ORIGINAL ARTICLE

The complexity of sleep disorders in dialysis patients

Sunny Eloot [iD] , Els Holvoet, Clement Dequidt, Sarah-Jane Maertens,
Floris Vanommeslaeghe and Wim Van Biesen [iD]

Nephrology Section, Ghent University Hospital, Ghent, Belgium

Correspondence to: Sunny Eloot; E-mail: sunny.eloot@ugent.be

ABSTRACT

Background. Dialysis patients experience a high burden of physical and emotional symptoms directly affecting their sleep and quality of life. In this study, objective and subjective measurements to quantify sleep were performed, compared with those of healthy controls, and associated with burden of comorbidity and uraemic toxicity.

Methods. A total of 64 dialysis patients were included—10 peritoneal dialysis, 42 in-centre daytime haemodialysis (HD) and 12 in-centre nocturnal HD patients—as well as one-to-one age- and gender-matched healthy controls. Assumed and actual sleep time, sleep efficiency and fragmentation index were measured by actigraphy for at least two consecutive nights. Patients and controls also completed Insomnia Severity Index (ISI) and Pittsburgh Sleep Quality Index (PSQI) questionnaires. The patients' blood was sampled to determine concentrations of a representative series of uraemic toxins and the Davies–Stoke comorbidity index was derived from medical records.

Results. Apart from the assumed sleep time, all objectively and subjectively measured sleep parameters were worse in the dialysis group compared with the healthy controls. No differences were seen in any of the measured sleep parameters among the different dialysis groups. None of the objectively measured sleep parameters were associated with ISI or PSQI scores in dialysis patients, while sleep times were related to the subjective scores in the healthy cohort. Objectively assessed sleep parameters were associated to neither the uraemic toxicity load nor the Davies–Stoke score.

Conclusions. Independent of the modality, dialysis patients have sleep quality much worse than age- and gender-matched healthy controls. The objectively measured sleep parameters could not be associated to the subjective score, uraemic toxicity or comorbidity score, highlighting the need for objective measurements of sleep and clinical guidelines to aid patient management.

Keywords: actigraphy, haemodialysis, peritoneal dialysis, sleep, uraemic toxins

INTRODUCTION

Disturbed sleep is associated with morbidity, quality of life (QoL) and even mortality in the general population [1, 2]. Impaired sleep duration and quality of sleep have been linked to hypertension, diabetes and cardiovascular disease [3, 4]. It remains unclear whether disturbed sleep is a symptom of underlying comorbidity and cardiovascular risk factors or whether there is a true direct causal impact of sleep disturbances on outcome. In people with chronic kidney disease (CKD), disturbed sleep is highly prevalent, with sleep apnoea and restless legs syndrome (RLS) as frequently reported symptoms [5–10]. Even an inverse dose–response curve with estimated

glomerular filtration rate has been reported [11, 12]. The underlying reasons for this association are incompletely understood. Accumulation of uraemic toxins (UTs) might play a role [13], though the causal relation remains unclear. In this respect, renal replacement therapy (RRT) modality could influence sleep quality not only because of the treatment setting itself, but also due to differences in levels of UTs. Nonetheless, only a few studies have addressed this topic [14, 15]. When patient-reported outcomes are solicited, most patients on RRT report sleep disturbances, but as sleep experience can be subjective, additional objectification of this is needed. Sleep quality can be assessed by subjective scoring systems, such as the Pittsburgh Sleep Quality Index (PSQI), but these have not been validated in patients on RRT. Previous reports indicate substantial differences in reported and measured sleep parameters, such as sleep duration or the presence of sleep apnoea [16–19]. It has also been reported that the concordance between subjective and objective sleep parameters is modulated by mood swings [20], which might occur because of a dialysis session. Subjective scores mostly rely on recall over the past period [21] and might be influenced by cognitive dysfunction, which is prevalent in patients on RRT. Research on this topic is further hampered by the fact that peritoneal dialysis (PD) and nocturnal haemodialysis (HD) are not available in all centres, making comparison difficult.

Objectively assessing sleep quality requires mostly polysomnography (PSG) [22], a cumbersome time-consuming and costly technique, adding to the burden of treatment-related time in patients who already spent many hours in the hospital for their dialysis sessions. In addition, such PSG evaluations only deliver point estimates and are not well-suited for regular follow-up. As a consequence, only a few studies using PSG comparing different RRT modalities are available [6, 15, 16, 23, 24]. It also remains unclear whether measures of subjective and objective sleep quality deliver similar results in patients on RRT. Over the last years, personal wearables that allow continuous monitoring of sleep parameters have become available (i.e. actigraphy) [25, 26]. These devices are suitable for monitoring sleep parameters during more prolonged or repetitive time periods, allowing better and more granular analysis of sleep patterns and impacting factors. Despite their user-friendliness and low intrusiveness, only a few studies report sleep parameters based on actigraphy measurements in patients on HD [12, 27] or PD [28], and none of them compared the different dialysis modalities.

Therefore this pilot study was set up to explore whether there are differences in subjective sleep quality between patients on different RRTs and a healthy cohort matched for age and gender, whether there are objective differences in sleep quality between these cohorts as measured with actigraphy, whether there is an association between objective and subjective sleep quality in patients on RRT, whether there is an association between uraemic toxicity as evaluated by serum levels of representative UTs and parameters of sleep quality and whether there is an association between the Davies–Stoke comorbidity score and sleep parameters.

MATERIALS AND METHODS

Patients and dialyses

The study included stable chronic dialysis patients on PD, in-centre daytime (ICD) HD or in-centre nocturnal (ICN) HD. Exclusion criteria were pregnancy, acute intervening illness and age <18 years. For every patient on dialysis, one gender- and age-matched healthy volunteer was also recruited.

The protocol adhered to the Declaration of Helsinki, was approved by the institutional research committee [Ethical Committee–Ghent University Hospital (EC 2015/0932, B670201525559 and EC 2017/0290, B670201731763)] and was registered as part of a larger study at www.clinicaltrials.gov (NCT03910426). Written informed consent was obtained from all included participants.

Objective measurement of sleep

Sleep quality was objectively measured using actigraphy using a MotionWatch (CamNtech, Cambridge, UK), a waterproof, non-invasive, wrist-worn accelerometer measuring tri-axial movement. Continuous recording was performed during at least two nights in all participants except the ICN patients, in whom three nights were recorded. All participants were equipped with the MotionWatch on their non-fistula and/or non-dominant wrist and were provided detailed information on its features (i.e. light sensor and event marker). They were instructed to press the event marker button in the centre of the watch every time they started trying to sleep and when they woke up. Activity was measured in epochs of 2 s, capturing movement and light.

Data were analysed using MotionWare version 1.1.15 (CamNtech). Per registered night, different sleep parameters were calculated, including assumed sleep time, which registers time between sleep onset and awakening; actual sleep time, which reflects total time effectively spent asleep; sleep efficiency, which reflects actual time spent sleeping as a percentage of the total time spent in bed; and fragmentation index, which is the percentage of the total time the patient is moving in his sleep and is considered a measure of sleep quality. For patients and controls, all parameters were extrapolated on a weekly basis.

Subjective measurement of sleep

Subjective measurement of sleep was assessed in patients and controls on the same day participants were fitted with the MotionWatch, using two validated questionnaires, the PSQI and the Insomnia Severity Index (ISI). The PSQI is a seven-component questionnaire about sleep quality and habits during the past month [29], including subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep medication and daytime dysfunction. Quantified sleep quality is lower for higher results on a 0–21 scale and global scores >5 are generally accepted to indicate poor sleep [30]. The ISI is a seven-item self-report questionnaire about a person's sleep experience over the past 2 weeks [31]. The dimensions evaluated are severity of sleep onset, sleep maintenance and early morning awakening problems, sleep dissatisfaction, interference of sleep difficulties with daytime functioning, noticeability of sleep problems by others and distress caused by sleep difficulties. Results are classified as 0–7 (no clinically significant insomnia), 8–14 (subthreshold insomnia), 15–21 (clinical insomnia—moderate severity) and 22–28 (clinical insomnia—severe).

Additionally, dialysis patients also completed the validated Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29) questionnaire, a generic health-related QoL measure, questioning seven domains with four questions each about the past week, including depression, anxiety, physical function, pain interference, fatigue, sleep disturbance and ability to participate in social roles and activities, the most relevant

areas for the majority of people with chronic illness. Within this study we focused on the *t*-scores of the subdomains fatigue and sleep disturbance.

Blood sampling and analyses. Blood samples were collected via venipuncture on the same day participants were fitted with the MotionWatch (PD patients) or from the patient's vascular access just before the start of a mid-week dialysis session (ICD and ICN patients) in the month preceding or following the sleep tests.

Samples were centrifuged within 20–30 min after collection for 10 min at 1250 *g* and 4°C. Subsequently the serum was stored at −80°C until batch analysis. All UTs were analysed at the Ghent University Hospital and were determined by reversed-phase high-performance liquid chromatography [32, 33] using the fluorescence detection method for the protein-bound toxins *p*-cresyl glucuronide (PCG), indole-3-acetic acid (IAA), indoxyl sulphate (IS) and *p*-cresyl sulphate (PCS) and the UV detection method for uric acid (168 Da) and the protein-bound toxins hippuric acid (HA) and 3-carboxy-4-methyl-5-propyl-2-furanpropionic acid (CMPF).

Total concentrations of protein-bound toxins were determined by consecutive 30 min deproteinizing by heat denaturation, 10 min cooling, 10 min centrifuging (7379 *g*) and filtering the serum for 20 min (3615 *g*, Amicon Ultra 0.5 mL Filters, Millipore, Billerica, MA, USA). Free fractions of protein-bound toxins were obtained using a Centrifreefilter device (Millipore).

Composite uraemic load was defined as one indicator of uraemic toxicity estimated by clustering the above-reported UTs in a regression model.

Davies–Stoke score. The burden of comorbidity was assessed using the Davies–Stoke score [34]. This score assigns one point for each of the following conditions: malignancy, ischaemic heart disease, peripheral vascular disease, left ventricular dysfunction, diabetes mellitus, systemic collagen vascular disease and other significant pathologies that have an impact on survival in the general population. The burden of the comorbidity is derived directly from the total score: Grade 0 (low risk) is a score of 0, Grade 1 (medium risk) is a score of 1–2 and Grade 2 (high risk) is a score ≥3. All parameters of the scores were surveyed by a trained research nurse and entered directly in a dedicated database. Diabetes was defined as patients taking one or more glucose-lowering drugs or diet.

Statistical analysis

Statistical analyses were performed using SPSS version 25 (IBM, Armonk, NY, USA). Baseline data were summarised as mean ± standard deviation (SD), median (25th–75th percentile) or frequency (%). Between-groups analysis was performed by one-way analysis of variance (ANOVA) or Kruskal–Wallis test, with the Scheffé or Mann–Whitney U-tests for *post hoc* comparisons, respectively. Associations between objective and subjective sleep measures, as well as between the Davies–Stoke score and sleep measures were investigated using the general linear model (GLM), accounting for age, gender and dialysis modality. The association between uraemic toxicity and sleep parameters was checked by allocating patients to one of three groups based on tertiles of single UT concentrations, using the Kruskal–Wallis test as between-group analyses. Least Absolute Shrinkage and Selection Operator (LASSO) was used to examine the eventual association between the composite uraemic load and the different objective sleep parameters.

RESULTS

This study included 10 PD patients (3 females, age 66 ± 17 years, 8 on automated PD). Also, 54 HD patients were included, of which 42 were on ICD HD (12 females, 64 ± 18 years) and 12 were on ICN HD (4 females, 55 ± 13 years). According to the intended one-to-one matching for gender and age, we included 64 healthy controls.

Objective and subjective sleep parameters are presented in Table 1 for the different groups. There was no difference for any of the sleep parameters between PD, ICD and ICN patients. With regard to the objective measures, dialysis patients as a group versus healthy controls had a comparable assumed sleep (7:57 ± 1:33 versus 7:51 ± 0:52 for controls), while actual sleep was lower (6:42 ± 1:24 versus 7:09 ± 0:46), sleep efficiency was worse (81 ± 12% versus 89 ± 4%) and the fragmentation index was higher (44 ± 20 versus 22 ± 11). Differences were also found for the subjective sleep measures, with higher PSQI scores (6.3 ± 3.1 versus 4.6 ± 2.9) and ISI scores (7.7 ± 4.9 versus 4.7 ± 4.1) for dialysis patients versus controls (Table 1).

Based on accepted thresholds of measured sleep efficiency (i.e. 85%) and fragmentation index (i.e. 25) [21], 59% and 81%, respectively, of the dialysis patients showed poor sleep, while for healthy controls this was only 13% and 34%, respectively (Table 2).

Differences in the results of the self-reported questionnaires PSQI and ISI were slightly less between the dialysis patients and controls, with 52% versus 30% (PSQI, threshold score 5) [30] and 42% versus 12% (ISI, threshold score 7) [31]. For the *t*-scores of PROMIS, only 20% and 9% of the dialysis patients indicated they suffered from fatigue and sleep disturbances, respectively; >1 SD worse than average.

For PD patients, sleep parameters, as registered by actigraphy, were not different among the different study nights. Daytime dialysis patients showed shorter assumed and actual sleep times the night before dialysis than the one following dialysis (both P < 0.001), while sleep efficiency and fragmentation index did not differ (Table 3). Also, for the patients on nocturnal dialysis, different assumed and actual sleep times were measured, with the shortest sleep during the night spent in the dialysis unit.

The GLM, including gender and age, showed that none of the objectively measured sleep parameters had a significant impact on ISI and PSQI scores in dialysis patients. In healthy controls, however, assumed and actual sleep times had a significant impact on the subjective ISI (P = 0.025 and 0.024, respectively) and PSQI scores (P = 0.020 and 0.009).

Table 4 shows that UT concentrations were not different among patients on different RRTs. For the different tertiles of UT concentrations, only fragmentation index was found to be different for IS (ANOVA P = 0.025) and free IS (P = 0.020). LASSO regression with the composite uraemic load revealed that only PCS (P = 0.023) had an impact on actual sleep time.

According to their Davies–Stoke scores, 18 patients were categorized as Grade 0 (no risk), 31 Grade 1 (medium risk) and 15 Grade 3 (high risk; Table 5). Although older patients showed higher risks (age P < 0.001), no differences in objective and subjective sleep measures could be seen among the three groups. However, the fragmentation index was higher when comparing the group with a non-zero Davies–Stoke score versus the no-risk group (54 ± 21 versus 41 ± 19; P = 0.025). The GLM, including dialysis mode, gender and age, indicated that the patient's Davies–Stoke score had no impact on the objectively measured sleep parameters, including assumed and actual sleep times, sleep efficiency and fragmentation index.

Table 1. Objective and subjective sleep measures in PD patients, daytime and nocturnal HD patients and corresponding healthy controls

Measured parameter	PD patients	ICD patients	ICN patients	All dialysis patients	Healthy controls	P-value, dialysis versus controls
Objective sleep measures (actigraphy)						
Assumed sleep (h:min)	8:21 ± 1:18	8:07 ± 1:39	7:04 ± 1:05	7:57 ± 1:33	7:51 ± 0:52	0.677
Actual sleep (h:min)	6:44 ± 0:53	6:55 ± 1:29	5:56 ± 1:12	6:42 ± 1:24	7:09 ± 0:46	**0.024**
Sleep efficiency (%)	78 ± 13	82 ± 11	78 ± 14	81 ± 12	89 ± 4	**<0.001**
Fragmentation index	50 ± 23	43 ± 18	40 ± 23	44 ± 20	22 ± 11	**<0.001**
Subjective sleep measures						
PSQI	7.1 ± 3.5	6.1 ± 3.3	6.0 ± 2.3	6.3 ± 3.1	4.6 ± 2.9	**<0.001**
ISI	7.0 ± 4.2	8.0 ± 5.4	6.9 ± 3.9	7.7 ± 4.9	4.7 ± 4.1	**0.002**
PROMIS(*t*-score)						
Fatigue	49 ± 9	51 ± 12	48 ± 10	50 ± 11	NA	NA
Sleep disturbance	48 ± 8	50 ± 11	50 ± 5	50 ± 9	NA	NA

Values presented as mean ± SD. Significant P-values are indicated in bold.
NA, not applicable.

Table 2. Participants in the different categories of objective and subjective sleep measures

Sleep measures	Dialysis patients, n (%)	Healthy controls, n (%)
Sleep efficiency		
≥85	26 (41)	56 (87)
<85	38 (59)	8 (13)
Fragmentation index		
≤25	12 (19)	42 (66)
>25	52 (81)	22 (34)
PSQI		
≤5	31 (48)	45 (70)
>5	33 (52)	19 (30)
ISI		
≤7	37 (58)	56 (88)
>7	27 (42)	8 (12)
PROMIS(*t*-score)		
Fatigue		
<40	15 (24)	–
40–60	36 (56)	–
>60	13 (20)	–
Sleep disturbance		
<40	10 (16)	–
40–60	45 (70)	–
>60	9 (14)	–

Table 3. Comparison between the nights before and after ICD HD and between the nights in the hospital during nocturnal HD and at home

ICD	Night after HD, mean ± SD	Night before HD, mean ± SD	P-value
Assumed sleep (h:min)	8:55 ± 2:22	7:31 ± 7:45	**<0.001**
Actual sleep (h:min)	7:38 ± 2:05	6:22 ± 1:31	**<0.001**
Sleep efficiency (%)	82 ± 13	82 ± 11	0.851
Fragmentation index	44 ± 17	43 ± 22	0.778
ICN	**Night in centre**	**Night at home**	
Assumed sleep (h:min)	6:11 ± 1:20	7:44 ± 1:38	**0.030**
Actual sleep (h:min)	5:09 ± 1:40	6:31 ± 1:34	**0.048**
Sleep efficiency (%)	75 ± 19	81 ± 13	0.171
Fragmentation index	42 ± 26	38 ± 23	0.580

Significant P-values are indicated in bold

DISCUSSION

This study collected objective and subjective sleep data from 64 dialysis patients treated with different RRTs as well as from just as many age- and gender-matched healthy controls. Our main findings are that subjective sleep quality was worse in dialysis patients versus the healthy cohort, but did not differ among the dialysis modalities; objectively measured actual sleep time, sleep efficiency and fragmentation index were worse in dialysis patients; subjective estimates of sleep quality did not reflect objectively measured sleep parameters in dialysis patients; no association was found between uraemic toxicity and sleep parameters; and patient's comorbidity score had no impact on measured objective sleep quality.

The incidence of sleep disturbance in dialysis patients, as measured objectively with actigraphy, is really striking, with 59% of patients having poor sleep efficiency and 81% of them having a high fragmentation index. These findings are in accordance with previously reported sleep parameters in dialysis patients all over the world, as measured by PSG [6, 15, 16, 23], actigraphy [12, 27, 28] or even by subjective sleep scores such as the PSQI questionnaire [35–41]. Reported sleep quality in dialysis patients is much worse than in healthy controls [16, 28], but also worse compared with CKD patients [6, 12]. While most of the previous studies focused on sleep parameters, comparing patients on two different RRTs or patients versus controls, our study is the first ever to compare patients being treated with PD, ICD and ICN HD, as well as perfectly age- and gender-matched healthy controls.

Each RRT has its treatment-related burdens for the patient, which may impact their sleep [27, 42]. Sleep times were shorter for the ICD patients the night before dialysis, as was the case for the ICN patients the night in the hospital. Still, overall sleep quality was not different among patients on the three dialysis modalities. Furthermore, as extrapolated for an entire week and apart from day-to-day differences, overall assumed and actual sleep times were not different in our study. We hereby confirm some previous findings from actigraphy and PSG [27, 42]. Apart from these general sleep quality indices, the incidence of RLS and sleep apnoea, two parameters that might be overlooked with actigraphy, were found to be different among dialysis

Table 4. UT concentrations in patients on different RRTs

Uraemic toxin	PD ($n = 10$)	ICD ($n = 42$)	ICN ($n = 12$)	P-value (Kruskal–Wallis)	All dialysis (N = 64)
Uric acid (mg/dL)	5.82 (5.07–6.45)	6.12 (5.21–7.00)	6.15 (5.28–6.83)	0.800	6.09 (5.20–6.76)
PCG (mg/dL)	0.09 (0.03–0.44)	0.18 (0.04–0.42)	0.16 (0.04–0.25)	0.675	0.17 (0.04–0.36)
PCG free (mg/dL)	0.09 (0.02–0.42)	0.16 (0.03–0.40)	0.15 (0.04–0.22)	0.720	0.15 (0.03–0.32)
HA (mg/dL)	1.52 (0.65–2.31)	2.30 (0.98–0.64)	3.08 (1.52–3.91)	0.363	2.12 (0.99–4.08)
HA free (mg/dL)	0.77 (0.26–1.31)	1.17 (0.40–2.74)	1.54 (0.70–1.78)	0.437	1.13 (0.43–1.91)
IAA (mg/dL)	0.11 (0.07–0.14)	0.14 (0.09–0.19)	0.15 (0.08–0.24)	0.399	0.13 (0.09–0.19)
IAA free (mg/dL)	0.03 (0.01–0.04)	0.04 (0.02–0.06)	0.04 (0.02–007)	0.348	0.04 (0.02–0.06)
IS (mg/dL)	1.74 (1.05–2.04)	1.86 (1.16–2.89)	1.60 (1.33–2.66)	0.655	1.71 (1.24–2.50)
IS free (mg/dL)	0.07 (0.04–0.15)	0.11 (0.05–0.20)	0.08 (0.05–0.18)	0.468	0.09 (0.05–0.19)
PCS (mg/dL)	2.87 (2.03–3.36)	3.15 (2.27–4.73)	1.71 (0.89–2.82)	0.050	2.87 (1.74–3.91)
PCS free (mg/dL)	0.16 (0.07–0.30)	0.22 (0.08–0.37)	0.15 (0.09–0.21)	0.355	0.19 (0.08–0.30)
CMPF (mg/dL)	0.24 (0.08–0.48)	0.44 (0.17–0.70)	0.58 (0.29–2.02)	0.072	0.39 (0.18–0.69)

Values presented as median (25th–75th percentile).

Table 5. Objective and subjective sleep measures according to the different Davies–Stokes scores

Davies–Stoke score	0	1–2	3–5	ANOVA P-value
Davies–Stoke grade	0	1	2	
n (%)	18 (28)	31 (48)	15 (24)	
Male/female, n/n	16/2	18/13	11/4	0.073
Age (years), mean ± SD	47.0 ± 17.8	67.4 ± 14.0[*]	69.2 ± 17.2[*]	<0.001
Objective sleep measures, mean ± SD				
Assumed sleep (h:min)	7:35 ± 1:28	8:11 ± 1:25	7:55 ± 1:56	0.431
Actual sleep (h:min)	6:23 ± 1:23	6:51 ± 1:10	6:44 ± 1:49	0.540
Sleep efficiency (%)	79 ± 11	81 ± 13	82 ± 13	0.812
Fragmentation index	36 ± 16	46 ± 20	49 ± 22	0.122
Subjective sleep measures, mean ± SD				
PSQI	7.1 ± 3.3	6.4 ± 3.1	5.0 ± 2.6	0.151
ISI	9.3 ± 4.6	7.5 ± 4.9	5.9 ± 5.2	0.153
PROMIS fatigue, mean ± SD	48 ± 9	52 ± 11	48 ± 14	0.291
PROMIS sleep disturbance, mean ± SD	51 ± 9	50 ± 8	46 ± 12	0.285

[*]P < 0.001 versus Davies–Stoke score of 0.

modalities. Using the criteria from the International Restless Legs Syndrom Study Group (IRLSSG) for the diagnosis and severity of RLS, patients on automated PD presented higher RLS severity compared with the HD group [43]. And previous PSG measurements also revealed that daytime dialysis may result in more obstructive and central apnoea as compared with nocturnal PD and HD [44, 45]. A review by Chu *et al.* [46] ascribed this sleep-disordered breathing to three different mechanisms: fluid accumulation resulting in pharyngeal narrowing, anaemia reducing the oxygen level and UT accumulation causing systemic inflammation, which in turn can cause pharyngeal narrowing and destabilization of chemoreceptors.

While uraemic toxicity in sleep studies was previously only checked by evaluating serum concentrations of small and water-soluble solutes like urea, creatinine, phosphate and potassium [14], this study focused on more representative UTs. A set of protein-bound toxins, with in particular IS and PCS, has been linked to the progression of renal failure, inflammation, vascular disease and mortality [47–51]. However, the hypothesis about the impact of toxicity on sleep quality could not be confirmed in this study since no differences in UT levels were found among the patients on different RRTs.

It has been postulated before that those objective measurements of sleep should accompany subjective measures, since the latter might be influenced too much by mood changes and the feeling at the moment of awakening [21]. In agreement with a previous study in HD patients, we did not find an association between objective and subjective sleep measures [16]. Apparently, healthy controls can accurately subjectively estimate their objective sleep time, whereas dialysis patients could subjectively estimate neither their objective sleep quality nor their sleep time. Noteworthy, but maybe not unexpectedly, we found greater differences between the percentages of patients and healthy controls experiencing bad sleep for objective versus subjective measures. This is in line with the accepted phenomenon of adaptation also observed in chronic patients for other symptoms.

Several mechanisms have been postulated to explain bad sleep quality in dialysis patients. Beside anaemia and fluid and toxin accumulation, patients can also suffer from pain, pruritus and psychological problems. Herewith, depression and poor QoL have been described as important risk factors [35, 37–41]. Also, the accumulation of UTs has been postulated to contribute to the neurological disorders inducing unpleasant and sometimes painful sensations, like RLS, directly impairing a patient's daily life and sleep [14, 52]. In this study, UT concentrations in all dialysis groups were sufficiently high to observe poor sleep compared with healthy controls, but variations among the groups were too limited to distinguish between the different

dialysis modalities. This implies that UT levels in all dialysis patients should be lowered by more adequate dialysis techniques.

In view of the secondary effects of poor sleep quality, and the fact that we found a dissociation between objective and subjective sleep quality, it can be recommended in clinical practice to evaluate sleep objectively. This might be even more important in PD and home dialysis patients, since these are vulnerable individuals with extended self-care responsibilities [28]. Independent of RRT modality, follow-up, individual guidance about sleep hygiene and especially advice about physical activity should be considered to improve sleep quality [53, 54].

The small patient number for the PD ($n = 10$) and ICN ($n = 12$) groups could be considered a limitation of the study, but the addition of a significant ICD group ($n = 42$) and the one-to-one age- and gender-matched healthy cohort makes this a unique study and provides material for comparison. Actigraphy is not providing as much detailed sleep data as in-centre PSG does. However, this is counterbalanced by the ability to make recordings during several nights in the patient's home setting, whereas PSG is nearly always performed in the atypical and artificial setting of the sleep laboratory and is mostly restricted to one night. An important element of weakness of this study is not having related sleep quality to the specific sleep disturbance RLS, which is highly prevalent in dialysis patients [7–9]. Indeed, actigraphy is only measuring arm movements and not sleep. Furthermore, it is also important to stress the difference between 'sleep' and 'sleep quality'. Excessive arm movements, although asleep, cannot be related to satisfying sleep quality, while the lack of arm movements does not guarantee sleep quality. In this respect, the present actigraphy results might be confusing by overestimating sleep quality in dialysis patients. Therefore, in terms of integral patient care, this pilot study should be followed by further exploration of sleep disturbances, preferably in an (as much as possible) non-invasive way. This can be performed using the IRLSSG questionnaires to diagnose RLS and assess its severity, eventually combined with actigraphy, specifically monitoring leg movements.

In conclusion, in this study we clearly found poor sleep quality in dialysis patients, which is remarkably worse than in healthy controls. We did not find differences in objective measurements of sleep quality between RRT modalities, degree of uraemic toxicity and comorbidity score.

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AUTHORS' CONTRIBUTIONS

CONFLICT OF INTEREST STATEMENT

None declared.

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