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A cross-sectional study of fatigue and sleep quality before and after kidney transplantation

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Abstract: Fatigue and sleep disturbances are common problems for adults with chronic kidney disease or end-stage renal disease. However, these issues have not been examined much in the context of kidney transplantation (KTx). This study characterizes these outcomes in the KTx population and examines their association with psychological functioning and quality of life (QOL). A cross-sectional cohort of 100 wait-listed pre-KTx and 100 post-KTx patients at one transplant center in the United States completed validated fatigue, sleep, mood, and QOL questionnaires, and their medical records were reviewed. Pre-KTx patients had higher levels of fatigue frequency, fatigue severity, and fatigue disruptiveness than post-KTx patients. Also, pre-KTx patients had more difficulty with sleep quality, latency, duration, efficiency, and disturbance and were more likely to have ''poor'' sleep quality compared with post-KTx patients. Multivariate predictors of high fatigue severity for both pre- and post-KTx patients were high body mass index (BMI), poor sleep quality, and mood disturbance, while poor sleep quality was predicted by high BMI and mood disturbance. Most sociodemographic and clinical parameters were not associated with fatigue severity or sleep disturbance. Fatigue and sleep disturbances are common before and after KTx, and study findings have important implications for their assessment and management.

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Fatigue and sleep disturbances are common problems for adults with chronic kidney disease (CKD) or end-stage renal disease (ESRD) (1, 2). Defined as a subjective and distressing state of persistent tiredness or exhaustion (3), fatigue is the most prevalent and distressing symptom associated with hemodialysis (2, 4). Most patients state a preference for more frequent dialysis sessions in exchange for more energy and less fatigue (5). Also, obstructive sleep apnea, insomnia, restless leg syndrome, and other sleep disturbances are common in this population (6). Hypothesized causal mechanisms of fatigue severity and sleep disturbances in adults with renal insufficiency are numerous and include physiological, psychological, behavioral, and treatment-related factors (1, 6).

Kidney transplantation (KTx) provides better patient survival and quality of life (QOL) outcomes than dialysis for those with progressive renal insufficiency (7). However, few studies have examined fatigue severity and sleep disturbances in the setting of KTx. Fatigue has not been studied following KTx, although significant improvements in vitality suggest that it is less problematic following transplantation (8). Post-KTx sleep quality findings are equivocal. Sabbatini et al. (9) found that sleep quality post-KTx was better than that for patients receiving hemodialysis but worse than in the general population. Novak et al. (10) reported insomnia prevalence rate of 8% in post-KTx patients, which was comparable to that of a matched community control group and substantially less than the 15% of wait-listed KTx patients with the disorder.

While fatigue severity and sleep disturbances have been studied extensively in other patient

populations, their assessment in KTx patients has not kept pace (11–15). Further evaluation of these clinical issues in KTx patients is important because they have the potential to compromise otherwise favorable QOL outcomes achieved by transplantation. Moreover, enhanced understanding of their prevalence and predictors will help guide intervention development. Therefore, we characterized the nature and severity of fatigue and sleep quality in a cohort of pre- and post-KTx patients. Also, we identified multivariate predictors of these outcomes, as well as their association with QOL. We hypothesized that fatigue and sleep quality would be more severe in pre-KTx patients, that fatigue severity would be associated with low QOL both pre- and post-KTx, and that mood disturbance would predict high fatigue severity and poor sleep quality.

Methods

Study participants were recruited from the transplant outpatient clinic at Beth Israel Deaconess Medical Center (BIDMC) in Boston, Massachusetts from February 2007 to August 2007. Eligibility criteria were ≥18 yr old, English proficiency, and either listed for KTx or a KTx recipient. All study questionnaires were completed in writing by the patient or via structured interview with a trained clinical research assistant. Study procedures were approved by the BIDMC institutional review board.

Fatigue

Fatigue was measured using the Fatigue Symptom Inventory (FSI) (16) and the Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF) (17). The FSI (Cronbach's alpha = 0.95) assesses the frequency, severity, and perceived disruptiveness of fatigue. *Frequency* is measured by the number of days in the past week that the patient felt fatigued and the percentage of each day, on average, that the patient felt fatigued. *Severity* is measured using four items (0 = not at all fatigued to 10 = as fatigued as I could be) tapping current fatigue and the most, least, and average fatigue experienced in the past week. A composite fatigue severity score is obtained by averaging the severity items, and a score ≥3 is the suggested cutoff for clinically meaningful fatigue (1). *Perceived disruptiveness* is measured using seven items (0 = no interference to 10 = extreme interference) that assess the degree to which fatigue in the past week interfered with general activity level, concentration, relationships, enjoyment of life, and mood.

The MFSI-SF (Cronbach's alpha = 0.89) includes 30 statements, and patients indicate the degree to which each statement is true for them in past week (0 = not at all to 4 = extremely). Scores are obtained along five fatigue dimensions: general fatigue, physical fatigue, emotional fatigue, mental fatigue, and vigor. A fatigue total score is also obtained.

Sleep quality

The Pittsburgh Sleep Quality Index (PSQI) (18) is a 19-item questionnaire that measures sleep quality and disturbances during the past month. The PSQI yields scores across seven dimensions: quality, latency (length of time it takes to transition from full wakefulness to sleep), duration, efficiency (total sleep time relative to amount of total time in bed), disturbance, use of sleep medication, and daytime dysfunction. Higher scores indicate worse sleep quality. A global sleep quality score is calculated with a cutoff score >5 used to identify clinically poor sleep quality (19, 20).

QOL and mood

The SF-36 Health Survey (SF-36) (21) (Cronbach's alpha = 0.91) is a widely used generic QOL measure with eight domains: physical functioning, role functioning-physical, role functioning-emotional, vitality, pain, general health, social functioning, and mental health. The SF-36 also yields two composite scores – Physical Component Summary (PCS) and Mental Component Summary (MCS). Higher scores reflect better QOL.

The Profile of Mood States-Short Form (POMS-SF) (22) (Cronbach's alpha = 0.90) is a measure of mood disturbance. Patients read 30 descriptive adjectives and indicate on a five-point scale (0 = not at all to 4 = extremely) the extent to which they have felt that way in the past week. Item scores are summed to yield a total mood disturbance score and six factor scores: anxiety, depression, anger, vigor, fatigue, and confusion. The total mood disturbance score was the primary unit of analysis in this study. A higher score indicates more mood disturbance.

Medical record information

Current age, gender, race, education, employment status, substance abuse history, current body mass index (BMI), primary diagnosis, disease duration, dialysis status and duration, hematocrit, type of KTx (living, deceased), immunosuppression type, and survival days (post-KTx

patients) were extracted from the patient's medical record.

Statistical analyses

This study was designed to have statistical power of ≥80% to detect a difference of at least one standard deviation between pre- and post-KTx patients on the FSI composite fatigue severity score and the PSQI global sleep quality score. Our target recruitment to achieve this level of statistical power was a total sample of 172 patients. Descriptive statistics (means and standard deviations, proportions) were calculated for all sample characteristics and dependent measures. Q-Q plots were used to examine distributional characteristics. MSFI total scores did not appear to be normally distributed, and log transformations were performed. Differences between the pre- and post-KTx patients were examined using *t*-tests and Fisher's exact tests. We then examined predictors of fatigue severity and sleep quality separately for pre- and post-KTx patients. Fatigue severity was categorized as "low" (FSI average severity score <3) or "high" (FSI average severity score ≥ 3). Sleep quality was categorized as "good" (PSQI global score ≤ 5) or "poor" (PSQI global score >5). Univariate analyses were first conducted, and sociodemographic, clinical, and mood disturbance variables found to be significantly associated ($p < 0.05$) with fatigue severity or sleep quality were included in subsequent multiple logistic regression analyses. Finally, we used *t*-tests to examine whether QOL was associated with the dichotomized fatigue severity and sleep quality variables. Statistical significance was defined as $p \leq 0.05$. All analyses were conducted using SPSS 16.0 for Windows (Chicago, IL, USA).

Results

One hundred wait-listed pre-KTx and 100 post-KTx patients provided informed consent and completed study questionnaires. Participation rates were 82% (100/122) and 89% (100/113) for pre- and post-KTx patients, respectively. Table 1 summarizes the sample characteristics. With a few exceptions, the sociodemographic characteristics of our study participants are comparable to those of our entire KTx patient population at our transplant program (data available at http://www.unos.org). Relative to those on the waiting list during the study period, there was a higher proportion of African Americans enrolled in the study (31% vs. 37%). Compared to all KTx recipients during the study period, our post-KTx cohort had higher proportions of women (38% vs. 46%) and white patients (63% vs. 82%). Relative to pre-KTx patients, post-KTx patients were more likely to be white ($p = 0.001$) and employed ($p = 0.03$), and they had significantly lower BMI ($p = 0.04$). Most pre-KTx patients (62%) were receiving dialysis (hemo = 59, peritoneal = 3). Most post-KTx patients (61%) received a live donor KTx, and about half had received KTx within the past two yr. Immunosuppression regimen was as follows: 60% tacrolimus, 31% sirolimus, and 9% both tacrolimus and sirolimus.

Table 1. Sociodemographic and clinical characteristics of pre-KTx and post-KTx patients

	Pre-KTx (n = 100)	Post-KTx (n = 100)	p Value
Age, yr	52.1 ± 12.2	53.1 ± 11.3	0.54
Gender, female (%)	38	46	0.32
Race (%)			
White	54	82	0.001
Black	37	17	
Hispanic	7	1	
Other	2	0	
Employed, yes	38	54	0.03
Education (%)			
No high school diploma	19	17	0.46
High school or equivalent	47	38	
Some college	17	22	
College graduate	17	23	
Married, yes (%)	62	66	0.56
Body mass index	29.5 ± 6.8	27.5 ± 6.2	0.04
Smoking history (%)	62	51	0.12
Alcohol abuse/dependence history (%)	28	21	0.25
Drug abuse/dependence history (%)	19	17	0.71
Primary diagnosis (%)			
Diabetes mellitus (I)	26	34	0.01
Diabetes mellitus (II)	17	6	
Focal glomerular sclerosis	6	9	
HIV	10	3	
Hypertension	18	10	
Polycystic kidneys	5	11	
Other	18	27	
Hematocrit	35.5 ± 4.8	36.9 ± 5.1	0.06
Dialysis, yes (%)	62		
Dialysis duration, months	36.8 ± 28.9		
Transplant type, % living donor (%)		61	
Immunosuppression regimen (%)			
Tacrolimus		60	
Sirolimus		31	
Tacrolimus + sirolimus		9	
Time since KTx (%)			
<1 yr		31	
1–2 yr		17	
3–5 yr		32	
>5 yr		20	

KTx, kidney transplantation.

QOL and mood disturbance

Significant differences were evident between pre-KTx and post-KTx patients on nearly all of the SF-36v2 and POMS-SF indices. In each instance, pre-KTx patients reported poorer functioning than post-KTx patients. Pre-KTx patients had worse physical functioning ($p = 0.008$), role-physical ($p = 0.003$), bodily pain ($p = 0.05$), general health ($p < 0.001$), vitality ($p = 0.003$), and social functioning ($p = 0.05$). Scores on the POMS-SF indicated more symptoms of depression ($p = 0.05$), anger ($p = 0.008$), and confusion ($p = 0.04$), less vigor ($p = 0.02$), and more total mood disturbance ($p = 0.007$) for pre-KTx patients.

Fatigue

Relative to KTx recipients, pre-KTx patients reported significantly higher levels of fatigue frequency, fatigue severity, and fatigue disruptiveness (Table 2). Current ($p = 0.02$) and average fatigue ($p = 0.009$) levels were higher in pre-KTx patients. Also, pre-KTx patients reported more fatigue interference with enjoyment of life ($p = 0.05$) and mood ($p = 0.04$). More pre-KTx than post-KTx patients were classified as having "high" fatigue severity (72% vs. 59%, $p = 0.04$).

Similar patterns emerged on the MFSI-SF, with pre-KTx patients reporting significantly higher general, physical, emotional, and mental fatigue and lower levels of vigor (Table 2). Pre-KTx patients also had a significantly higher fatigue score on the POMS-SF.

Approximately one-third of both pre-KTx (32%) and post-KTx patients (37%) reported no consistent pattern of daily fatigue ($p = 0.49$), although a higher proportion of pre-KTx patients (28%) reported worse fatigue in the afternoon (vs. 18% for post-KTx patients).

Table 2. Means and standard deviations for the Fatigue Symptom Inventory (FSI), Multidimensional Fatigue Symptom Inventory (MFSI-SF), and Profile of Mood States (POMS-SF) Fatigue subscale in pre-KTx and post-KTx patients

	Pre-KTx (n = 100)	Post-KTx (n = 100)	p Value
FSI frequency			
Days in past week felt fatigued[a]	4.32 ± 2.5	3.80 ± 2.6	0.16
How much of days felt fatigued[b]	4.56 ± 3.1	3.49 ± 2.9	0.01
FSI Severity[c]			
Current fatigue	3.61 ± 2.8	2.67 ± 2.6	0.02
Most fatigued	6.12 ± 2.6	5.44 ± 3.0	0.09
Least fatigued	3.55 ± 2.5	2.38 ± 2.3	0.001
Average fatigue	4.52 ± 2.3	3.64 ± 2.4	0.009
FSI Disruptiveness[d]			
General activity level	3.93 ± 2.9	3.22 ± 2.9	0.09
Ability to bathe and dress self	1.86 ± 2.6	1.18 ± 2.0	0.04
Normal work activity	3.64 ± 3.1	2.99 ± 3.1	0.14
Concentration ability	2.86 ± 2.7	2.30 ± 2.5	0.14
Relations with others	2.85 ± 2.9	2.34 ± 2.5	0.18
Enjoyment of life	4.00 ± 3.2	3.08 ± 3.2	0.05
Mood	3.47 ± 3.1	2.41 ± 2.8	0.04
MFSI general fatigue	11.46 ± 7.0	8.77 ± 6.7	0.01
MFSI physical fatigue	8.33 ± 5.9	5.10 ± 4.3	<0.001
MFSI emotional fatigue	5.81 ± 5.4	4.32 ± 4.6	0.04
MFSI mental fatigue	5.62 ± 5.0	3.75 ± 3.9	0.003
MFSI vigor	10.10 ± 4.8	12.27 ± 5.9	0.005
MFSI total	21.12 ± 21.5	9.66 ± 19.3	<0.001
POMS fatigue	8.99 ± 5.5	6.81 ± 5.5	0.02

KTx, kidney transplantation.
[a]0–7 days.
[b]0 (none of the day) to 10 (the entire day).
[c]0 (not at all fatigued) to 10 (as fatigued as I could be).
[d]0 (no interference) to 10 (extreme interference).

Sleep quality

Pre-KTx patients had significantly higher PSQI global mean scores than post-KTx patients, indicating more sleep disturbance (Table 3). Pre-KTx patients had more difficulty with sleep quality, latency, duration, efficiency, and disturbance, and they were more likely to be classified as having "poor" sleep quality compared with post-KTx patients (78% vs. 52%, $p < 0.001$).

Pre-KTx patients reported taking longer minutes to fall asleep (43.8 ± 44.9 vs. 24.9 ± 22.1, $p < 0.001$), and they were more likely to use sleep medications ≥3 times per week in the past month (31% vs. 16%, $p = 0.01$). While there was no significant difference in total hours slept per night in the past month (6.5 ± 2.0 vs. 6.9 ± 1.6, $p = 0.18$), pre-KTx patients were less likely to sleep ≥6 hr per night (70% vs. 84%, $p = 0.01$). Most pre-KTx (77%) and post-KTx (68%) patients

Table 3. Pre-KTx and post-KTx scores on the Pittsburgh Sleep Quality Index (PSQI)

	Pre-KTx (n = 100)	Post-KTx (n = 100)	p Value
Global score[a,b]	9.55 ± 4.8	6.84 ± 4.0	<0.001
Component scores[a,c]			
Sleep quality	1.44 ± 1.0	1.05 ± 0.9	0.003
Sleep latency	1.73 ± 1.1	1.08 ± 1.0	<0.001
Sleep duration	1.44 ± 1.1	1.02 ± 1.0	0.01
Habitual sleep efficiency	1.13 ± 1.2	0.65 ± 0.9	0.002
Sleep disturbance	1.69 ± 0.6	1.35 ± 0.5	<0.001
Use of sleep medications	0.94 ± 1.3	0.64 ± 1.1	0.09
Daytime dysfunction	1.20 ± 0.9	1.05 ± 0.8	0.22

KTx, kidney transplantation.
[a]Higher scores reflect more sleep disturbance.
[b]Global scores range from 0 to 21.
[c]Component scores range from 0 to 3.

reported trouble waking up during the night. The most common reasons for nighttime awakening were breathing difficulties (74%), pain (40%), and coughing or snoring loudly (33%).

Correlates of fatigue severity and sleep quality

FSI Severity scores were positively correlated with both MFSI total scores (pre-KTx $r = 0.72$, $p < 0.001$; post-KTx $r = 0.69$, $p < 0.001$) and PSQI global scores (pre-KTx $r = 0.44$, $p < 0.001$; post-KTx $r = 0.46$, $p < 0.001$). MFSI total scores were also significantly correlated with PSQI global scores (pre-KTx $r = 0.49$, $p < 0.001$; post-KTx $r = 0.48$, $p < 0.001$). Additional correlational analyses showed that several variables were associated with fatigue and sleep outcomes (all p values <0.05). High pre-KTx fatigue severity was significantly associated with older age, diabetes, higher BMI, poor sleep quality, and more mood disturbance. Poor pre-KTx sleep quality was significantly associated with hemodialysis, higher BMI, and more mood disturbance.

For post-KTx patients, both high fatigue severity and poor sleep quality were significantly associated with higher BMI and more mood disturbance. Fatigue severity also was significantly associated with older age and poor sleep quality, while poor sleep quality was associated with high fatigue severity. Fatigue level was slightly higher in patients taking sirolimus versus tacrolimus (65% vs. 55%), but this did not reach statistical significance ($p = 0.38$).

We also examined correlates of the different types of fatigue assessed by the MFSI-SF. For both pre- and post-KTx patients, more physical fatigue was associated (all p values <0.05) with older age, dialysis, poor sleep quality, and more mood disturbance. Higher mental fatigue was correlated with dialysis, poor sleep quality, and total mood disturbance, while higher emotional fatigue was associated with more mood disturbance.

Predictors of fatigue severity and sleep quality

In the logistic regression models, significant multivariable predictors of high pre-KTx fatigue severity were diabetes, higher BMI, poor sleep quality, and total mood disturbance. Poor pre-KTx sleep quality was predicted by hemodialysis, higher BMI, and total mood disturbance. High post-KTx fatigue severity was predicted by higher BMI, poor sleep quality, and total mood disturbance, while poor post-KTx sleep quality was predicted by higher BMI and total mood disturbance (Table 4).

Table 4. Results of multivariate logistic regression analysis for fatigue severity and sleep quality

Variables	Odds ratio	95% CI	p Value
Pre-KTx			
High fatigue severity[a]			
Diabetes	1.58	1.21, 2.80	0.05
Higher body mass index	1.12	1.03, 1.21	0.03
Poor sleep quality (PSQI)	1.13	1.02, 1.21	0.03
Total mood disturbance (POMS-SF)	1.09	1.04, 1.14	0.001
Poor sleep quality[b]			
Dialysis	3.00	1.13, 7.96	0.03
Higher body mass index	1.09	1.06, 1.12	0.01
Total mood disturbance (POMS-SF)	1.05	1.02, 1.09	0.01
Post-KTx			
High fatigue severity[c]			
Higher body mass index	1.08	1.02, 1.15	0.04
Poor sleep quality (PSQI)	1.10	1.01, 1.24	0.03
Total mood disturbance (POMS-SF)	1.11	1.06, 1.16	0.001
Poor sleep quality[d]			
Higher body mass index	1.06	1.01, 1.12	0.02
Total mood disturbance (POMS-SF)	1.04	1.01, 1.07	0.003

High fatigue severity is defined as Fatigue Symptom Inventory (FSI) composite score ≥3.
Poor sleep quality is defined as Pittsburgh Sleep Quality Index (PSQI) global score >5.
KTx, kidney transplantation; POMS-SF, Profile of Mood States-Short Form.
[a]Total model is significant ($p = 0.03$) and the Hosmer–Lemeshow test showed good model fit ($\chi^2 = 9.2$, $p = 0.24$) with high discrimination (0.79).
[b]Total model is significant ($p < 0.0001$) and the Hosmer–Lemeshow test showed good model fit ($\chi^2 = 6.4$, $p = 0.50$) with high discrimination (0.86).
[c]Total model is significant ($p < 0.0001$) and the Hosmer–Lemeshow test showed good model fit ($\chi^2 = 10.8$, $p = 0.21$) with high discrimination (0.80).
[d]Total model is significant ($p = 0.005$) and the Hosmer–Lemeshow test showed good model fit ($\chi^2 = 11.4$, $p = 0.18$) with high discrimination (0.76).

Fatigue, sleep quality, and QOL

High fatigue severity and poor sleep quality were significantly associated with all SF-36 scores in both the pre- and post-KTx cohorts. Therefore, we combined the two cohorts and classified patients into four groups: (i) low fatigue severity, good sleep quality, (ii) low fatigue severity, poor sleep quality, (iii) high fatigue severity, good sleep quality, and (iv) high fatigue severity, poor sleep quality. The analysis of variance group effect was statistically significant across all SF-36 indices (all p values <0.001). Post hoc tests showed that KTx patients classified as having high fatigue severity and poor sleep quality had significantly lower QOL scores relative to those with low fatigue, regardless of sleep quality (Fig. 1).

Discussion

Three main findings emerged from this study that support our a priori hypotheses. First, fatigue severity is high and sleep quality is poor in a

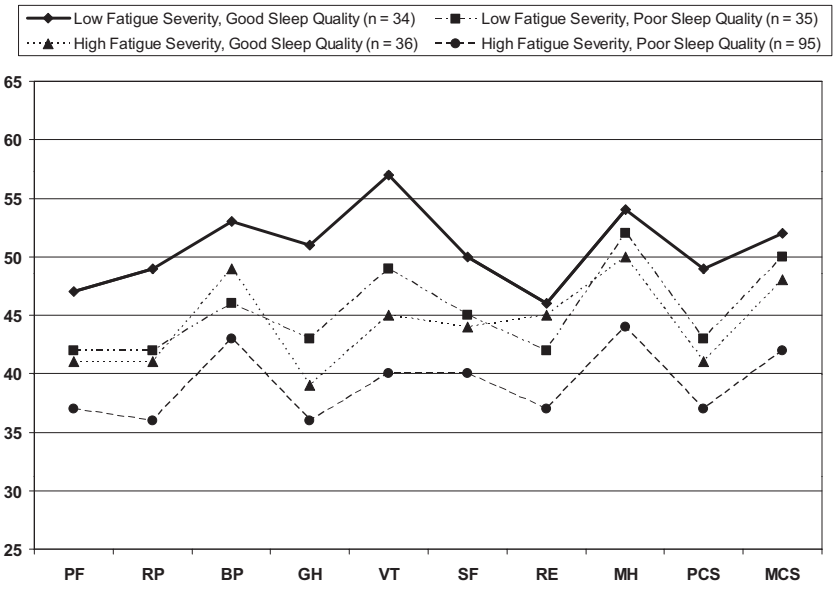

Fig. 1. Mean scores on the SF-36 subscales broken down by fatigue severity and sleep quality. PF, physical functioning; RP, role functioning – physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role functioning – emotional; MH, mental health; PCS, Physical Component Summary; MCS, Mental Component Summary. Higher scores indicate better quality of life.

substantial proportion of both pre- and post-KTx patients. Second, higher BMI and mood disturbance consistently emerged as salient predictors of fatigue severity and poor sleep quality in both pre- and post-KTx patients. Third, patients with high fatigue severity and poor sleep quality have significantly lower QOL. Collectively, these findings have important implications for the assessment and management of fatigue and sleep disturbances in patients across the KTx spectrum.

The finding of high fatigue severity in pre-KTx patients is not surprising because fatigue is among the most common and problematic symptom for adults with renal insufficiency (1, 4, 23). Indeed, FSI scores in the current study exceeded those reported for adults receiving treatment for breast cancer (24) and were comparable to those of adults with end-stage liver disease (Rodrigue JR, Nelson DR, Reed AI, Hanto DW, Curry M, in press). Our findings further suggest that fatigue is multidimensional and includes comparably high rates of physical, emotional, and mental fatigue. It is important to assess for these different components of fatigue because they may have distinctive etiologies and manifestations. For instance, we found that physiological and sociodemographic (e.g., low hematocrit, older age) variables were associated with physical fatigue, but not emotional or mental fatigue. Also, patients on hemodialysis reported more physical and mental fatigue, relative to emotional fatigue, than patients not on dialysis. Renal insufficiency is known to have physical as well as neuropsychological and emotional manifestations, and this may be especially true for elderly patients (25–27).

The finding of poor sleep quality among those with CKD or ESRD (78% in the current study) was expected because prevalence rates of insomnia, obstructive sleep apnea, restless leg syndrome, and excessive daytime sleepiness are high (50–80%) in this population (9, 28–33). However, we also found that more than half (52%) of KTx recipients had poor sleep quality, suggesting that this problem also is highly prevalent after transplantation. This finding mirrors that of Sabbatini et al. (9) and Kachuee et al. (34), who found that 53% and 62% of KTx recipients, respectively, were classified as poor sleepers based on PSQI scores. Collectively, these figures are much higher than the estimated one-third of adults who have insomnia or poor sleep quality of the general population (35). While KTx largely restores renal function and improves symptoms associated with uremia, sleep problems may persist in a large subset of patients and should be routinely assessed and treated. Indeed, even for those without a history of chronic health problems, sleep problems such as insomnia tend have a chronic course (35, 36).

We found that higher BMI was a robust predictor of both fatigue severity and poor sleep quality. Obesity (BMI $\geq$ 30) is a known risk factor for fatigue and sleep disorders (37–39). It is possible that the relationship we found between high BMI and fatigue levels is mediated by the presence of obstructive sleep apnea. Unfortunately, we did not assess whether patients were diagnosed or treated for obstructive sleep apnea. The rising BMI of the US population has implications for KTx that extend beyond fatigue and sleep quality, including access to transplantation, graft survival,

and heightened cardiovascular risk (40–42). In addition to reducing the risk of metabolic syndrome, weight loss in the KTx population may lead to improvements in fatigue and sleep quality, although this has yet to be demonstrated in any clinical trials.

As many as two-thirds of adults with ESRD may have clinical depression (43), and adult KTx recipients also are at risk for depression and anxiety (44). Mood disturbance, fatigue, and sleep disturbances are closely linked. Symptoms of depression, for instance, may include insomnia, low energy, and physical and cognitive fatigue. In our study, mood disturbances – including depression, anxiety, and anger – not only were strong predictors of higher fatigue severity and poorer sleep quality but also were associated with different types of fatigue (physical, mental, and emotional) before and after KTx. These findings highlight the importance of systematic psychological symptom assessment and management.

Diabetes predicted more fatigue and hemodialysis predicted more sleep problems in pre-KTx patients. The relationship between endocrine disorders and sleep disturbances is multifaceted and complex, including the potential role of sleep disorders in promoting insulin resistance (45). In a post hoc analysis, we found that 33 of 36 (92%) pre-KTx diabetic patients receiving hemodialysis had poor sleep quality, suggesting that this combination of clinical features may elevate the risk for sleep disturbances. Evidence for a relationship between these clinical outcomes and other sociodemographic or medical parameters has been inconclusive (9, 32), and they failed to consistently emerge as predictors of fatigue or sleep problems in our multivariate analyses.

Effective strategies to assess and treat fatigue and sleep problems in KTx patients have the potential to improve functional capacity and QOL. Several validated sleep assessment tools have been developed including the FSI and PSQI that are brief and easy to administer in outpatient clinics. There are many challenges to developing interventions to improve fatigue and sleep disturbances in the KTx population, including the lack of practice guidelines and different causal mechanisms for different types of fatigue and sleep disturbances. While both pharmacological and non-pharmacological interventions have been evaluated in different medical populations, their effectiveness in KTx patients is largely unknown (46–49). Jhamb et al. (1) advocate for a multidisciplinary clinical approach to managing fatigue and sleep disturbance and further stress the importance of training nephrologists and transplant specialists to better assess these clinical issues. We also suggest that KTx programs develop a collaborative relationship with a sleep health center to assist in the clinical evaluation and management of sleep-related problems.

This study has several important limitations. First, this was a cross-sectional study, and we could not examine fatigue and sleep quality changes over time. We cannot determine, for instance, whether post-KTx fatigue problems represent a continuation of pre-KTx fatigue or new-onset fatigue problems. Second, patients were recruited from only one KTx program, thus limiting the generalizability of the findings. Third, patients were self-selected, and those who chose to take part in the study may have more/less fatigue and sleep problems. Fourth, we did not include a healthy comparison group to determine whether rates of fatigue and sleep disturbance in our samples were higher than those in the general population, although this has been shown by other investigators (9, 10). Finally, there are many other contributors to fatigue and sleep disturbance, especially in the pre-KTx dialysis population, that we did not examine, but that may be important to assess in future research. For instance, uremia, dialysis adequacy, hyperparathyroidism, medication side effects, comorbid medical conditions, dietary and fluid restrictions, and physical inactivity have all been implicated as potential causal mechanisms of fatigue (1). Also, there is emerging research, suggesting that changes in proinflammatory cytokine levels, particularly IL-1, IL-6, and TFN-α, may play an important mediating role in fatigue (50).

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Conflict of interest

None.

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