only 0.4–10% of the variance of the HRQoL scores (Table 3). Relatively, the largest effect was seen for the kidney disease-targeted 'burden' and 'effect of kidney disease' scales and the 'general health perceptions' scale of the SF-36 instrument.

All the models improved significantly and substantially after entering socio-demographic characteristics (age, sex, education, self-reported financial situation) and clinical variables (serum albumin, Hb, comorbidity, ESRD vintage) as one block. The association between 'modality' vs HRQoL remained significant for only five of the eight domains assessed. Importantly, this association remained significant for all the kidney disease-targeted dimensions (Table 3). These models explained ~9–20% of the total variability of the HRQoL scores. The relative contribution of this block was the largest for the 'physical function' and the 'general health perception' domains, but it was substantial for the kidney disease-targeted scales, as well (Figure 1).

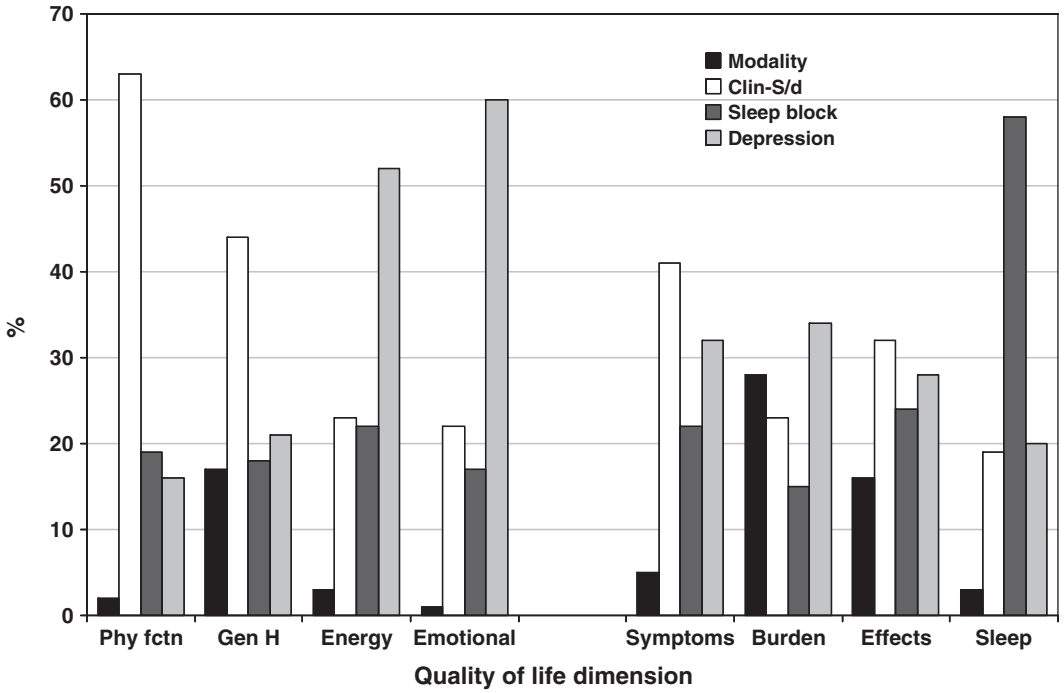

Fig. 1. Relative contribution of blocks of independent variables to the fully adjusted *R* squared of the HRQoL domains. Modality: Tx or WL; Clin-S/d (clinical and socio-demographic): age, gender, education, self-reported financial situation, serum albumin, haemoglobin, number of comorbid conditions, ESRD vintage; Sleep (sleep disorders): self-reported restless legs syndrome, obstructive sleep apnoea, insomnia; Depression: depressive symptoms (CES-D score). Abbreviations: Phy fctn, physical function; Gen H, general health perceptions; Energy, energy-fatigue; emotional, emotional well-being; symptoms, symptoms/problems list; Burden, burden of kidney disease; Effects, effects of kidney disease; Sleep, sleep.

Entering the 'sleep problem' block (the presence of self-reported insomnia, RLS or high risk of OSAS) was associated with an *R* squared change ~0.05–0.10, which corresponds to ~20% of the variance of the fully adjusted models, except for the sub-scale of 'sleep'. The 'sleep problem' block explained ~60% of the variance of this domain (Table 3 and Figure 1), and the association between 'modality' and the 'sleep' score has expectedly become non-significant after controlling for the presence of 'sleep problems' (Table 3).

The fully adjusted models (which included the CES-D score in addition to the previous blocks) explained between 29% ('general health') and 0.51% ('emotional well-being') of the variance of the quality of life scores (Table 3). The relative contribution of the CES-D score to the overall variance was above 40% for most of the general HRQoL dimensions and 20–30% for the kidney disease-targeted domains (Figure 1). In the final, fully adjusted model 'modality' was still significantly associated with one of the four general HRQoL domains ('general health perceptions') and two of the four kidney disease-targeted dimensions ('burden' and 'effect' of kidney disease) (Table 3).

Discussion

In this study, we found significantly better HRQoL in a large sample of kidney transplant recipients compared to a group of WL haemodialysis patients with very similar characteristics. This difference, however, has become non-significant in three out of the four generic HRQoL domains of the SF-36 instrument after adjusting for socio-demographic and clinical variables. Importantly, kidney disease-targeted sub-scales of the KDQoL-SF questionnaire persistently yielded significantly better HRQoL for the Tx patients even after adjusting for the presence of sleep disorders and difference in depressive symptoms. These results confirm that kidney transplantation is associated with better HRQoL compared to dialysis. We also demonstrated the complexity of HRQoL assessment and emphasize the need of using multifaceted approach when comparing HRQoL data between groups of patients treated with different treatment modalities.

There seems to be a general consensus that kidney transplantation improves quality of life compared to dialysis treatment [6–8,18]. Data from numerous, predominantly cross-sectional studies seemed to support this notion. Most of those studies, however, used non-selected patients on maintenance dialysis as comparator group and did not control for potentially important differences in case mix between patients after kidney transplantation vs on dialysis treatment. The importance of this is clearly pointed out by the result of the recent meta-analysis which suggested that the difference in HRQoL measured by the SF-36 instrument between kidney transplant recipients vs patients on dialysis was substantially reduced after controlling for age and diabetes [18]. Furthermore, Rosenberger *et al.* found no difference in HRQoL between groups of WL and Tx patients matched for age, gender and comorbidity [19]. Our results are in accord with these published data and extend our understanding further. The basic socio-

demographic and clinical characteristics of our large samples of Tx and WL patients were very similar. Both generic and kidney disease-targeted HRQoL dimensions were significantly better in the Tx group, but RRT modality accounted for only a small proportion of the variance of the HRQoL scores. After adjusting for socio-demographic and clinical variables, the HRQoL scores on the generic sub-scales were not associated with modality any more, except the 'general health perception' sub-scale (which was not assessed in the paper of Rosenberger *et al.*). These results point out that even seemingly similar groups of patients will have subtle differences which influence the comparison between those groups. Importantly, the variance explained by these models (including RRT modality and eight additional variables) was only 10–20%.

Sleep disorders, namely RLS, insomnia and OSA, are prevalent among patients with CKD and are reportedly associated with HRQoL both in patients on dialysis and after Tx. Our WL population is characterized by lower prevalence of sleep disorders compared to previous reports [40–42]. One possible explanation for this is that our WL dialysis population is younger and healthier than the non-selected prevalent HD populations involved in other studies. The prevalence of insomnia reportedly increases with age and also with comorbidity [43]. Secondly, the methods used to assess sleep problems may result in differences in the reported prevalence. In this study, we used standard instruments and stringent criteria to define the sleep problems assessed.

Similarly to insomnia, the difference in the prevalence of RLS in this paper compared to previous reports is likely explained by sample characteristics. The prevalence of RLS defined by the criteria of the International Restless Legs Syndrome Study Group in maintenance dialysis populations is 7–23% [11,41,42]. Using the RLSQ, our group has found 15% RLS in a prevalent dialysis population while the prevalence of RLS was 11% in WL patients [12]. This latter is similar to the prevalence of the condition reported by Merlino *et al.* for non-dialysis dependent-CKD patients [44]. The prevalence of sleep conditions is generally less among kidney transplant recipients compared to patients on maintenance dialysis [26,27,40,45]. Having self-reported sleep problems in the multivariable models did not seem to account for the difference between the Tx and WL groups, at least for three sub-scales (the strong association between the presence of sleep disorders and the 'sleep' sub-scale was expected).

Depression is a powerful predictor of quality of life [46–48]. Both clinically diagnosed depression and the presence of depressive symptoms have repeatedly been shown to be associated with impaired HRQoL in various patient populations. Depressive symptoms are frequently present in patients on dialysis, and their severity and/or prevalence decreases after kidney Tx [33,49]. The CES-D score in our final set of multivariable models explained ~20–30% of the total variance of the HRQoL scores not directly associated with mood. Importantly, the association between 'modality' and the HRQoL scores remained consistently significant in the three sub-scales mentioned previously ('general health perceptions', 'effects' and 'burden' of kidney disease) even after adjusting for differences in depressive symptoms.

These results clearly demonstrate that several aspects of quality of life, specifically generally feeling 'healthy' and also more specifically kidney disease-related concerns, are better in kidney transplant recipients even after extensive adjustment for socio-demographic, clinical characteristics and even sleep problems and depressive symptoms.

As indicated earlier, the three HRQoL dimensions that are robustly and consistently better in the Tx vs WL groups were 'general health perceptions', 'effects' and 'burden' of kidney disease. The first dimension combines notions about 'feeling healthy' in general and compared to others, and also about expectations about one's future health. The better HRQoL of the Tx patients on this subscale is likely a reflection of the difference between the perceptions of being a 'transplanted patient' vs a 'patient on dialysis'. The 'objective health status' of the WL patients may be very similar to their transplanted counterparts; the subjective perception of one's own health is largely influenced by their very different treatment modality and treatment environment.

Renal transplantation is not a uniformly and exclusively positive experience for all patients. Factors related to the kidney disease, such as medication side effects, psychosocial distress, anxiety, employment problems [5], are still present and have a negative impact on quality of life. Transplanted patients, however, still perceive less interference of their condition with valued everyday activities and are less concerned about their condition compared to WL patients as indicated by the significantly better scores on the 'effects' and 'burden' of kidney disease sub-scales. These are particular areas of quality of life which are not captured by the generic instruments. These results underline the need for disease-specific instruments when assessing QoL in patients with CKD.

Our study is notable for the large sample size, well-matched groups. Numerous clinical, socio-demographic parameters were collected. Importantly, rarely assessed psycho-social characteristics and sleep problems were also recorded and used in the multivariable models. The multidimensional nature of the KDQoL-SF instrument allowed us to analyse specific aspects of HRQoL and also the relative contribution of various sets of independent variables to these individual dimensions of quality of life.

Several important limitations of our study should also be noted when interpreting the results. Patients from a single centre were enrolled; therefore, our results are not to be generalized without further considerations. Generalizability is further limited, particularly as compared with the US CKD population, because of the relatively young age, low percentage of diabetics, lack of African-Americans or other ethnic groups and the low number of comorbid conditions in our sample.

The cross-sectional nature of our study does not allow us to conclude about the temporality or a causal relationship between treatment modality and HRQoL.

The proportion of non-participants was substantial. These patients, however, had similar socio-demographic characteristics to those who completed the questionnaire; consequently, it is unlikely that this has caused a systematic bias in our results.

Depressive symptoms and the presence of sleep disorders were assessed by self-reported scales, which does not allow us make clinical diagnosis. Questionnaires, on the other hand, remain valuable tools in large scale epidemiologic studies. Our earlier results suggest that the Hungarian version is a reliable tool to measure depressive symptoms in different CKD populations [3,32,33].

Information about comorbid conditions was based on self-report of the patients. However, elements of the ESRD-SI, a valid comorbidity questionnaire [36], were integrated into our tool. In a cross-sectional analysis, the self-reported comorbidity score was significantly correlated with serum albumin [37]. Self-reported comorbidity was also significantly associated with mortality in this patient population [38]. We suggest, therefore, that this score provides valuable information about the overall clinical condition of the patients.

Conclusion

In summary, we reported here that several, but not all, dimensions of HRQoL were significantly better in a large sample of kidney transplant recipients compared to a well-matched group of WL haemodialysis patients after extensive adjustment for socio-demographic, clinical and psycho-social characteristics. The most substantial difference between the two groups was seen in kidney disease-targeted sub-scales of the KDQoL-SF questionnaire. These results demonstrate the complexity of HRQoL assessment and emphasize the need of using a multifaceted approach when comparing HRQoL data between groups of patients treated with different treatment modalities.

Acknowledgements. The authors thank the patients and the staff of dialysis units in Budapest and the Department of Transplantation and Surgery, Semmelweis University, Budapest, Hungary for their assistance in this survey.

This study was supported by grant from the National Research Fund (OTKA) (T-38409, TS-049785, F-68841), ETT (240/2000, 218/2003), the Hungarian Kidney Foundation, Hungarian Society of Hypertension, Hungarian Society of Nephrology and the Foundation for Prevention in Medicine. This paper was supported by the Janos Bolyai Research Scholarship of the Hungarian Academy of Sciences (M.N. and M.Z.M.).

M.N. and M.Z.M. were recipients of the Hungarian State Eotvos Fellowship (MÖB/66-2/2010). M.N. has been supported by a grant from the Center for Integrative Mood Research, Toronto, Canada.

Conflict of interest statement. None declared.

References

1. Valderrabano F, Jofre R, Lopez-Gomez JM. Quality of life in end-stage renal disease patients. *Am J Kidney Dis* 2001; 38: 443–464
2. Mucsi I, Kovacs AZ, Molnar MZ *et al*. Co-morbidity and quality of life in chronic kidney disease patients. *J Nephrol* 2008; 21: S84–S91
3. Szentkiralyi A, Molnar MZ, Czira ME *et al*. Association between restless legs syndrome and depression in patients with chronic kidney disease. *J Psychosom Res* 2009; 67: 173–180
4. Finkelstein FO, Wuerth D, Finkelstein SH. Health related quality of life and the CKD patient: challenges for the nephrology community. *Kidney Int* 2009; 76: 946–952
5. Matas AJ, Halbert RJ, Barr ML *et al*. Life satisfaction and adverse effects in renal transplant recipients: a longitudinal analysis. *Clin Transplant* 2002; 16: 113–121
6. Cameron JI, Whiteside C, Katz J *et al*. Differences in quality of life across renal replacement therapies: a meta-analytic comparison. *Am J Kidney Dis* 2000; 35: 629–637
7. Jofre R, Lopez-Gomez JM, Moreno F *et al*. Changes in quality of life after renal transplantation. *Am J Kidney Dis* 1998; 32: 93–100
8. Franke GH, Reimer J, Philipp T *et al*. Aspects of quality of life through end-stage renal disease. *Qual Life Res* 2003; 12: 103–115
9. Rebollo P, Ortega F, Baltar JM *et al*. Health related quality of life (HRQOL) of kidney transplanted patients: variables that influence it. *Clin Transplant* 2000; 14: 199–207
10. Prihodova L, Nagyova I, Rosenberger J *et al*. Impact of personality and psychological distress on health-related quality of life in kidney transplant recipients. *Transpl Int* 2009; 23: 484–492
11. Unruh ML, Levey AS, D'Ambrosio C *et al*. Restless legs symptoms among incident dialysis patients: association with lower quality of life and shorter survival. *Am J Kidney Dis* 2004; 43: 900–909
12. Mucsi I, Molnar MZ, Ambrus C *et al*. Restless legs syndrome, insomnia and quality of life in patients on maintenance dialysis. *Nephrol Dial Transplant* 2005; 20: 571–577
13. Roumelioti ME, Argyropoulos C, Buysse DJ *et al*. Sleep quality, mood, alertness and their variability in CKD and ESRD. *Nephron Clin Pract* 2010; 114: c277–c287
14. Pietrabissa A, Ciaramella A, Carmellini M *et al*. Effect of kidney transplantation on quality of life measures. *Transpl Int* 1992; 5: S708–S710
15. Fujisawa M, Ichikawa Y, Yoshiya K *et al*. Assessment of health-related quality of life in renal transplant and hemodialysis patients using the SF-36 health survey. *Urology* 2000; 56: 201–206
16. Bohlke M, Marini SS, Rocha M *et al*. Factors associated with health-related quality of life after successful kidney transplantation: a population-based study. *Qual Life Res* 2009; 18: 1185–1193
17. Liem YS, Bosch JL, Hunink MG. Preference-based quality of life of patients on renal replacement therapy: a systematic review and meta-analysis. *Value Health* 2008; 11: 733–741
18. Liem YS, Bosch JL, Arends LR *et al*. Quality of life assessed with the Medical Outcomes Study Short Form 36-Item Health Survey of patients on renal replacement therapy: a systematic review and meta-analysis. *Value Health* 2007; 10: 390–397
19. Rosenberger J, van Dijk JP, Prihodova L *et al*. Differences in perceived health status between kidney transplant recipients and dialyzed patients are based mainly on the selection process. *Clin Transplant* 2009; 24: 358–365
20. Rosenberger J, van Dijk JP, Nagyova I *et al*. Predictors of perceived health status in patients after kidney transplantation. *Transplantation* 2006; 81: 1306–1310
21. Rosenberger J, van Dijk JP, Nagyova I *et al*. Do dialysis- and transplantation-related medical factors affect perceived health status? *Nephrol Dial Transplant* 2005; 20: 2153–2158
22. Hays RD, Kallich JD, Mapes DL *et al*. Development of the kidney disease quality of life (KDQOL) instrument. *Qual Life Res* 1994; 3: 329–338
23. Barotfi S, Molnar MZ, Almasi C *et al*. Validation of the Kidney Disease Quality of Life-Short Form questionnaire in kidney transplant patients. *J Psychosom Res* 2006; 60: 495–504
24. Molnar MZ, Szentkiralyi A, Lindner A *et al*. High prevalence of patients with a high risk for obstructive sleep apnoea syndrome after kidney transplantation—association with declining renal function. *Nephrol Dial Transplant* 2007; 22: 2686–2692
25. Molnar MZ, Novak M, Szeifert L *et al*. Restless legs syndrome, insomnia, and quality of life after renal transplantation. *J Psychosom Res* 2007; 63: 591–597
26. Molnar MZ, Novak M, Ambrus C *et al*. Restless Legs Syndrome in patients after renal transplantation. *Am J Kidney Dis* 2005; 45: 388–396
27. Novak M, Molnar MZ, Ambrus C *et al*. Chronic insomnia in kidney transplant recipients. *Am J Kidney Dis* 2006; 47: 655–665
28. The Modification of Diet in Renal Disease Study: design, methods, and results from the feasibility study. *Am J Kidney Dis* 1992; 20: 18–33
29. Hays R KJ, Mapes D, Coons S *et al*. Kidney Disease Quality of Life Short Form (KDQOL-SFTM), Version 1.3: A Manual for Use and Scoring. Santa Monica, CA: RAND, 1997

30. Bonomi AE, Cella DF, Hahn EA *et al*. Multilingual translation of the Functional Assessment of Cancer Therapy (FACT) quality of life measurement system. *Qual Life Res* 1996; 5: 309–320
31. Radloff LS. The CES-D Scale: a self-report depression scale for research in the general population. *Appl Psychol Meas* 1977; 1: 385–401
32. Zoller R, Molnar MZ, Mucsi I *et al*. Factorial invariance and validity of the Hungarian version of the center for epidemiological studies-depression (CES-D) scale. *Qual Life Res* 2005; 14: 2036
33. Szeifert L, Molnar MZ, Ambrus C *et al*. Symptoms of depression in kidney transplant recipients: a cross-sectional study. *Am J Kidney Dis* 2010; 55: 132–140
34. Molnar MZ, Szentkiralyi A, Lindner A *et al*. Restless legs syndrome and mortality in kidney transplant recipients. *Am J Kidney Dis* 2007; 50: 813–820
35. Molnar MZ, Czira M, Ambrus C *et al*. Anemia is associated with mortality in kidney-transplanted patients—a prospective cohort study. *Am J Transplant* 2007; 7: 818–824
36. Allen RP. Validation of a diagnostic questionnaire for the restless legs syndrome (RLS). *Neurology* 2001; 56: 4A
37. Allen RP, Picchietti D, Hening WA *et al*. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. *Sleep Med* 2003; 4: 101–119
38. Soldatos CR, Dikeos DG, Paparrigopoulos TJ. Athens Insomnia Scale: validation of an instrument based on ICD-10 criteria. *J Psychosom Res* 2000; 48: 555–560
39. Netzer NC, Stoohs RA, Netzer CM *et al*. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Intern Med* 1999; 131: 485–491
40. Sabbatini M, Crispo A, Pisani A *et al*. Sleep quality in renal transplant patients: a never investigated problem. *Nephrol Dial Transplant* 2005; 20: 194–198
41. Gigli GL, Adorati M, Dolso P *et al*. Restless legs syndrome in end-stage renal disease. *Sleep Med* 2004; 5: 309–315
42. Merlino G, Piani A, Dolso P *et al*. Sleep disorders in patients with end-stage renal disease undergoing dialysis therapy. *Nephrol Dial Transplant* 2006; 21: 184–190
43. Foley DJ, Monjan A, Simonsick EM *et al*. Incidence and remission of insomnia among elderly adults: an epidemiologic study of 6,800 persons over three years. *Sleep* 1999; 22: S366–S372
44. Merlino G, Lorenzut S, Gigli GL *et al*. A case-control study on restless legs syndrome in nondialyzed patients with chronic renal failure. *Mov Disord* 2010; 25: 1019–1025
45. Mallamaci F, Leonardis D, Tripepi R *et al*. Sleep disordered breathing in renal transplant patients. *Am J Transplant* 2009; 9: 1373–1381
46. Finkelstein FO, Wuerth D, Finkelstein SH. An approach to addressing depression in patients with chronic kidney disease. *Blood Purif* 2010; 29: 121–124
47. Abdel-Kader K, Unruh ML, Weisbord SD. Symptom burden, depression, and quality of life in chronic and end-stage kidney disease. *Clin J Am Soc Nephrol* 2009; 4: 1057–1064
48. Watnick S, Kirwin P, Mahnensmith R *et al*. The prevalence and treatment of depression among patients starting dialysis. *Am J Kidney Dis* 2003; 41: 105–110
49. Akman B, Ozdemir FN, Sezer S *et al*. Depression levels before and after renal transplantation. *Transplant Proc* 2004; 36: 111–113

Received for publication: 20.5.10; Accepted in revised form: 12.7.10

Nephrol Dial Transplant (2011) 26: 1065–1073
doi: 10.1093/ndt/gfq531
Advance Access publication 30 August 2010

Acute graft pyelonephritis in renal transplant recipients: incidence, risk factors and long-term outcome

Silvana Fiorante[1], Mario Fernández-Ruiz[1], Francisco López-Medrano[1], Manuel Lizasoain[1], Antonio Lalueza[1], José María Morales[2], Rafael San-Juan[1], Amado Andrés[2], Joaquín R Otero[3] and José María Aguado[1]

[1]Unit of Infectious Diseases, University Hospital 12 de Octubre, Universidad Complutense, Madrid, Spain, [2]Department of Nephrology, University Hospital 12 de Octubre, Universidad Complutense, Madrid, Spain and [3]Department of Microbiology, University Hospital 12 de Octubre, Universidad Complutense, Madrid, Spain

Correspondence and offprint requests to: José María Aguado; E-mail: jaguadog@medynet.com
This study was partially presented at the 48th Annual Interscience Congress on Antimicrobial Agents and Chemotherapy (ICAAC), Washington DC (25–28 October, 2008) (abstract K-1487).

Abstract

Background. The influence of acute graft pyelonephritis (AGPN) on graft outcome in renal transplant recipients still remains controversial.

Methods. We retrospectively analysed 189 patients (113 males; mean age: 49.7 ± 13.1 years) undergoing renal transplantation at the University Hospital 12 de Octubre (Madrid, Spain) from January 2002 to December 2004, with a minimum follow-up of 36 months. Factors associated with AGPN were assessed by logistic regression analysis. Long-term graft function was compared according to the occurrence of this complication during follow-up. 'Decline in renal graft function' was defined as the increase in serum creatinine (SC) levels >0.33 mg/dL between Month 3 and Year 1 after transplantation.

Results. Nineteen patients (10.0%) were diagnosed with 25 episodes of AGPN (incidence rate: 4.4 episodes per 100 patient-years). The presence of glomerulonephritis