Nephrol Dial Transplant (2008) 23: 998–1004
doi: 10.1093/ndt/gfm630
Advance Access publication 1 October 2007

Original Article

NDT
Nephrology Dialysis Transplantation

Sleep quality predicts quality of life and mortality risk in haemodialysis patients: Results from the Dialysis Outcomes and Practice Patterns Study (DOPPS)

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Abstract

Background. Poor sleep quality (SQ) affects many haemodialysis (HD) patients and could potentially predict their morbidity, mortality, quality of life (QOL) and patterns of medication use.

Methods. Data on SQ were collected from 11 351 patients in 308 dialysis units in seven countries in the Dialysis Outcomes and Practice Patterns Study (DOPPS) between 1996 and 2001 through a patient self-reported SQ scale, ranging from 0 (worst) to 10 (best). A score of <6 reflected poor SQ. Sleep disturbance was also assessed by self-reported daytime sleepiness, feeling drained and nocturnal awakening. Logistic and multiple linear regression were used to assess predictors of SQ and associations with QOL. Cox regression examined associations with mortality. Analyses accounted for case-mix, facility clustering and country.

Results. Nearly half (49%) of patients experienced poor SQ. Mean SQ scores varied by country, ranging from 4.9 in Germany to 6.5 in Japan. Patients with poor SQ were more likely to be prescribed antihistamines, antidepressants, anti-inflammatories, narcotics, gastrointestinal (GI) medications, anti-asthmatics or hypnotics. Physical exercise at least once a week (*vs* < once a week) was associated with lower odds of poor SQ (AOR = 0.55–0.85, $P < 0.05$). Poorer SQ was associated with significantly lower mental and physical component summary (MCS/PCS) scores (MCS scores 1.9–13.2 points lower and PCS scores 1.5–7.7 points lower when SQ scores were <10 *vs* 10). The RR of mortality was 16% higher for HD patients with poor SQ.

Conclusions. Poor SQ is common among HD patients in DOPPS countries and is independently associated with several QOL indices, medication use patterns and mortality. Assessment and management of SQ should be an important component of care.

Keywords: DOPPS; haemodialysis; mortality; pain; quality of life; smoking

Introduction

Poor sleep quality (SQ) is common among patients on maintenance haemodialysis (HD). The associated factors are not well understood. Insomnia, defined as the difficulty either to start or maintain sleep, has been shown to be highly associated with SQ, as have disorders such as restless leg syndrome (RLS), periodic limb movement and sleep apnea. These disorders are formally diagnosed through polysomnography performed in a sleep laboratory or through the use of a portable device to assess respiration during sleep in a home setting. Prior studies have shown poor SQ in HD patients to be associated with female sex, older age, caffeine intake, recombinant erythropoietin therapy, years on dialysis, depression, cardiovascular disease, physical functioning, larger body mass index (BMI), exercise, dialysis adequacy, parathyroid hormone, serum creatinine and quality of life (QOL) [1–3].

Questionnaire-based surveys have found a prevalence of poor SQ in HD patients ranging between 41 and 83% [4–7]. However, the majority of these studies involved relatively small numbers of patients ($n < 100$). The DOPPS is a prospective, observational study designed to examine the relationships between HD practices and patient outcomes and, as such, provides an opportunity to study this topic

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in large numbers of HD patients around the world. In this study, we examined the prevalence of self-reported poor SQ and patient characteristics associated with it. In addition, we investigated associations with mortality, QOL indices, depression, pruritus, exercise frequency, certain laboratory values, other factors pertaining to sleep and use of different types of medication among those with poor SQ to gain important clinical insights into this problem for those on HD.

Methods

Data sources

Sleep quality was assessed using data collected in DOPPS I (1996–2001), wherein adult HD patients were randomly selected for study participation from 308 dialysis facilities ($n = 17\,034$ patients from seven countries: France, Germany, Italy, Japan, Spain, the United Kingdom and the United States). Facilities were randomly selected in each country to be representative of the types and geographic distribution of facilities within each country. The DOPPS sampling plan and study methods have been described previously [8].

Patient information was collected without patient identifiers, and patient consent was obtained as required from local or national ethics committees or institutional review boards. In DOPPS I, US facilities began study participation in 1996, European facilities in 1998, and Japanese facilities in 1999. Data were collected from 20 to 40 prevalent HD patients at each facility (depending upon facility size), and also from new end-stage renal disease (ESRD) patients when they initiated chronic HD. The total number of patients for whom SQ data were available was 11 351 from 308 facilities. Detailed patient data were collected at study entry (baseline) and at 4-month intervals thereafter.

Statistical methods

The main variable of interest was patient self-reported SQ as derived from the Kidney Disease Quality of Life Short Form (KDQOL-SF-36^{TM}). Patients were asked, "On a scale of 0 to 10 (where 0 represents 'very bad' and 10 represents 'very good'), how would you rate the quality of your sleep overall?" Those who rated their SQ as 0–5 were characterised as having poor SQ; an SQ of 6–10 was considered good.

The correlation between the patient self-reported sleep score and different types of sleep-related problems identified at the patient level was also examined. Information about these problems was elicited with these questions: (1) How often during the past 4 weeks did you awake at night and have problems falling asleep again? (2) How often did you have problems getting the amount of sleep needed? (3) How often did you have trouble staying awake during the day? Each of these questions had six possible responses: none of the time, a little of the time, some of the time, a good bit of the time, most of the time and all of the time. For our analysis, respondents were considered not to have the individual sleep problem if they answered "none of the time", "a little of the time" or "some of the time" to the following questions: "How often did the patient awaken and have trouble falling asleep again?" and "How often did the patient have trouble staying awake during the day?" However, those who answered "a good bit of the time", "most of the time" or "all of the time" were classified as having a sleep problem. The converse was used for the question that asked how often a patient got the amount of sleep needed.

Another outcome examined was "feeling washed out or drained", which was defined as a patient being moderately, very much, or extremely bothered by this feeling. In addition, patient self-reported SQ was used to predict physician-diagnosed depression, risk of mortality and differences in mental and physical component summary (MCS and PCS) scores, as calculated from responses to the KDQOL-SF^{TM}. The scores for MCS and PCS were derived from eight subscales originally developed for the Short-Form Health Survey (SF-36): physical functioning, role—physical, bodily pain, general health, vitality, social functioning, role—emotional and mental health. Various medications including antihistamines, antidepressants, anti-inflammatories, narcotics, GI medications, anti-asthmatics, hypnotics, beta blockers and anti-hypertensive medications were also investigated as predictors of patient SQ.

Logistic regression was used to examine (1) predictors of SQ; (2) the relationship of a patient's self-reported SQ score with the outcomes of "feeling washed out or drained" and physician-diagnosed depression and (3) the relationship of exercise frequency and degree of bodily pain with the odds of poor SQ. Predictors included age; sex; race; single-pool Kt/V (spKt/V); haemoglobin levels; serum albumin levels; albumin-corrected serum calcium levels; serum phosphorus levels; time with ESRD; BMI; smoking status; pruritus (as defined by Pisoni *et al*. [9], moderately, very much, and extremely itchy were considered to be pruritus); country of residence and 13 summary comorbid conditions (coronary artery disease (CAD), congestive heart failure (CHF), cardiac disease other than CAD or CHF, hypertension, diabetes, cerebrovascular disease, peripheral arterial disease (PAD), cancer, HIV/AIDS, lung disease, neurologic disorders, GI bleeding and recurrent cellulitis/gangrene). In addition, all logistic models were adjusted for physician-diagnosed depression except when depression was the outcome. In the logistic regression models, generalised estimating equations were used to account for clustering at the facility level, assuming a compound symmetry covariance structure.

For the analyses involving exercise frequency, patients were asked, "How often do you exercise (do physical activity during your leisure time)?" The six possible responses were: daily or almost daily, 4–5 times a week, 2–3 times a week, about once a week, less than once a week and almost never or never. Concerning pain, patients were asked, "How much bodily pain have you had during the past 4 weeks?" Possible responses were: none, very mild, mild, moderate, severe, and very severe. For the pain analysis, the responses of severe and very severe were combined.

Mixed linear regression was used to examine the association between a patient's MCS or PCS score and SQ with adjustments for age, race, sex, 13 summary comorbid conditions, depression, years on dialysis, BMI, smoking status

and country of residence while adjusting for facility clustering effects.

Cox proportional hazards regression was used to examine the relationship between mortality and SQ, with adjustments for age, race, sex, Kt/V, haemoglobin, albumin, phosphorus, calcium adjusted for albumin, 13 summary comorbid conditions, depression, BMI, smoking status and years on dialysis. Cox models were stratified by country and used a robust sandwich estimator to account for facility clustering. Time at risk was defined as the period from when the patient questionnaire was completed (usually within 4 months of entering the DOPPS) until death, departure from the study or end of study follow-up.

All analyses were performed using the SAS, version 9.1 (SAS Institute, Cary, NC, USA).

Results

Descriptive statistics

Figure 1 shows the considerable variation in SQ among prevalent HD patients on a scale of 0–10, where 0 represented the poorest possible SQ and 10 represented the best. The mean sleep score was 5.8 and the median was 6. Therefore, we categorised patients with a sleep score below 6 to be poor sleepers (49%) and those with a score of 6 or greater to be good sleepers (51%).

Mean sleep score varied by country. The lowest average score was 4.9 in Germany; the highest was 6.5 in Japan. France, Italy, Spain, the United Kingdom and the United States were all very similar in their mean sleep scores, ranging from 5.2 (United Kingdom) to 5.6 (France, United States). Compared with Japan, mean sleep scores for the remaining six countries were significantly different ($P < 0.0001$). The percentages of patients with poor SQ also varied by country, ranging from 63% in Germany to 53–56% in France, Italy, Spain, the United Kingdom and the United States to 37% in Japan (data not shown).

Table 1 shows demographic and comorbid characteristics for the prevalent patient sample. Significant differences among patients who had poor *vs.* good SQ included female sex; higher BMI; presence of bodily pain; and a higher prevalence of CAD, CHF, other cardiovascular diseases, diabetes, GI bleeding in the prior 12 months, lung disease, psychiatric disorders, PAD, depression and pruritus. The largest difference was seen in the prevalence of patients with depression, which was more than two times higher in those with poor SQ (17.5%) than with good (8.4%). The percentage of patients who were current smokers or had quit smoking within 1 year of completing the patient questionnaire was also higher among the group with poor SQ.

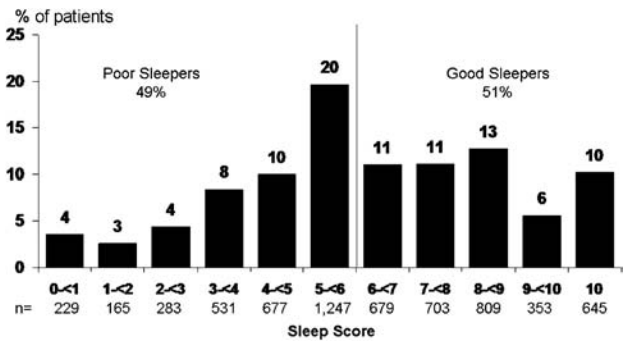

Fig. 1. Distribution of SQ scores among prevalent HD patients in DOPPS I (1996–2001). Responses regarding SQ on a scale of 0–10 are based upon self-reported data collected from a prevalent cross section of HD patients at 308 dialysis units participating in DOPPS I (1996–2001) from France, Germany, Italy, Japan, Spain, the United Kingdom, and the United States. The line between the scores of 5–6 and 6–7 represents an arbitrary division between poor SQ and good SQ, with poor SQ represented as a sleep score <6.

Table 1. Summary of prevalent patient demographics and comorbidities and associations with good SQ and poor SQ

Demographic/Comorbidity	Good sleepers Mean (SD) or % ($n = 3189$)	Poor sleepers Mean (SD) or % ($n = 3132$)
Age (years)	59.0 (14.7)	58.9 (14.3)
Male	60.7%	55.4%*
Black	14.8%	14.7%
Body mass index (kg/m^2)	23.2 (4.8)	23.9 (5.3) *
Smoking status (y/n)	16.4%	18.3%*
Pruritus**	36.8%	52.2%*
Bodily pain	33.3%	55.1%*
Diabetes	28.2%	31.6%*
Coronary artery disease	29.4%	36.0%*
Congestive heart failure	22.2%	29.8%*
Other cardiovascular disease	29.6%	34.3%*
Hypertension	71.0%	74.1%
Cerebrovascular disease	13.5%	14.4%
Recurrent cellulitis	4.9%	7.4%
Gastrointestinal bleeding	4.6%	7.1%*
HIV/AIDS	0.4%	0.5%
Cancer	7.7%	7.9%
Lung disease	6.6%	10.9%*
Peripheral arterial disease	16.8%	22.5%*
Neurologic disease	6.3%	7.2%
Psychiatric disorder	12.2%	22.3%*
Depression diagnosis	8.4%	17.5%*
Years on dialysis [median (IQR)]	3.3 (1.2, 7.2)	3.0 (1.2, 6.8)
Sleep medication use	19.0%	29.5%*

Note: Poor SQ = sleep score <6, IQR = Inter-quartile range (25th percentile, 75th percentile).
*Significantly different mean (%) from good sleepers ($P < 0.05$).
**Defined as moderately to extremely bothered by itchy skin in the past 4 weeks as reported by the patient.

Characteristics associated with greater likelihood of poor sleep quality in haemodialysis patients

We explored patient characteristics including demographics, baseline comorbidities and most recent laboratory values to determine their relationship to the likelihood of having poor SQ (Table 2). Patients had significantly higher odds ($P < 0.05$) of poor SQ if they were smokers or had pruritus, a BMI >30 kg/m^2 *vs* 20–30 kg/m^2, CAD, diabetes, GI bleeding, lung disease, PAD, depression or high baseline serum phosphorus levels. Those with a lower likelihood of suffering from poor SQ tended to be male, black, or living in Japan or Spain rather than the United States. A model using the number of summary comorbid conditions present in patients to quantify/indicate their level of illness showed that the odds of having poor SQ

Table 2. Predictors of poor SQ

Characteristic	AOR* poor SQ *vs* not	*P*-value
Black (*vs* non-black)	0.74	0.0008
Male (*vs* female)	0.78	<0.0001
Smoker	1.24	0.005
Pruritus	1.33	<0.0001
Body mass index (kg/m^2)		
<20	1.08	0.28
20–30	1.00	Ref.
>30	1.26	0.01
Years with ESRD (per one year)	1.01	0.05
Gastrointestinal bleeding	1.34	0.02
Lung disease	1.29	0.009
Peripheral arterial disease	1.18	0.04
Depression diagnosis	1.69	<0.0001
Japan (*vs* United States)	0.49	<0.0001
Spain (*vs* United States)	0.73	0.06
Serum phosphorus (mg/dl)		
<3.5	1.08	0.48
3.5–5.5	1.00	Ref.
5.6–7.0	1.07	0.27
>7.0	1.24	0.007
Calcium phosphorus product (mg^2/dl^2)		
<40	1.02	0.84
40–50	1.00	Ref.
51–60	1.04	0.65
61–70	1.16	0.07
71–80	1.24	0.04
>80	1.52	0.0005

*Adjusted odds ratio.
Note: Also adjusted for 10 other comorbidities, years on dialysis, spKt/V, albumin, albumin-adjusted serum calcium, haemoglobin, and country; accounted for facility clustering effects; $n = 6{,}321$.

was 1.08 times higher ($P < 0.0001$) for every additional comorbid condition a patient had (data not shown). Patient characteristics not significantly associated with poor SQ included CAD, CHF, cardiac disease other than CAD or CHF, hypertension, diabetes, cerebrovascular disease, cancer, HIV/AIDS, neurologic disorders, recurrent cellulitis/gangrene, years on dialysis, spKt/V and albumin. At higher levels of serum phosphorus, there was also a steady rise in the odds of having poor SQ. The likelihood of suffering from poor SQ was 1.24 times higher ($P = 0.007$) when serum phosphorus was >7.0 mg/dl, compared with 3.5–5.5 mg/dl. Furthermore, the likelihood of poor SQ was 1.52 times higher at a calcium phosphorus product level of >80 mg^2/dl^2 *vs* 50–60 mg^2/dl^2 ($P = 0.0005$). Length of dialysis session and number of sessions per week were also tested, but neither was significantly associated with SQ.

Pattern of medication use and poor sleep quality in haemodialysis patients

Because certain medications can affect SQ, we compared patients prescribed medications thought to affect SQ with those not taking them. For patients with poor *vs* good SQ, 14.3% *vs* 11.1% were prescribed an antihistamine, 8.2% *vs* 5.1% an antidepressant, 34.1% *vs* 22.4% a narcotic, 36.4% *vs* 32.2% a GI medication and 29.5% *vs* 19.0% a sleep medication. In multivariable analyses, patients using an antihistamine, antidepressant, anti-inflammatory, narcotic, GI medication, anti-asthmatic or sleep medication were significantly more likely to have poor SQ compared with patients with good SQ (Table 3). Beta blockers and other antihypertensive medications were not found to be associated with SQ.

Table 3. Adjusted odds ratios of poor SQ by medication use

Medication use (yes *vs* no)	AOR poor SQ *vs* not	*P*-value
Antihistamine	1.25	0.002
Antidepressant	1.35	0.0001
Anti-inflammatory	1.30	0.02
Narcotic	1.55	<0.0001
Gastrointestinal medication	1.14	0.004
Anti-asthmatic	1.51	0.0007
Sleep medication	1.59	<0.0001

Note: Based on seven individual logistic regression models adjusted for age, sex, race, BMI, smoking status, physician-diagnosed depression, 13 summary comorbid conditions, albumin-corrected serum calcium, serum phosphorus, serum albumin, haemoglobin, years on dialysis, and country (antidepressant model not adjusted for depression); accounted for facility clustering effects; $n = 10\,171$.

Other sleep-related problems and sleep quality score in haemodialysis patients

We compared other sleep-related variables between those with poor and good SQ: patients who awoke during the night and had trouble falling asleep again at least a good bit of the time, 62% *vs* 12%; patients who felt sleepy during the day at least a good bit of the time, 24% *vs* 15%; those who reported not getting enough sleep, 72% *vs* 32%; patients who reported being moderately to extremely bothered by feeling drained, 56% *vs* 32%. Patients who awoke during the night and had trouble falling asleep again at least a good bit of the time or reported not getting enough sleep were highly correlated with poor SQ ($R^2 = 0.83$, $P < 0.0001$), providing further validation of this score (Table 4).

Association of self-reported exercise frequency and sleep quality in haemodialysis patients

Patients indicated their frequency of physical exercise in response to the question, "How often do you exercise (do physical activity during your leisure time)?" Possible responses to this question appear on the *x*-axis in Figure 2. Significant associations with poorer SQ were noted when

Table 4. Associations of SQ score with other sleep-related problems

	Odds ratio	
Outcome: experiencing sleep-related problem (yes *vs* no)	SQ score (per one unit lower)	*P*-value
Waking at night ($n = 10\,372$)	1.89	<0.0001
Feeling sleepy during day ($n = 10\,519$)	1.17	<0.0001
Not getting enough sleep ($n = 10\,193$)	1.55	<0.0001
Bothered by feeling drained ($n = 10\,489$)	1.22	<0.0001

Note: Based on four individual unadjusted logistic regression models; accounted for facility clustering effects.

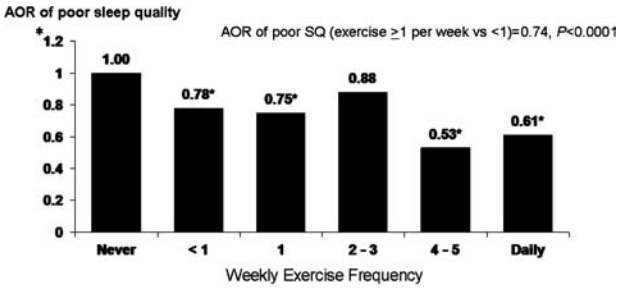

Fig. 2. Likelihood of poor SQ with patient-reported exercise frequency per week. Multivariate logistic regression was used to determine the relationship between patient-reported frequency of exercise and the odds of a patient having poor SQ. The model was adjusted for age, sex, race, years with ESRD, spKt/V, haemoglobin, serum albumin, albumin-adjusted serum calcium, serum phosphorus, BMI, smoking status, 13 comorbid conditions, physician-diagnosed depression, pruritus, and country. The model accounted for facility clustering effects and included a cross SQ quality and exercise frequency ($n = 6321$).

comparing patients who reported never exercising with those who exercised at least one time per week. Patients who exercised 1–7 times per week *vs* <1 time per week had significantly lower likelihood of poor SQ (AOR = 0.74, $P < 0.0001$).

Association of bodily pain and sleep quality in haemodialysis patients

Patients indicated their degree of bodily pain when asked, "How much bodily pain have you had during the past 4 weeks?" Possible responses appear on the *x*-axis of Figure 3. The likelihood of suffering from poor SQ was shown to rise dramatically with greater degrees of bodily pain (AOR = 1.32–3.54).

Mental component summary and physical component summary scores by sleep quality score

An investigation into the relationship between QOL and SQ scores was performed using MCS and PCS scores

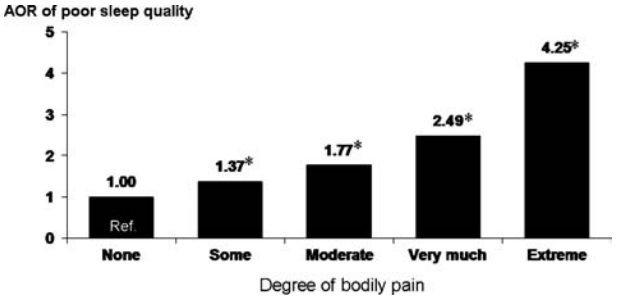

Fig. 3. Likelihood of poor SQ with patient-reported degree of bodily pain. Multivariate logistic regression was used to determine the relationship between patient-reported degree of bodily pain and the odds of a patient having poor SQ. The model was adjusted for age, sex, race, years with ESRD, spKt/V, haemoglobin, serum albumin, albumin-adjusted serum calcium, serum phosphorus, BMI, smoking status, 13 comorbid conditions, physician-diagnosed depression, pruritus and country. The model accounted for facility clustering effects and included a cross section of patients from DOPPS I who completed the questions concerning SQ and bodily pain ($n = 6321$).

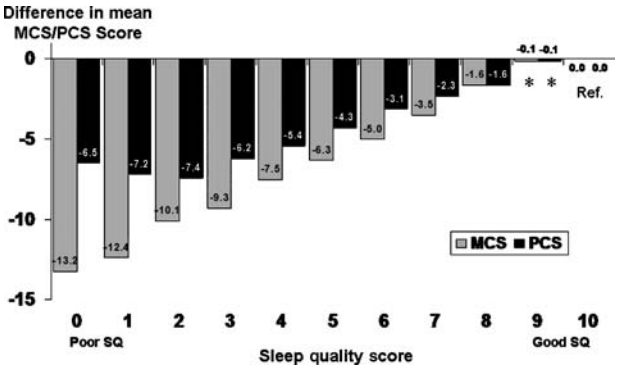

Fig. 4. Relationships of QOL mental/physical component summary scores with patient-reported SQ score. Mixed linear regression was used to determine the relationship between patient-reported SQ and MCS/PCS scores. Each model was adjusted for age, sex, race, years with ESRD, BMI, smoking status, 13 summary comorbid conditions, and country. Models accounted for facility clustering effects and were restricted to a prevalent cross section of HD patients ($n = 10\,158$). Bars indicate the magnitude of difference between the mean value for a given SQ score and the mean MCS/PCS value of the reference group. The mean value was 44.8 for the MCS reference group and 35.4 for the PCS reference group. Each mean score differed from the mean value of the corresponding reference group with a $P < 0.003$, except where noted (*).

(Figure 4). Results indicate that higher SQ scores were significantly associated with higher MCS and PCS scores. Patients who had a sleep score of 0 displayed a 13.2 point lower MCS score ($P < 0.0001$) than patients with a sleep score of 10. PCS scores steadily dropped as SQ scores decreased, except in the lowest reported SQ score (0), where the PCS score was slightly higher than if the sleep score was 1 or 2. However, these differences were not significant.

Association of mortality and sleep quality in haemodialysis patients

The relationship of a patient SQ score to mortality risk also was explored, using the best SQ score, 10, as a reference. Significant associations between higher relative risks of death and sleep scores of 1–3 *vs* 10 were noted (RR = 1.28–1.37, $P < 0.03$) (Figure 5).

Relative risk of death was also analyzed dichotomously using poor SQ *vs* good SQ. The risk of death was significantly associated with poor SQ (RR = 1.16, $P = 0.002$). When the data were analyzed using the sleep scale as a continuous variable, results showed that higher sleep scores were significantly associated with lower risk of death (RR [per one point higher] = 0.97, $P = 0.0003$).

Risk of death also was analyzed at a facility level, where the percentage of those with poor SQ was used to predict risk of death. No significant relationship was observed (RR [per 10% more] = 1.02, $P = 0.47$).

Discussion

These data represent the largest international study of self-reported SQ and its correlates among HD patients. Poor SQ is highly prevalent among HD patients worldwide and is significantly associated with many factors, including lower

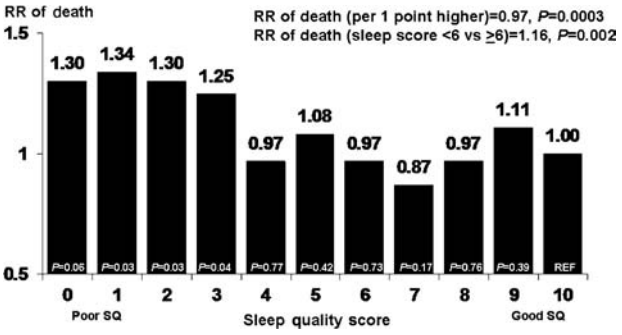

Fig. 5. Relative risk of mortality for HD patients by SQ score. Relative risk of mortality for patients by SQ score was assessed using Cox survival models adjusted for age, race, sex, 13 comorbid conditions, physician-diagnosed depression, baseline measures of haemoglobin, albumin-corrected serum calcium, serum albumin, serum phosphorus, BMI, smoking status, Kt/V and years on dialysis ($n = 11\,088$). Models were stratified by country, accounted for facility clustering effects, and were based on data collected in DOPPS I (1996–2001). Results are also shown for SQ modeled as a continuous variable and as a dichotomous variable (<6 *vs* ≥ 6). Mean follow-up time = 1.4 years (range = 0–5.2).

QOL scores, less frequent performance of physical exercise, higher degrees of bodily pain, higher use of certain classes of medications and higher serum phosphorus and calcium phosphorus levels. A schematic of these relationships can be seen in Figure 6. Importantly, this study finds that poor SQ, as assessed by a single question from the KDQOL SF-36 instrument, predicts a higher relative risk of mortality.

The prevalence of poor SQ in HD patients was 49%, which is consistent with the range found in other studies (41–83%) [5–7]. The prevalence of poor SQ in the general population internationally, ranges from 7 to 40% [10–15], showing that poor SQ is considerably higher in the HD patient population. Other studies have reported the prevalence of daytime sleepiness to be 33–53% in patients with poor SQ [11–16], slightly higher than that found in the present study (24%), although definitions between studies of poor SQ may differ. Sabbatini *et al*. reported nighttime waking in 92% of patients considered to have an inability to sleep [1], compared with 62% in the present study.

In the general population, studies have shown that poor SQ is associated with cigarette smoking [17–20] as noted in the present DOPPS analysis in HD patients.

As serum phosphorus levels increased, so did the odds of suffering from poor SQ. While previous studies have also found serum phosphorus to be related to poor SQ [21], others have failed to identify significant relationships between phosphorus and RLS [22,23]. This may indicate that sleep problems other than RLS may be associated with higher phosphorus levels.

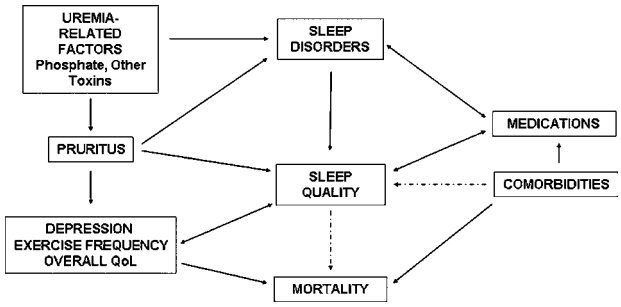

Fig. 6. Possible relationships between factors associated with SQ. This illustration shows the relationships between factors that have been shown to be associated with SQ.

Poor SQ was not associated with serum albumin, Kt/V, or treatment time, consistent with findings of Mucsi *et al*. [24]. Poor SQ was highly associated with MCS and PCS scores, showing that patients with better SQ are significantly more likely to have higher MCS and PCS scores. A dose-response type trend was seen with both component summary scores; as sleep scores decreased, so did the component summary scores. Iliescu *et al*. found significant and independent associations between SQ, determined using the Pittsburgh Sleep Quality Index (PSQI), and MCS and PCS scores in dialysis patients even when controlling for a variety of factors [5]. Curtin *et al*. [25] constructed a summary index incorporating five symptoms related to fatigue or sleep problems that were independently and significantly associated with MCS or PCS scores in dialysis patients. They found that higher (poorer) scores on their fatigue/sleep index were significantly associated with lower MCS and PCS scores.

The degree of patient-reported pain was significantly associated with greater likelihood of poor SQ and showed a dose-response type trend; the higher the degree of pain, the greater the odds of suffering from poor SQ. These results are consistent with Davison and Jhangri [26], who showed that HD patients suffering from moderate or severe pain had a significantly higher prevalence of insomnia than those with mild or no pain. Increased odds of poor SQ with greater degrees of pruritus was shown, a finding also noted by Pisoni *et al*. [9]. Our study also shows that reduced odds of poor SQ are associated with greater frequency of exercise.

Poor SQ was associated with use of several different medications. A limitation of DOPPS data is that it is impossible to know for certain the directionality of these associations. This is a clear example of confounding by indication. For example, it is reasonable to assume that poor SQ precedes the use of sleep medication and persists despite medications. Indeed, a recent randomised, double-blind, placebo-controlled crossover study by Sabbatini *et al*. [27] demonstrated that zaleplon, a new sleep drug, significantly improved SQ (assessed by the PSQI) in 10 HD patients; nonetheless, most of treated patients remained poor sleepers, suggesting the resistance of sleep disorders even to efficient treatments.

Another limitation of our study is its use of a question concerning sleep that has not been formally validated. Importantly, this question, however, is highly correlated with other sleep-related variables in our study (Table 4). It is notable that this single question pertaining to 'global' SQ is independently predictive of mortality risk in this patient population. The DOPPS study questionnaires do not permit investigation of specific sleep disorders such as RLS, periodic limb movement, or sleep apnea. However, in a recent analysis of data received from DOPPS III, which includes the previously validated PSQI, we found that 52% of HD patients from this sample were categorised as having poor SQ (unpublished observations). This lends further credence to our results and suggests that the single question alone in

the KDQOL-SF-36 could be useful in the clinical context. It has been suggested that nocturnal HD may improve SQ through the reduction of central sleep apnea, although the mechanism by which this improvement occurs remains uncertain. One consideration is that there is better clearance of uremic toxins with nocturnal dialysis [28,29]. The DOPPS does not collect data on patients who undergo nocturnal dialysis, so conclusions cannot be made in this regard.

Our study, based upon a large international sample of HD patients, clearly showed a significantly higher risk of mortality in HD patients as assessed by a simple question addressing SQ. This question could easily be administered by a practicing clinician in the dialysis unit. We postulate that lower QOL and depression associated with poor SQ may be contributing factors to higher mortality risk. Although statistical efforts have been made to correct for comorbidities, it cannot be determined whether the associations are causal, and the issue of residual confounding remains. Further research is needed to determine the complex nature of the individual relationships involving poor SQ to develop a better understanding of its pathogenesis and consequences in HD patients. Programs that encourage exercise and smoking cessation, as well as other therapeutic measures, such as relieving pruritus and reducing bodily pain, should be explored to determine any benefit for the nearly 50% of HD patients who suffer from poor SQ. Many of the variables associated with poor SQ are modifiable and may influence the condition. The associations, as shown in this study, between SQ and modifiable risk factors point to clinical opportunities to improve morbidity and mortality in a large number of HD patients by taking steps to improve their SQ. The single question about SQ used in this study could potentially be used as a simple bedside screening tool in clinical evaluation of HD patients and should be the subject of future studies.

Acknowledgements. The DOPPS is supported by research grants from Amgen and Kirin Pharma without restrictions on publications. The results presented in this paper have not been published previously in whole or part, except in abstract format.

Conflict of interest statement. Dr. Port holds grants from Amgen and Kirin Pharma. The remaining authors report no conflict.

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Received for publication: 9.1.07
Accepted in revised form: 20.8.07