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Original Article

Proactive telemedicine monitoring of sleep apnea treatment improves adherence in people with stroke— a randomized controlled trial (HOPES study)

Stefan T. Kotzian [a, 1], Michael T. Saletu [a, b, *, 1], Angela Schwarzinger [a], Sandra Haider [a, c], Josef Spatt [a], Gottfried Kranz [a], Bernd Saletu [d]

[a] Neurologisches Rehabilitationszentrum Rosenhügel, Vienna, Austria
[b] Department of Sleep Medicine, LKH Graz II, Austria
[c] Medical University of Vienna, Department of Social and Preventive Medicine, Center for Public Health, Austria
[d] Medical University of Vienna, Department of Psychiatry and Psychotherapy, Austria

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ABSTRACT

Objective: Obstructive sleep apnea (OSA) impacts stroke recovery and outcome negatively. Although its identification and treatment are part of the current stroke guidelines, standard management with positive airway pressure (PAP) therapy is not routinely performed and adherence rates are very low. The purpose of this study was to determine whether PAP adherence can be improved by a PAP training strategy during in-hospital rehabilitation combined with a telemedicine monitoring system after discharge.

Methods: In this study, we performed a controlled trial (RCT) on standard PAP treatment (SG) as compared with proactive telemonitored PAP treatment (TG). After three months and one year, PAP adherence (min of use per day) and clinical outcome variables were compared.

Results: In 33 (47.1%) out of 70 patients diagnosed with therapy-relevant OSA [70% male, 62 (5) years, body mass index (BMI) 30 (4) kg/m^2, Barthel Index 90 (20), NIHSS 3 (3)] in-hospital PAP titration was performed. Subsequently, they were randomized to SG or TG. Drop-out rates after three months and after one year were 12% and 30%, respectively, with no differences between the groups. After three months, telemonitored patients used the PAP device 76 min longer per night (SG: 299 (76), TG: 375 (86) minutes per night; $p = 0.017$), after one year there was no significant difference.

Conclusion: People with stroke and therapy-relevant OSA who accept PAP therapy should receive additional telemedicine monitoring at least for three months.

Clinical trial registration-url: http://www.clinicaltrials.gov; Unique identifier: NCT02748681.

1. Introduction

Obstructive sleep apnea (OSA) is the most common sleep-related breathing disorder in people who survived a stroke [1]. OSA may either be a risk factor for stroke or a consequence of stroke and affects short- and long-term stroke recovery and outcome [2,3]. It is considered a negative predictor of all-cause mortality and recurrent vascular events following stroke or a transitory ischaemic attack [4,5] independent of other risk factors, including hypertension [6]. The identification and treatment of OSA in people who survived a stroke was added to the stroke guidelines of the American Heart Association/American Stroke Association (AHA/ASA) in 2014 [7], which supports the systematic implementation of clinical procedures for the diagnosis and treatment of post-stroke sleep-

Abbreviations: BI, Barthel Index; HSAT, home sleep apnea testing; MOCA, Montreal Cognitive Assessment Test; NHPT, Nine-Hole Peg Test; NIHSS, National Institute of Health Stroke Score; PAP, positive airway pressure; SG, standard PAP treatment group; SSA, Self-Assessment Scale for Sleep and Awakening Quality; SDB, sleep-disordered breathing; TG, telemonitored PAP treatment group; TIA, transitory ischemic attack; TOAST, Trial of ORG; TUG, Timed Up and Go Test.

* Corresponding author. Associate Professor of Neurology, LKH Graz II, Department of Sleep Medicine, Wagner Jauregg Platz 17, 8053, Graz, Austria.
E-mail addresses: michael.saletu@gmail.com, michael.saletu@kages.at (M.T. Saletu).

[1] The first two authors have contributed equally to the manuscript.

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disordered breathing (SDB) in stroke units. In spite of the high prevalence of SDB in patients after stroke and the fact that OSA therapy may increase rehabilitation success, sleep studies and subsequent therapeutic interventions are still neglected in stroke rehabilitation units [8]. Subjective evaluation is not sufficient to diagnose OSA in patients after stroke [9]. A method that has recently shown good feasibility and sufficient accuracy [10] in OSA diagnosis is home sleep apnea testing (HSAT).

The standard OSA treatment is continuous positive airway pressure (CPAP) therapy, as suggested in the 2014 AHA/ASA guidelines [7]. It lowers the risk of further cardiovascular events [11–13], especially stroke [14], and leads to a better neurofunctional outcome [13,15,16]. The real challenge in neurologically impaired stroke survivors is adherence [17] (ie, PAP use in minutes per hour). A recent meta-analysis demonstrated a remarkably high overall adherence of 4.5 h a night, but also showed the difficulties in recruiting patients after stroke and high dropout rates ranging from 0 to 46% [4,18].

Low adherence rates may be explained by a discomfort with the device [4] and increased air leakage [19]. Heated humidification, mask optimization or topical nasal therapy can improve adherence [20]. Moreover, stroke-related motor and cognitive impairment, especially difficulties handling the mask and the PAP device, might be responsible for higher dropout and low adherence rates.

In people with OSA and without a history of stroke, educational, supportive and behavioural interventions have been shown to improve adherence [21]. Telemedical monitoring by proactive management for patients, as already examined in patients without stroke [22], provides a new option and is generally well accepted [23]. A recent systematic review suggests that tele-rehabilitation interventions in stroke have either better or equal salutary effects on motor, higher cortical, and mood disorders as compared with conventional face-to-face therapy [4].

Current technology provides access to PAP therapy data (pressures applied, air leaks, the apnea-hypopnea index (AHI), and objective adherence) with the opportunity to timely intervene and proactively provide quality care to patients at a distance [22]. Recent studies demonstrated a reduction in labor requirements [24] nursing time [25] and costs [26] due to telemedical care. Alternately, telemedical monitoring is a time- and human resource-intensive tool for sleep centers and homecare providers. Moreover, it is not clear for how long “special patient groups” like people who had a stroke might benefit from telemedicine in PAP management.

The primary objective of this study was to investigate whether a telemedical monitoring system can improve three-month PAP adherence in people with stroke and therapy-relevant OSA (trOSA), who initially accepted PAP therapy in a rehabilitation setting. Secondary objectives were to assess the influence of telemedical monitoring on one-year PAP adherence, to establish predictive variables for PAP adherence and examine the impact of telemonitored PAP therapy on cognitive and motor neurorehabilitation outcome parameters after three months and one year.

2. Materials and methods

2.1. Study design

This single-blind randomized controlled trial is part of the Home Polygraphic Recording with Telemedicine Monitoring for Diagnosis and Treatment of Sleep Apnea in Stroke (HOPES study) and was conducted at the NRZ Rosenhügel (Vienna, Austria) from April 18, 2016 to April 18, 2018. The study protocol was published earlier [27]. All people with stroke referred to rehabilitation were initially included in the study. Those who fulfilled the eligibility criteria underwent in-hospital OSA evaluation with HSAT. Patients with trOSA were suggested for PAP treatment. If they tolerated PAP treatment after a coaching strategy of over a week and treatment was successful in ways of PAP-PSG studies, they were randomly assigned to a standard group (SG) or a telemedical group (TG) stratified by age (>/≤59 years) with the help of the “Randomizer for Clinical Trials 1.8.1” [28]. Investigators were blinded as long as no medical interventions were necessary during the three months of treatment.

2.2. Sample size calculation

A power calculation was based on the results of the study by Fox et al., in people with sleep apnea [29] with an effect size >0.80, as proposed by Cohen [30]. Therefore, we conducted a two-sided t-test with a significance level of 0.05 and a difference in groups of 114 min PAP usage per night with a standard deviation of 93 min. The result of this calculation was 11 patients per group. To allow for dropouts, we planned to include all patients eligible during the study period despite the fact of over-recruiting.

2.3. Inclusion/exclusion criteria

Subacute adult (19–70 years of age) stroke survivors (>1 month to <1 year post stroke) with a completed stroke confirmed by a neurologist based on the history of a sudden onset of a neurological deficit lasting longer than 24 h, the presence of a neurological deficit upon physical examination, and a brain lesion compatible with the neurological deficit in computerized tomography or magnetic resonance imaging of the brain were included.

Exclusion criteria were as follows: patients unable to understand the protocol due to cognitive impairments; patients with chronic obstructive pulmonary disease > Gold III; chronic kidney disease > stage 4; coexisting causes of daytime sleepiness (eg, narcolepsy, night or rotating shift-work; self-reported average sleep duration <4 h); experiences of major psychiatric or any other acute medical condition; previously established PAP therapy; patients with central sleep apnea; and patients unable or unwilling to comply with the protocol.

2.4. OSA evaluation

For evaluation of OSA, eligible patients underwent in-hospital sleep studies. For details, please see the study protocol [27] and the diagnostic part of the study [10].

Therapy-relevant OSA was defined as showing an AHI >15 per hour of sleep, indicating moderate sleep apnea, as recommended by the international task force on the standardization of definitions for sleep-related breathing disorders [31]. This task force differentiates mild (AHI = 5–14), moderate (AHI = 15–30), and severe (AHI > 30) sleep apnea.

2.5. Initiation of PAP therapy and titration

All patients referred to PAP therapy received a 30-min introductory lesson with nasal or oro-nasal mask fitting, device handling and information about PAP therapy. Patients were provided with an AirSense™ 10 AutoSet CPAP (Resmed) including a humidifier and were set to auto-titrate at pressures between 6 and 13 cm H2O. Patients were motivated to use the PAP device for at least 4 h of sleep/night. The PAP-training period lasted at least one week, with bedside coaching in the morning and the evening. During the night, patients were coached by trained nurses. Relatives were also trained in using the humidifier and cleaning the mask and the humidifier chamber. The AHI, oximetry and leakage information

were collected every day in coaching sessions with the patient. Pressure limits could be increased or decreased to improve patient comfort. If the patient had problems to tolerate high pressures while falling asleep in the first week, the fixed window was reduced to sub-therapeutic pressures (eg, 4–8 mbar) for a few nights to enable the patient to get used to therapy. If the AutoSet PAP device did not react to obstructive events, titration was too slow or did not decrease (according to PSG or the internal AHI detection), either a fixed CPAP or a narrow Auto CPAP window was attached. Those who tolerated PAP therapy with a median PAP use of >4 h/night underwent polysomnography (PSG) with PAP. To take part in the study, a good titration according to Berry et al. [32] (AHI <10/h, REM sleep on the treatment pressure, desaturation index ≤10/h) was required.

2.6. Interventions in both groups

Patients were asked to call their homecare provider if any problems with the device occurred or their physician in case of medical problems. Two days after discharge from hospital, they were contacted by their homecare provider and were asked about progress and adherence, as well as about any other problems. They were asked to return to the hospital after three months for evaluation of therapy including review of PAP pressure, mask leakage, residual respiratory events, and compliance. Any problems with treatment were addressed. HSAT sleep studies were performed.

2.7. Telemedical interventions

The PAP coordinator at the homecare provider reviewed the downloaded information every morning except on weekends and holidays and contacted the patient if the 90th percentile of pressure was >16 cm H_2O or mask leakage of the 95 percentiles was >24 l/min or use was <4 h or the AHI was >10 events/h for three consecutive days.

2.8. Clinical measurements

The following scores were obtained from all patients at baseline, after three months and one year: Epworth Sleepiness Scale (ESS) [33], Quality of Life Index (QoL) [34], PAP Satisfaction Questionnaire [32], National Institutes of Health Stroke Scale (NIHSS) [35], Timed Up and Go Test (TUG) [36], Nine Hole Peg Test (NHPT) [37], Barthel Index for disability [38], and the Montreal Cognitive Assessment Test (MOCA) [39]. Clinical classification of stroke was performed according to the Oxfordshire Community Stroke Project (OCSP) criteria [40]. Aetiology was classified according to the Trial of ORG 10172 (TOAST) criteria [41]. For a detailed description of our clinical scales, please see the study protocol [27].

2.9. Statistics

Descriptive data are shown in frequencies and percentages or means and standard deviation (SD) or median and range. If data were skewed, non-parametric tests such as Wilcoxon and Mann–Whitney U test or Spearman's correlation coefficients were chosen. Otherwise, T-Test and ANOVA were used. To examine categorical baseline characteristics, χ^2 and F-test were used. The primary outcome was PAP adherence after three months (min of use per day), which was analysed according to the per-protocol-analysis with ANOVA for independent samples. If differences between groups were significant, ANOVA was corrected for these parameters. Additionally, in order to examine predictive variables for PAP adherence, univariate and multiple linear and logistic regression analyses were performed, with age, gender, impairments in activities of daily living and cognitive status as independent variables. To examine the impact of telemonitored PAP therapy on cognitive and motor neuro-rehabilitation outcome parameters, ANOVA for repeated measurements after three months and one year were conducted. The IBM SPSS Statistics for Windows, V.22 software (IBM, Armonk, NewYork, USA) was used for all statistical analyses. All tests, except PAP adherence after three months, were two-sided and a P value < 0.05 was considered statistically significant.

2.10. Ethical considerations

The study was approved by the Clinical Research Ethics Board of Vienna (EK-15-231-1115) and was performed in accordance with the relevant guidelines of the Declaration of Helsinki, 1964 [42]. Written informed consent for all examinations was obtained upon patients' admission. The protocol was registered at clinicaltrials.gov (Identifier: NCT02748681).

3. Results

3.1. Prevalence of OSA

During the one-year study period, 932 people after stroke were admitted to rehabilitation. Persons >70 years of age (n = 396), with a stroke suffered >1 year ago (n = 153), previously diagnosed OSA (n = 12), previously negative diagnosed for OSA (n = 2), other relevant medical conditions (n = 47) and patients unable to understand the protocol (n = 26) were not included in further investigations.

Overall, 296 individuals were eligible for HSAT sleep studies, which were finally performed in 265 (89.5%) patients (age 58 (9) years, male 70%). (19 patients rejected HSAT sleep studies and in 12 HSAT sleep studies could not be scheduled during rehabilitation for time management reasons). A total of 258 (97.4%) sleep studies were eligible for estimation of SA and further evaluation. Seven sleep studies were not eligible for SA estimation also after repetition of HSAT because of insufficient recording quality. Moreover, 82 patients (31.8%) were classified as having “no SA”; in 99 (38.4%) “Mild SA”, in 31 (12%) “Moderate SA” and in 46 (17.8%) “Severe SA” was diagnosed. In 77 patients (29.8%) the SA was found to be therapy-relevant (AHI >15, moderate and severe SA). A central sleep apnea was diagnosed in seven (9.1%) Thus, 70 patients were diagnosed with trOSA.

For characterisation of patients with trOSA, see Table 1:

Patients with trOSA were older, had a higher BMI, a lower Barthel Index and time after stroke was longer, but did not differ from patients without trOSA concerning gender, etiology or stroke location.

3.2. PAP titration

All 70 people diagnosed with trOSA received a 30-min PAP introductory lesson. Of those, 11 (15.7%) were not willing to start PAP therapy after suggestion by their physician and three (4.3%) were not willing to do so after introduction into therapy and mask fitting. Furthermore, two patients (2.9%) declined after one night, 11 (15.7%) patients after several nights of PAP training because of disturbed sleep quality and pressure intolerance; eight (11.4%) patients declined further PSG sleep studies for CPAP evaluation; one (1.4%) patient could not be titrated successfully during rehabilitation and in one (1.4%) patient PAP therapy could not be initiated for administrative reasons.

A total of 33 (47.1%) people with trOSA were successfully titrated, adhered to PAP treatment during in-hospital rehabilitation and were eligible for inclusion into one of the study arms.

Table 1
Characteristics of patients with and without trOSA.

	No trOSA (n = 181	trOSA (n = 70)	P value
Demographic data			
Male, n (%)	122 (67.4)	50 (71.4)	0.538
Age (years), mean (SD)	56.8 (9.1)	61.4 (6.6)	<0.001
BMI (index), mean (SD)	26.7 (4.8)	29.5 (5.2)	<0.001
Clinical data			
Barthel Index, mean (SD)	93.4 (15.4)	82.9 (25.1)	<0.001
Stroke history in months,[a] mean (SD)	3.1 (2.9)	3.7 (2.8)	0.013
Etiology			0.717
Large-artery atherosclerosis, n (%)	60 (33.1)	27 (38.6)	
Cardioembolism, n (%)	43 (23.8)	8 (11.4)	
Small-vessel occlusion, n (%)	49 (27.1)	19 (27.1)	
Other determined etiology, n (%)	15 (8.3)	9 (12.9)	
Intracerebral hemorrhage, n (%)	11 (6.1)	4 (5.7)	
Undetermined, n (%)	2 (1.1)	2 (2.9)	
Stroke location			0.103
Total anterior circulation, n (%)	11 (6.5)	14 (19.4)	
Lacunar, n (%)	43 (25.3)	13 (18.1)	
Partial anterior circulation, n (%)	70 (41.2)	29 (40.3)	
Posterior circulation, n (%)	46 (27.1)	16 (22.2)	

BMI indicates Body Mass Index.
[a] Time from stroke onset to OSA diagnosis.

Seventeen were randomized into the TG and 16 into the SG. All of them gave their written consent.

3.3. PAP adherence and telemedical proactive management

For inclusion into the two study arms and follow-up analysis, see study flow chart (Fig. 1).

After three months, 88% of patients were available for analysis, which reduced to 70% of patients after one year. Two patients (6%) discontinued for medical reasons and one patient had to switch to another OSA therapy with a mandibular advancement device because of skin irritations from the mask. Six patients (18%, three from each group) dropped out because of discomfort with the device.

One patient was titrated with a fixed CPAP pressure, all other patients with a narrow Auto PAP window. The residual AHI after three months and one year was significantly higher in the TG group. As the residual AHI was <5/h in both groups, a good titration according to Berry was reached after three months and one year [32]. In two patients, APAP therapy was changed to BIPAP after three months.

For characteristics of all randomized patients, see Table 2.

The only statistically significant difference was found in sleepiness, although sleepiness did not correlate with the AHI ($r = -0.032$, $p = 0.860$) and was lower in the SG.

The primary outcome variable mean adherence to PAP use all days after three months was 76 min longer in the TG ($p = 0.017$) if adjusted for sleepiness (see Table 3). There were no significant differences in the number of days the PAP was used. The AHI measured by the device, exposed PAP pressure as well as PAP satisfaction (PAP questionnaire) did not differ between the two groups. After one year of treatment, there was no more statistically significant difference in mean PAP use all days, although the TG used PAP therapy 45 min longer than the SG.

Patients in the TG received 65 phone calls (3.8, range = 2–8 per person) from the provider, compared to 25 phone calls in the SG (see Table 4). Phone calls from patients were 13 in the SG and 15 in the TG. Interventions at the patients' homes were marginally more frequent in the TG: six for mask fitting and seven for consultations about the device as compared with three and five in the SG. Table 4 shows the data from the tele-module that resulted in proactive management.

A logistic regression model with the dichotomised variable PAP use more than median use and the independent factors age, gender, Barthel index, living status, ESS and intervention group, showed the TG group as independent factor ($\beta = 0.200$, $p = 0.046$).

3.4. Impact of PAP treatment on clinical outcome variables

Table 5 shows the changes in the clinical outcome variables. Mobility assessed by TUG improved significantly after one year in the SG, with no intergroup difference. The NIHSS improved significantly in both groups after three months and one year, with no intergroup effect. After three months, the TG significantly increased their cognitive performance measured by the MOCA Test, with no intergroup effect. There was no change in disability and quality of life.

4. Discussion

4.1. Prevalence of trOSA in people with stroke – the effect of age, stroke etiology, stroke location and disability

In the present study, 265 patients with stroke, admitted to our rehabilitation unit were investigated with HSAT sleep studies for OSA. Thirty percent were diagnosed with trOSA, which reflects a lower prevalence compared to other studies with 38% (AHI >10) to 63% (AHI >20) [1]. The wide range of prevalence rates can be explained by the timing of post-stroke screening (the earlier the sleep study the higher the prevalence), but especially by differences in age as the most relevant factor. Sleep-disordered breathing is much more prevalent in elderly people than in middle-aged or young populations, but on the other hand its clinical significance in the elderly is unclear [43,44]. Therefore, patients over the age of 70 were excluded from the study. In-hospital evaluation of OSA also showed that in people who survived a subacute stroke, central sleep apnea is relatively rare and was only diagnosed in 9.1%. This might also reflect a good time for starting PAP treatment following stroke, as central sleep apnea is more frequently seen in acute stroke [2]. A recent meta-analysis suggests that a non-invasive ventilatory therapy might be associated with greater improvement of neurological deficits during the first days after stroke onset [45]. However, there are no data on PAP dropout rates comparing the acute with the subacute phase. Stroke patients in the acute phase are certainly confronted with more PAP use confounders (infections, intensive care environment, higher immobility and cognitive dysfunction) than in the subacute phase at a rehabilitation center.

Diagnosis of OSA was not associated with etiology, anatomic lesion or gender, but with higher age, a higher body mass index

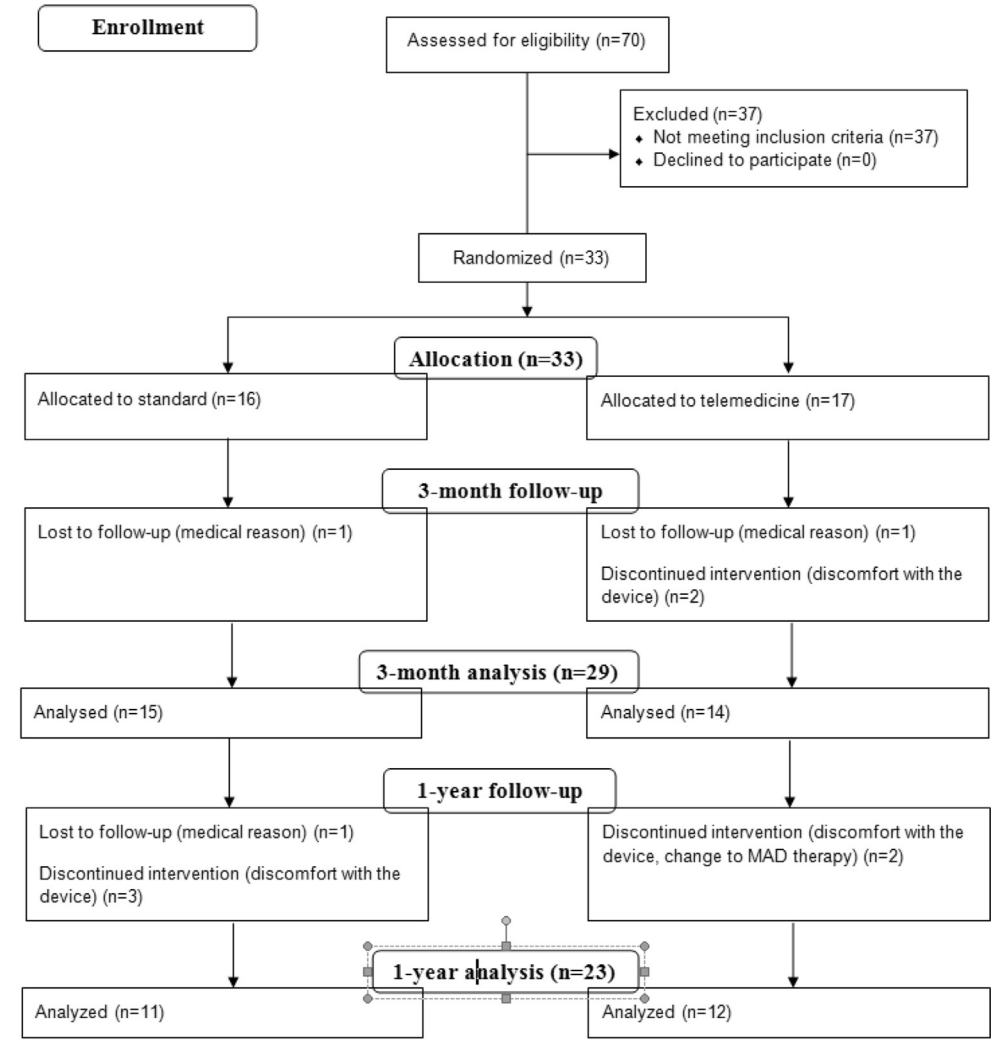

Fig. 1. Study flow chart. MAD = mandibular advancement device.

Table 2
Baseline characteristics of SG and TG.

	SG	TG	P value
	n = 16	n = 17	
Male; %	75.0	64.7	0.708
Age (years); mean (SD)	61.8 (5.3)	62.9 (5.3)	0.567
Age >60 years; %	68.8	76.5	0.708
BMI kg/m^2; mean (SD)	29 (3.1)	30.9 (4.8)	0.197
Living alone; %	18.8	29.4	0.688
Barthel Index; median (range)	100 (35–100)	100 (35–100)	0.683
Disability BI < 80	18.8	17.6	1.000
AHI; mean (SD)	37 (12.8)	37 (14.1)	0.980
ESS; median (range)	6 (0–12)	10 (3–20)	0.004
MOCA; median (range)	25 (14–29)	25 (16–30)	0.707
NIHSS; median (range)	3.5 (0–11)	1 (0–12)	0.314
QOL; median (range)	7.2 (5–10)	7.2 (5–10)	0.559
TUG; mean (SD)	12.5 (5.5)	9.3 (2.7)	0.071
NHPT; mean (SD)	35.1 (11.9)	37.3 (17.7)	0.727

AHI indicates apnea-hypopnea index; ESS, Epworth Sleepiness Scale; MOCA, Montreal Cognitive Assessment; NIHSS, National Institute of Health Stroke Score; QOL, Quality of Life Index; TUG, Timed Up and Go Test; NHPT, Nine-hole Peg Test.

(BMI) and a lower Barthel Index, reflecting a relevant disability in daily living. This association had already been shown before [46]. However, disability was not an exclusion criterion as we tried to include a representative sample of survivors from stroke admitted to rehabilitation. One quarter of our patients had a Barthel Index lower than 80, reflecting a challenging group for successful and independent PAP use.

4.2. Successful PAP titration and device acceptance - the importance of an interdisciplinary coaching strategy within rehabilitation

Adherence to PAP is a difficult issue, even in the general population experiencing SDB. In the Sleep Apnea Cardiovascular Endpoints (SAVE) study (n = 2717), after 3.7 years there was no cardiovascular outcome difference in the PAP arm versus usual care alone [47]. A low PAP adherence rate of 3.3 h per night lessened the impact of therapy on outcome. However, a propensity score–matched analysis in the same study showed that patients who adhered to PAP therapy had a lower risk of stroke than those in the usual-care group as well as a lower risk of the composite end of cerebral events. Adherence might therefore be even more challenging in survivors experiencing neurological impairment after stroke and in the particularly difficult environment of stroke units.

In a meta-analysis, dropout rates ranged from 0% to 46%, with more dropouts in the PAP groups than for sham PAP or usual care

Table 3
Adherence data after 3 months and 12 months.

	Group	3 months	p-value	12 months	p-value
Mean adherence all days (min per day), mean (SD)	SG	299 (76)	0.017	307 (62)	0.204
	TG	375 (86)		352 (97)	
Mean adherence days with PAP use (min per day), mean (SD)	SG	338 (83)	0.035	351 (44)	0.082
	TG	402 (73)		400 (78)	
Mean % days used, mean (SD)	SG	88 (10)	0.771	88 (12)	0.865
	TG	90 (16)		89 (14)	
Days PAP used >4 h, mean (SD)	SG	66 (25)	0.406	282 (55)	0.740
	TG	74 (25)		271 (99)	
AHI, mean (SD)	SG	2.2 (2.3)	0.212	1.6 (1.3)	0.046
	TG	4.1 (5.3)		4.2 (3.9)	
Median pressure, mean (SD)	SG	11 (4.2)	0.684	6.7 (2.7)	0.071
	TG	9 (4.2)		11 (1.0)	
PAP satisfaction, median (range)	SG	12.5 (5–15)	0.221	12.5 (8–15)	0.865
	TG	14 (9–15)		13.5 (3–15)	

AHI indicates apnea-hypopnea index, PAP, positive airway pressure.

Table 4
Proactive management.

Conditions[a]	Documented contacts n	Number of patients (%)
AHI>10/h	1	1 (5.9)
Leakage 95 percentiles >24 l/min	13	8 (47.1)
Adherence<4 h	26	10 (58.8)

AHI indicates apnea-hypopnea index.
[a] Patients were contacted if one of the conditions persisted for three days.

Table 5
Clinical outcome variables.

	Group	Clinical data			Within-subject Effect[b]		Inter-group Effect[a]	
					3 months	1 year	3 months	1 year
		Baseline	3 months	1 year	P-value	P-value	P-value	P-value
NIHSS, score	SG	3.7 (3.3)	1.9 (2.6)	2.1 (2.6)	0.011	0.011	0.878	0.775
Mean (SD)	TG	2.8 (3.4)	1.9 (3.1)	2.2 (3.0)	0.007	0.007		
MOCA, score	SG	24.1 (3.9)	24.9 (3.4)	27.2 (3.4)	0.191	0.012	0.542	0.812
Mean (SD)	TG	24.5 (3.7)	25.8 (3.2)	26.3 (3.9)	0.036	0.122		
Barthel Index	SG	92.2 (14.6)	96.4 (10.8)	93.5 (14.2)	0.109	0.713	0.576	0.640
Mean (SD)	TG	90.9 (21.6)	93.0 (17.8)	85.8 (21.8)	0.109	0.916		
TUG, seconds	SG	12.5 (5.5)	9.6 (3.5)	13.7 (12.9)	0.091	0.021	0.924	0.226
Mean (SD)	TG	9.3 (2.7)	10.1 (5.9)	11.9 (7.8)	0.241	0.484		
NHPT, seconds	SG	57.1 (77.3)	41.6 (22.8)	87.3 (89.3)	<1.000	<1.000	0.319	0.563
Mean (SD)	TG	40.0 (19.6)	31.4 (7.4)	34.2 (5.9)	0.050	0.080		
QOL, score	SG	7.3 (1.4)	7.7 (1.2)	7.7 (1.6)	0.571	0.359	0.914	0.861
Mean (SD)	TG	7.6 (1.6)	7.7 (1.7)	7.7 (1.4)	0.666	0.443		

NHPT indicates Nine-hole Peg Test; TUG, Timed Up and Go Test; NIHSS, National Institute of Health Stroke Score; MOCA, Montreal Cognitive Assessment; QOL, Quality of Life.
[a] Differences between the SG and the TG groups were calculated using ANCOVA for repeated measurements with TG as the reference group.
[b] Differences from baseline to three months were calculated using Wilcoxon.

[13]. Seven RCTs reported a mean PAP use of ≥4 h per night, and two showed a mean PAP use of <4 h per night, resulting in a combined mean PAP use of 4.53 h per night, but with considerable heterogeneity ($I2 = 87.2\%$, $p < 0.0001$) across the studies. Factors associated with reduced adherence were neurological impairment, mask discomfort, depressive symptoms, or subjective sleep disturbance.

Earlier studies have shown that only a small percentage of patients with stroke start PAP therapy. In a stroke unit study, 51% of patients primarily accepted PAP therapy, but only 15% continued treatment chronically [48]. A meta-analysis showed adherence rates of only 37% [18]. In our study, a comparable subsample of 47.1% started PAP therapy. After three months, 88% still used therapy and after one year, 70% PAP were still users. This might be due to the coaching strategy during rehabilitation. It gives patients the chance to become familiar with the device over a longer period than in standard care at sleep laboratories. The time from initiation of treatment to independent use differed from two days up to two weeks in patients with severe limb/trunk weakness. In contrast to nurses and physicians at rehabilitation units, sleep laboratory staff are often not experienced in bed/wheelchair transfer and management of severely affected patients. In occupational therapy, these patients received special training on how to apply the mask with only one hand. This might be the reason for a higher adherence in our study independent from telemedicine management. These findings should be evaluated in a further study comparing a coaching strategy at a rehabilitation unit with OSA management at a sleep center.

4.3. Proactive telemedicine monitoring of PAP therapy improves adherence for three months

After three months, there was a significant difference in the duration of PAP use between the two groups, with the TG using it

76 min longer. This difference was not significant after one year. This might be due to the high standard deviation of mean adherence in minutes and the increase in dropout rates to 30% in a relatively small sample size.

Our findings would prioritise stroke patients to be receiving additional telemonitoring at least for three months after initiation of PAP treatment. As this tool is human resource intensive, the three-month benefit might also be interesting for health care insurances from a cost-effectiveness point of view.

There was no significant difference between the two groups in the regularity (days of PAP use >4 h) or in the persistence of PAP use (days used). Having received PAP coaching during rehabilitation, both groups felt highly motivated to use the mask regularly at night.

However, it might be hypothesized that the significant difference in the duration of PAP use is due to the fact that patients in the TG knew that they were monitored.

In both groups, adherence was higher than in other studies. PAP adherence per night should be more than 4 h [13,47]. In the study by Fox et al., in patients with trOSA without any comorbidities, mean adherence was 105 (118) and 191 (147) min, respectively [29]. In our sample of patients experiencing motor impairment after stroke, mean adherence was 299 (76) and 375 (86) min, respectively. Only three patients used their device less than 4 h in the first three months. The authors suggest that this might be due to the coaching strategy at the hospital, which of course limits the effect of telemedical treatment as a confounder. This might be seen as a limitation of the study. In addition to that, patients in the TG had a higher EES score. However, as shown before, stroke patients with trOSA are not sleepy in general [9]. In a recent study, a greater CPAP adherence was linked to greater functional capacity and not endorsing daytime fatigue [49].

4.4. Impact of PAP treatment on clinical outcome variables - no group difference

Neurofunctional changes in patients with stroke receiving PAP were assessed in six RCTs [13]. In the combined analysis of the neurofunctional scales (NIHSS and CNS), the standardized mean difference showed overall a neurofunctional improvement with PAP with a standardized mean difference of 0.5. The heterogeneity of the studies was high with I2 = 78.9 and a subgroup analysis of early and delayed PAP trials showed no significant changes. However, a greater improvement in the NIHSS score was mentioned in patients with a better adherence to PAP in two publications [50,51]. In our study, the NIHSS improved in both groups and the MOCA score in the TG after three months with a high standard deviation but without intergroup difference. This might also be related to the above-mentioned high heterogeneity of stroke samples as well as the overall high PAP adherence in both groups. Nevertheless, our sample size was too small for this question, as the power analysis was based on telemedicine usage and there was no control group without PAP therapy. Therefore, these results can only be considered explorative and further studies with this question as primary objective are required.

5. Conclusion

An interdisciplinary coaching strategy during in-hospital rehabilitation combined with a telemedicine monitoring tool after discharge can reduce dropout rates and improve PAP adherence in patients with stroke and trOSA after three months. Thus, demonstrating a benefit in stroke patients would prioritise them to be receiving additional telemonitoring at least for three months. This might also be interesting for health care providers from a cost-effectiveness point of view.

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Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2019.06.004.

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