Effect of kidney transplantation on sleep quality in patients admitted in ICU:a cross-section study in China

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Abstract

Background Although evidences showed that sleep disorder is common in patient with end stage renal disease (ESRD), less is known about their sleep quality after early post-kidney transplantation (kTx) especially in Intensive Care Unit (ICU). Thus, the purpose of this study is to investigate sleep quality of kTx recipients in ICU and explore factors related poor sleep, second, to measure the correlation of subjective sleep quality and sleep architecture assessed by PSG in kTx recipients.

Methods This study recruited participants from ESRD patients registered in transplantation waiting list at the third xiangya hospital of central south university in China. Participants required to complete the Pittsburgh sleep quality index(PSQI) and demographic questionnaire as baseline data and received one night of Polysomnography (PSG) in the ICU within 96 hours of surgery, during which time sound and light data were monitored. After that Richards Campbell sleep questionnaires (RCSQ) also need completed.

Results 26 participants self-reported sleep quality and sleep efficiency based on RCSQ was at middle level (49.2 ± 25.6 mm), and 14/26(53.8%) kTx recipients in ICU were poor sleepers defined by RCSQ <50. PSG showed that most kTx recipients in ICU had shallow sleep with mainly stage 2 sleep time (80.90 ± 70.10 min), lower total sleep time (136.50 ± 86.41 min), higher awakening frequency after sleep onset (8.87 ± 5.92 times) and long awaken time (94.67 ± 75.09 min) when a sleep disruption occurred. multiple linear regression analysis showed that self-reported noise and pain were the significant factor affecting sleep($P < 0.05$).

Conclusion Subjective sleep quality based on RCSQ scored better than objective one measured by PSG in kTx recipients, sleep disruption always remained a substantial problem and affected by self-reported noise and pain.

1. Background

Sleep disorder is one of the most common comorbidities in patients with end-stage renal disease (ERDS), and the prevalence rate is gradually increasing. It causes abnormal sleep and poor sleep quality, which could generate some undesirable health consequences, such as fatigue^[1], depression^[2], decreased quality of life^[3], premature mortality^[4] as well as major economic consequences^[5].

Kidney transplantation (kTx) is the main treatment for patients with ERDS. It seems that successful transplantation could restore normal metabolism and is likely to improve sleep quality^[6]. Most studies suggested that sleep quality improved in kTx recipients (30%-52%)^[1,7] than patients with ERDS (49%-78%)^[8-10]. Our previous research^[11] also showed the percentage of "poor sleep" in kTx recipients during follow-up was much lower about 29.2% (defining as global Pittsburgh sleep quality index (PSQI) >7). These results from previous reports all seem to be very good, but most of the subjects were only targeted at recipients with longer transplant times, none studies cared about individuals who stayed in ICU at earlier postoperative times.

Poor sleep could be defined using specific diagnostic criteria subjectively and objectively. In general, subjective questionnaires are the simple and convenient methods for preliminary sleep screen and diagnosis. Commonly used questionnaires include PSQI^[12], Epworth Sleepiness Scale^[13], and the Berlin

Questionnaire^[14]. However, all the screening survey questionnaires only provided general described or categorized results about sleep symptoms and there is no physiological analysis of sleep. Polysomnography (PSG) is a significant tool for sleep related evaluations and sleep studies. It could provided quantitative information of sleep and its deviation from the normal by analyzing sleep physiological parameters. Although PSG is the gold standard for diagnosing sleep disorders, only a few published articles^[15-18] reported PSG assessment of sleep in kTx recipients for it requires long wear times that limited its use in sleep research. However, Considering that PSG can still provide relatively detailed sleep physiological information and intuitively reflect the patients' sleep situation at night in ICU. Therefore, the purposes of this study were:

1. to describe the sleep quality characteristics of kTx recipients in ICU based on subjective questionnaires and PSG, and to explore factors related poor sleep.
2. to measure the correlation of subjective sleep quality and sleep architecture assessed by PSG in kTx recipients.

2. Methods

2.1 design, setting and participants

This was a prospective, cross-sectional study using convenient sampling. All kTx recipients who admitted in ICU at the Third Xiangya Hospital of Central South University in Hunan Province, China from August 2018 to April 2019 were recruited. The inclusion criteria were: age 18 years to 60 years, being at least stay 96 hours in ICU after surgery and with no physical or mental conditions that would prevent the participants from completing the survey and the measurement of PSG.

Ethical approval was obtained from the Institutional Review Board (IRB) of the Third Xiangya Hospital of Central South University. Participants need to signed consent at the beginning of the study. Every participant received an open published book of "Essentials you need to know after kidney transplantation" (12 RMB) or a medicine container (15 RMB) for free.

2.2 variables and measurement

Eligible participants needed to complete the demographic, medical history questionnaire and self-reported sleep quality as baseline data before surgery . Then an objective and subjective sleep assessment were respectively performed at postoperative transplantation ICU. Meanwhile, Pain, sound, and light were also collected during the sleep monitoring.

2.2.1 Demographics, clinical characteristics

Age, gender, height, weight, occupation, status of marriage or fertility, degree of education, monthly income, the type of sleep and waiting time for transplantation were collected by interviewing. Primary disease, the type of dialysis before kTx, times of operation, creatinine ($\mu\text{mol/l}$), creatinine clearance rate (ml/min), hemoglobin (g/l), immunosuppressors and sleep drugs before and after operation were also retrieved from the participants' hospital information system.

2.2.2 self-reported sleep quality

The self-reported sleep quality of kTx recipients before and after surgery was investigated using the PSQI and Richards Campbell sleep questionnaires (RCSQ). Self-reported sleep quality of kTx recipients within one month prior to surgery and 96 hours after surgery using the PSQI and RCSQ.

The PSQI is one of the most widely used and most easily self-reported sleep quality questionnaires. It has been validated and used in a variety of clinical populations by differentiating between “poor-” and “good-” quality sleepers. The PSQI includes 19 questions to assess seven domains of sleep: subjective sleep quality, sleep latency, duration, efficiency, disturbances, use of sleep medication, and daytime dysfunction over the past month. Scoring is based on a 0–3 Likert scale, which a score of 3 reflects the negative extreme. Global PSQI scores range from 0 to 21 with a cutoff score of >5 indicating poor sleep in the general population^[12]. Liu et al^[19] used the PSQI > 7 as the cutoff to differentiate the poor sleep quality in the Chinese version of PSQI, which showed a higher sensitivity (98.3%) and specificity (90.2%).

RCSQ was developed by Richards et al^[20] specifically for patients admitted in ICU. The RCSQ scale consisted of 5 items including sleep depth, difficulty falling asleep, number of awakenings, difficulty in re-sleeping, and overall sleep quality. Each item was scored using visual analogue scale from 0~100mm. Patient marks the distance on the line that represents each item score. The total RCSQ score is the average score of 5 items, with higher scores indicating better sleep. Naik et al^[21] defines good sleep in one study as a total RCSQ score of ≥ 50 (sensitivity 88.24%, specificity 86.67%), patients with total RCSQ score <50 were considered to have poor sleep. The Chinese version of the RCSQ scale has a content validity of 0.840 and a Cronbach's α coefficient of 0.874^[22].

2.2.3 objectively measured sleep quality

PSG is known as the current gold standard for measuring sleep. Attended one overnight PSG would be performed for each participant. This technique employs numerous collections of surface electrodes, which measures physiologic parameters of sleep including brain dynamics of EEG, eye movements, muscle activities, heart physiology, and respiratory function^[23]. Finally, data from the PSG were downloaded into a computer, and the sleep characteristics were concluded by following parameters: sleep onset latency (SOL: The duration of time between the patient tried to sleep when the lights are turned off until the time patient actually falls asleep); wake after sleep onset (WASO: time spent awake from sleep onset to finally awakening); total sleep time (TST: the entire time spent sleeping); times and percentages of non-rapid eye movement stages (N1, N2, N3) and latency of rapid eye movement (REM), sleep efficiency (SE); . All these sleep characteristics from the PSG are also reflective of five domains: sleep depth, difficulty in falling asleep, number of wakes, percent of awakening time, and overall quality of sleep.

2.2.4 Other variables

Pain, sounds and lights are the common factors affecting sleep, these variables would be also collected when PSG was performed. Visual analogue scale (VAS) were used to assess the pain degree of recipients, it's easy and simple to use for post-surgery patients. Sounds were detected by digital sound level meter (SMART AR844), lights by luminometer (TES-1330A).

2.3 Analysis of sleep micro-structure

The sleep micro-structure was analyzed by PSG technicians according to the sleep staging rules promulgated by the American Academy of Sleep Medicine. Through the analysis of different frequency and amplitude sleep signals, the information of the N1, N2, N3, REM and awakening periods, the proportion of each period, the number of awakenings, the number of sleep transitions and other indicators were extracted.

2.4 Statistical analysis

All data were reviewed by the double check. If the missing values in the questionnaire was >20% or key values were missing in the PSG, the data in this case was invalid. Statistical analyses were performed using SPSS 25.0 (SPSS Inc., Chicago, IL). The continuous data were described as mean and standard deviation, while the categorical data were described as frequencies and percentages. Correlation between RCSQ and PSG was tested using the Spearman correlation test. Multivariable linear regression analysis was used for exploring the influencing factors of subjective sleep quality.

3. Results

3.1 Sample characteristics

40 participants were enrolled, of those 8 were excluded for invalid RCSQ questionnaires and 6 for incomplete PSG data. Finally, 26 participants were eligible. The study profile, including reasons for loss to follow-up is summarized in figure 1.

The participants had a mean age of 38.08 ± 9.68 year, 17/26 were male and their waiting time for kTx less than 1 year, 24/26 individuals received hemodialysis (HD), the mean HD time was 13.7 ± 11.6 months, 9/26 had a bad sleep quality (PQSI>7) before the transplant (Table 1).

3.2 subjective sleep quality in post-operative ICU

The mean RCSQ score of kTx recipients in ICU was 48.8 ± 20.6 mm, which indicated that self-reported sleep quality and sleep efficiency was on the middle levels. According to the sleep disruption definition(total RCSQ<50 mm) by Naik, 14/26(53.8%) individuals were poor sleepers when stayed in ICU at earlier postoperative times.

3.3 objective sleep quality and their association with RCSQ score

According to the analysis of PSG sleep characteristics, it showed that kTx recipients in ICU had shallow sleep with mainly stage 2 sleep time (80.90 ± 70.10 min), lower total sleep time (136.50 ± 86.41 min), higher awakening frequency after sleep onset (8.87 ± 5.92 times), long awakening time (94.67 ± 75.09 min) when they waked up.

In the next step, the association between RCSQ score and PSG sleep characteristics was analyzed. Known from the original questionnaire, RCSQ item corresponds to multiple sleep characteristics of PSG in each sleep

domain. As presented in the Table 2, there was no statistically significant correlation between PSG sleep characteristics and RCSQ items.

3.4 pain, noise(VAS), sound(dB) and light

Pain (38.5 ± 17.1) and noise (34.2 ± 27.2) were at low level based on the visual analogue scale (VAS), the noises detected by digital sound level meter was at middle level (49.7 ± 3.4 dB), so as the intensity of light (49.2 ± 31.4 Lux) (Table 3).

3.5 subjective sleep quality and associated factors

Correlation analysis was performed for each predictor and potential confounder variables, only pain (Spearman $r=0.42$, $P=0.03$) and noise (Spearman $r=0.67$, $P=0.00$) correlated with RCSQ score.

Furthermore, pain and noise with multivariable linear regression were analyzed. The result showed that higher RCSQ score was significantly associated with higher pain and noise (Table 4).

4. Discussions

Although there is a growing evidence show the importance of sleep quality on kTx recipients^[2,3,6,24], most of them only focused on patients from outpatient or clinic with some subjective sleep questionnaires. Few studies investigated the sleep quality of kTx recipients who stayed in postoperative ICU, especially rarely used objective sleep assessment tool. This study provides a current characteristic of the quality and quantity of sleep of kTx recipients in ICU based on the subjective and objective methods.

This study found that self-reported sleep quality and sleep efficiency of recipients was at a middle level which were consistent with previous reports^[21,25]. Study^[26] has shown that as the transplantation time prolongs, sleep quality of kTx recipients will gradually improve, but the symptoms of sleep disorder will be still worse than the general population. Difference from the previous researches, this study described the sleep characteristic and level using RCSQ rather than PSQI in the people who stayed at transplantation ICU. RCSQ described a specific and concurrent sleep pattern of an overnight sleep monitoring in ICU, and the mean total score (49.2 ± 25.6 mm) obtained in our study was lower than mean score (51.42 ± 21.48 mm) obtained in other study^[25]. Both these two study sites were in the surgery ICU, but our participants were younger (38.1 ± 9.7 vs 57.72 ± 14.81 yr), it is a well-known fact that perception of sleep quality decrease with advancing age^[27]. Also, there are only 9/26 (34.6%) recipients diagnosed with “poor sleep” defined by PSQI >7 before the transplant, while 14/26 (53.8%) recipients were poor sleepers defined by RCSQ <50 after the transplant.

To gain the sight of sleep architecture in kTx recipients, PSG was employed for one-night sleep, the result showed that participants typically experienced more shallow sleep, especially stage 1 and 2 sleep, frequent awake, increased the total awakening time, decreased restorative sleep like N3 and REM sleep. This result was similar with other ICU sleep survey results^[28], which manifest that reduced REM sleep, sleep fragmentation, increased arousal, and deep sleep reduction. was evident in ICU. In fact, some studies^[29-30] reported that short and fragmented sleep architecture had occurred in patients with chronic dialysis before kTx. For the problem of poor sleep in the ICU, various factors have been proposed, including patient-related factors and

environmental factors. There is an agreement in the literature that environmental factors might greatly impact the patients' quality of sleep in ICU^[31].

To further analyze the relationship between subjective sleep and objective sleep, bivariate analysis was used. Due to a single item of RCSQ may correspond to multiple sleep characteristics of PSG, so a single sleep item cannot be used as a proxy for a PSG sleep characteristic. The results showed that all RCSQ items are less correlated with corresponding PSG characteristics with no statistically significant. The study was different from the Richards et al^[20] study which demonstrated there was a moderate correlation between RCSQ and PSG, The five item RCSQ score can predict 33% of the variance in the sleep efficiency index. Several reasons could explained it when there was a subjective-objective mismatch. First of all, age could affected the perceived sleep. In one study^[32], the relation between subjective sleep quality and PSG variables in older and younger women was investigated, it found that perceived poor sleep was related to short TST, long awakening time, low sleep efficiency and high frequency of awakenings. For those older women, even they had lower TST and sleep efficiency and longer awakening time, their rate of good sleep was still higher than younger women, because older women would adjust objective criteria for good sleep downwards. Second, cognitive and psychological could be another factors including time perception. For poor sleepers, they always tended to underestimate nocturnal sleep and overestimated awake times related to their own sleep problem^[33]. In our study, The small sample size, the younger subjects may be factors influencing inconsistency between the subjective and objective sleep. Also Consider that the kTx recipients wore with a PSG monitor for the first time and the "first-night effect" could increase both stage 1 sleep time and REM latency^[34].

Moreover, multivariable linear regression analysis showed that sleep quality was affected by noise and self-report pain. The noise detected by digital sound level meter was middle level (47.34 ± 3.01 dB), it equivalent to average noise levels in ICU which can reach 55 to 65 dB over a 24-hour period^[35-36]. Noise has been considered to be a key factor of poor sleep in the ICU in some studies. It shows that noise is responsible for 11% to 24% of the total number of arousal^[37]. However in our study, the recipients' subjective perception of sound was much lower than the actual monitoring sound, this average noise levels in ICU has little practical impact on patients though it excess of recommendations by the WHO (45 dB in the daytime and above 35 dB at night. These indicate that recipients subjectively reduce the tolerance of noise in the ICU, making it one of the affected factors of sleep disorders, other objective factors must be taken into consideration in this phenomenon, such as the environmental layout of the ICU may enhance the subjective noise response.

Pain was known as one of most terrible experience in ICU and had a negative effect on the sleep quality. The result also showed that self-report pain was associated with sleep quality though pain detected by VAS at a relative low level. It means that in the state of sedation and analgesia, the patient still has a certain perception of pain, which may be related to the shallower analgesic intensity and kidney transplant recipients may be unable to communicate their level of pain if sedated and anesthetized.

5. Strengths And Limitations

As far as we know, this study was the first study to explore the sleep of kidney transplant recipients in ICU by using both subjective and objective methods in China. It can be seen that the objective outcome of the

patient's sleep was not ideal, the subjective sleep score was still at a low level, and the degree of association between subjective and objective sleep was inconsistent, which was similar to the results of other studies. This suggests that the patient's response to subjective sleep is more in line with their sleep experience. In transplanted patients, difficult sleep is more likely to be connected with the existence of some psychological problems than with sociodemographic or biochemical parameters^[8]. Although patient's sleep in ICU is difficult to achieve by changing the physiological indicators that affect sleep, it may be effective to change the external physical environment in ICU and do some the psychosocial interventions.

Several limitations of this study should be considered when interpreting our results. First of all, admittedly, our study sample was small. When analyzing the influencing factors of sleep, some indicators such as hemoglobin, hormonal dosage were not included in the regression equation. However, these were related factors affecting sleep in other studies. Molnar et al^[38] reported that Hb was significantly correlated with AHI and was higher in patients with apnea. A potential explanation for this association is the recurrent reduction of oxygen saturation caused by apnea, which stimulates erythropoietin production. Corticosteroids are well-known to cause sleep disturbance, insomnia, and unpleasant dreams, which insomnia is the most frequently reported sleep-related side effect of steroids and immunosuppressive medications^[39]. As this study included these indicators but did not produce a dominant result, this may be related to the sample size of this study is too small.

6. Conclusions

The quantity and quality of kidney transplant recipients sleep in ICU by using both objective and subjective assessment methods were not in consistency, while the subjective sleep quality based on RCSQ score better than objective one measured by PSG. However, sleep disruption always have remained a substantial problem and affected by self-reported noise and pain. Importantly, though the RCSQ is easy and simple to used for patients in ICU, the current study has questioned about the association between PSG and RCSQ score. Therefore, self-reported sleep of patients in ICU also requires assessment by others to further understand the sleep disruption of this vulnerable patient population. Another potential way to improve prediction is to add an additional section to the questionnaire consisting of observation of patient sleep by nurses. Then , it would be able to develop more targeted and operative interventions .

Declarations

Abbreviations

ESRD:End stage renal disease; kTx:Kidney transplantation;ICU:Intensive care unite; PSQI:Pittsburgh sleep quality index;PSG:Polysomnography; RCSQ: Richards Campbell sleep questionnaires; EEG:Electroencephalogram; IRB:Institutional Review Board;SOL: sleep onset latency; TST:Total sleep time; WASO:Wake after sleep onset; SE:sleep efficiency; N1:Percentages of stages 1; N2:Percentages of stages 2; SWS:Slow wave sleep; REM:Rapid eye movement; VAS:Visual analogue scale;HD:hematodialysis

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None

Author's contributions

LL carried out the study and drafted manuscript; JL JY designed the study and revised the manuscript; JFX designed the study and supervision of data collection; HL KHY carried out the study and data analysis. All authors have read and approve of the final manuscript.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethical approval was obtained from the Institutional Review Board of the Third Xiangya Hospital of Central South University. Consent to participate was required and not applicable. We retrospectively used medical records.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1 Demographics and clinical characteristics of participants (n=26)

Parameters	Mean (SD)	Percentage[%]
Age	38.1(9.7)	
Sex		
Males		17(65.4)
Females		9(34.6)
BMI (kg/m ²)	22.6(3.3)	
HD		24(92.3)
HD duration[month]	13.7(11.6)	
Creatinine[umol/l]	938.6(308.2)	
Creatinine clearance rate(ml/min)	9.06(3.39)	
Haemoglobin (g/l)	114.2(23.0)	
The waiting time for kTx		
<1 year		17(65.4)
1~3 years		9(34.6)
Global PQSI score		
PQSI>7		9(34.6)
PQSI≤7		17(65.4)

Descriptive statistics and Correlation of PSG sleep characteristics with RCSQ items

domains	PSG sleep characteristics	PSG mean $\pm$ SD	Corresponding RCSQ item	RCSQ mean $\pm$ SD	r
h	Percent N2	38.38 $\pm$ 26.12	Item1 light sleep /deep sleep	52.31 $\pm$ 25.50	-0.06
ep	percent N3	4.13 $\pm$ 8.84			0.26
	sleep onset latency	14.19 $\pm$ 16.27	Item 2 fall asleep immediately/never could fall asleep	49.62 $\pm$ 36.16	0.21
s	Number of awakenings	8.52 $\pm$ 6.06	Item 3 awake very little/awake all night alone	46.54 $\pm$ 26.67	0.19
time	Percent of time awake	46.64 $\pm$ 34.90	Item 4 go back to sleep immediately/ couldn't get back to sleep	46.15 $\pm$ 32.63	0.21
sleep	Total sleep time	136.50 $\pm$ 86.41	Item 5 a good night sleep/ a bad night sleep	49.23 $\pm$ 25.60	-0.31
	Latency to sleep onset	14.19 $\pm$ 16.27			-0.19
					0.26
	Total sleep time	136.50 $\pm$ 86.41			0.14
	Number of awakenings	8.52 $\pm$ 6.06			0.27
	Percent N2	38.38 $\pm$ 26.12			-0.19
	Percent REM	0.9 $\pm$ 3.0			-0.35

Table 3 pain, noise(VAS), sound(dB) and light

Items	Mean	Standard	Minimum	Maximum
Pain (VAS)	38.5	17.1	10	80
Noise (VAS)	34.2	27.2	0	100
Sound (dB)	49.7	3.4	43.2	59.5
Light (lux)	49.2	31.4	3.4	102.6

Table 4 Association of pain, noise and RCSQ score in multivariable linear regression model

Variables	β coefficient	95% CI	P
Pain (VAS)	0.409	0.058-0.759	0.024*
Noise(VAS)	0.466	0.245-0.687	0.000**

* $P < 0.05$, ** $P < 0.01$.

Figures

Figure 1

study profile

Supplementary Files

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- [STROBEchecklistcrosssectional.doc](#)