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Impact of a multimodal telemonitoring intervention on CPAP adherence in symptomatic low-cardiovascular risk sleep apnea: a randomized controlled trial

Short title: Telemonitoring for low cardiovascular risk OSA

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Abbreviations

AASM – American Academy of Sleep Medicine

AHI – apnea-hypopnea index

BMI – body mass index

CPAP – continuous positive airway pressure

DBP – diastolic blood pressure

ESS – Epworth Sleepiness Scale

HDL – high-density lipoprotein

IQR – interquartile range

ITT – intention-to-treat

LDL – low-density lipoprotein

ODI – oxygen desaturation index

OSA – obstructive sleep apnea

PaCO₂ – arterial partial pressure of carbon dioxide

PaO₂ – arterial partial pressure of oxygen

PG – respiratory polygraphy

PP – per-protocol

PROMs – patient reported outcomes

PSG – polysomnography

RCT – randomized controlled trial

SaO₂ – arterial oxygen saturation

SBP – systolic blood pressure

SD – standard deviation

SDB – sleep disordered breathing

SF-12 – Health Outcomes Short Form

SpO₂ – oxygen saturation

TM – telemonitoring

UC – usual care

WHO – World Health Organization

Abstract

Background: One of the major challenges in treating obstructive sleep apnea (OSA) is to achieve adequate continuous positive airway pressure (CPAP) adherence. Telemonitoring has the potential to provide individualized management and early recognition of problems during treatment.

Research question: What is the effect of a multimodal telemonitoring intervention on treatment adherence, quality of life and functional status in symptomatic OSA patients with low cardiovascular risk?

Study Design and Methods: In a multicenter, randomized controlled trial, newly diagnosed OSA patients were randomly assigned to multimodal telemonitoring for 6 months versus usual care (UC). Telemonitoring consisted of built-in electronic alert algorithms for early adjustment of CPAP treatment in case of side effects, leaks or persistent residual events. The primary outcome was CPAP adherence (in hours/night). Secondary outcomes included daily symptoms such as fatigue and sleepiness, and quality of life measured by self-reported questionnaires.

Results: Of 206 OSA patients aged 50.6 [42.1 ; 58.1] (median [IQR]) years; predominantly male (63%) with body mass index of 30.6 [26.8 ; 35.1] kg/m² and an apnea-hypopnea index of 45.2 [34.0 ; 60.0] events/hour) 102 received UC and 104 telemonitoring. After 6 months of treatment, CPAP adherence was similar in the two groups when assessed either by mean duration of usage (4.73 ± 2.48 hours/night in the TM group and 5.08 ± 2.44 hours/night in the UC group, $p = 0.30$) or in % of patients adherent to treatment (over 4 hours usage/night, > 70% nights; 64% in TM versus 72% in UC, $p = 0.24$). There was no significant difference between the groups in effect size of improvement in fatigue and sleepiness.

Interpretation: In severe OSA patients with low cardiovascular risk, multimodal telemonitoring did not increase CPAP adherence. For both telemonitoring and usual care groups similar improvements in daytime symptoms were achieved.

NCT: 01796769

Keywords: obstructive sleep apnea, telemonitoring, telemedicine, CPAP adherence.

Introduction

Obstructive sleep apnea (OSA) is characterized by repeated episodes of apneas and hypopneas during sleep producing intermittent hypoxia and sleep fragmentation which in turn generate disturbing symptoms including daytime sleepiness, impairment of daily functioning, deterioration of memory and cognition, and a higher risk of developing cardiovascular, metabolic and cerebrovascular diseases.^{1,2} OSA is one of the most frequent chronic diseases, affecting nearly one billion people worldwide.³ Sleep apnea demonstrates extreme heterogeneity⁴ in clinical presentation and several cluster analyses have identified homogeneous subgroups of OSA patients sharing the same pattern of symptoms, similar levels of cardio-metabolic risk and uniform responses to continuous positive airway pressure (CPAP). Among OSA subgroups there is considerable variability in age, gender, symptoms, obesity, co-morbidities and exposure to environmental risk factors.⁵⁻⁷

Currently the optimization of OSA treatment strategies requires the allocation of patients to a specific phenotype and then to propose personalized therapeutic strategies adapted to these subpopulations.^{8,9} Sleepiness and fatigue, two of the main symptoms of OSA, are strongly associated with a poorer quality of life and functional status and should be priorities when treating these patients.^{10,11} Previous studies have demonstrated that adequate adherence to CPAP treatment is the pre-requisite for reducing symptoms.^{12,13} It is well established that good adherence to CPAP early-on is the strongest predictor of long-term compliance and that interventions should focus on the period of treatment initiation.¹⁴ CPAP telemonitoring and telemedicine might provide innovative and practical solutions to identifying the OSA patients at highest risk of future nonadherence to treatment, allowing home care providers and physician resources to be primarily allocated to those who most need it.

Every night telemonitoring of patients treated with CPAP devices provides information on CPAP adherence, efficacy and leaks. Telemonitoring strategies can also include the use of electronic messages¹⁵ and self-management platforms. Such platforms help physicians and healthcare providers to rapidly identify potential sources of poor CPAP adherence: mask leaks, CPAP side effects, unfounded patient beliefs and/or inappropriate behaviors regarding their therapy.¹⁶⁻¹⁹ Although some studies have suggested higher CPAP usage with telemonitoring compared to usual care^{15,20-22} most studies have failed to show better CPAP adherence.²³⁻²⁸ These discrepancies might be partly explained by the fact that

the impact of telemonitoring on CPAP adherence is OSA phenotype dependent. Low cardiovascular risk OSA patients without associated comorbidities, even although they are symptomatic, might underestimate the consequences of their disease and be at higher risk of poor CPAP adherence.²⁹

We hypothesized that patients with severe and symptomatic sleep apnea but with low cardiovascular risk (no cardiovascular comorbidity) would benefit from a multidisciplinary and coordinated follow-up based on telemonitoring to achieve better adherence to CPAP treatment. This improvement in adherence to CPAP might result in gain in the quality of life of these patients. In this randomized controlled trial, we investigated the effects of a multidisciplinary and coordinated telemonitoring intervention in improving treatment adherence (primary outcome) along with its impact on quality of life and functional status as measured by self-reported questionnaires (secondary outcomes).

Methods

Design and participants

OPTISAS 1 was a prospective, randomized, multi-center, parallel trial comparing 6-month CPAP adherence after allocation of symptomatic OSA patients with low cardiovascular risk to a usual CPAP care (UC) group or to a group with multidisciplinary and coordinated follow-up based on telemonitoring (TM). This study was part of a larger project (OPTISAS), which encompassed OSA patients with low cardiovascular risk (Systematic Coronary Risk Evaluation Project SCORE<5%, OPTISAS 1, NCT: 01796769) and OSA patients with high cardiovascular risk (SCORE>5%, OPTISAS 2, NCT: 01505959). OPTISAS 1 is reported here, and the results of OPTISAS 2 were recently published.³⁰ The primary research objective was to determine the impact of telemonitoring performed by health professionals on 6-month CPAP adherence (in hours/night) compared to usual care (See Online supplement for definitions of usual care and telemonitoring with interventions). Secondary research objectives were to determine the impact of TM versus UC, on quality of life (Health Outcomes short form - SF-12), sleepiness (Epworth Sleepiness Scale (ESS)) and fatigue (Pichot fatigue scale).

This study was conducted in accordance with applicable good clinical practice requirements in Europe, French law, ICH E6 recommendations, and the ethical principles of the Helsinki Declaration (South Africa 1996 and Edinburgh 2000). The trial was approved by an independent ethics committee (Comité de Protection des Personnes Sud Est V, Grenoble, France, N° IRB: 0006705) and registered on the ClinicalTrials.gov site (NCT: 01796769). All participants signed the written informed consent before enrollment in the study. All recruiting centers were in France, with Grenoble as the coordinating center. All centers, public university hospitals as well as private practice facilities had well established sleep units with the personnel trained for diagnosis, treatment and follow-up of patients with OSA. The associated home healthcare providers were trained and certified in technical support and follow-up of CPAP therapies (see online supplement for inclusion among healthcare provider agencies).

Between February 2013 and October 2013, patients with suspected OSA attending one of the participating sleep centers were screened for inclusion. Patients were selected based on their complain of sleepiness whatever their ESS value. Eligible patients were aged

18 to 78 years, with severe OSA defined by an apnea hypopnea index (AHI) > 30 events/hour based on respiratory polygraphy (PG) or polysomnography (PSG). Inclusion criteria included no known cardiovascular disease at baseline and a cardiovascular risk of less than 5% (assessed by the ten-year risk of fatal cardiovascular event SCORE calculation adapted specifically for European countries).³¹ The exclusion criteria were any history of a cardiovascular pathology, a central sleep apnea index above 20% of AHI, hypercapnic chronic respiratory failure (daytime PaCO₂ > 50 mmHg), and insufficient skill in the use of the telemonitoring system. Inclusion and exclusion criteria are detailed in the online supplement.

Intervention

Patients in both UC and remote multimodal TM arms received the same 1-hour CPAP initiation educational program. In the multimodal TM group, CPAP telemonitoring provided adherence, leaks, and residual events. Symptoms and quality of life were recorded via electronic questionnaires to be filled-in by patients. Patients were shown how to use the remote home telemonitoring equipment and were given an explanation of why monitoring of these variables was relevant to their care. Secured data transmission of patients reported outcomes to the medical staffs' computers and secured websites completed the integrated care management system.

Automatic algorithms have been developed for the rapid adjustment of CPAP treatment in the event of side effects, leaks (specific thresholds depending on the brand of CPAP device), residual sleepiness (ESS > 10) or persistent residual events (residual AHI > 10 events/hour). For the main side effects (aerophagia, dry mouth, abrasion of the ridge of the nose, sneezing and nasal drip³²) specific and homogeneous procedures were defined prior to the study and agreed between the different study sites. The addition of a humidifier, changes in interface and reduction in pressure were among the most frequently proposed actions. In CPAP adherent patients, with persistent sleepiness or residual respiratory events above 10events/hour, a sleep study under CPAP was generally scheduled. The efficacy of actions taken was systematically reassessed by asking patients to report any new side effects and evaluate patient centered outcomes via electronic questionnaires presented by the web platform. The multimodal telemonitoring system assigned predefined interventions to trained home-care providers (managing leaks, mask problems or other side effects).

Physicians were in charge of the appropriate management of residual events or lack of efficacy of CPAP. Additional home visits or visits to the sleep clinic were organized when required (see figure 1 in Pepin et al³⁰).

Randomization and masking

Patients were randomized to multimodal remote telemonitoring or usual care (1:1 ratio) using computer-generated allocation. Randomization was stratified by center, home-care provider and CPAP brand (the 4 main brands used in France at the time of the study). Neither patients nor investigators were masked to group assignment. Patient outcomes (sleepiness, fatigue, depression, and side effects) were self-reported at home without any intervention by the investigators. All data of the study were analyzed by a personnel blinded to study arm allocation.

Procedures

Assessments for the primary and secondary outcomes were done immediately before CPAP initiation and after 6 months of treatment.

Sleep studies (See Online supplement for description)

The diagnosis of OSA was obtained by full-night PSG performed at a sleep center or by PG performed at home. Sleep stages were scored manually according to the American Academy of Sleep Medicine criteria.³³ The scoring of respiratory events was done according to the rules described by the AASM.³⁴ AHI was defined as the number of apneas and hypopneas per hour of sleep (full-night PSG) or per hour of recording (PG). Sleep studies are described in detail in the online supplement.

CPAP treatment (See Online supplement for description)

After diagnosis, all patients were treated using an automatic CPAP device, as described in the online supplement and in a similar manner to treatment in the OPTISAS 2 study.³⁰ Optimal usage was characterized as more than 4 hours/night for > 70% nights used.

Quality of life and functional status: (See Online supplement for description)

Patient reported outcomes (PROMs)³⁴ were evaluated using validated French versions of self-reported questionnaires: Health Outcomes Short Form - SF-12³⁵, ESS³⁶ and the Pichot fatigue scale³⁷, detailed in the online supplement.

Cardiovascular Risk SCORE

The ten-year risk of fatal cardiovascular events was calculated using the SCORE calculation for European countries: Systematic Coronary Risk Evaluation Project³¹. Variables used for calculation of the score are detailed in the online supplement. Only patients with low cardiovascular risk defined as <5% and/or in primary prevention were included in the study.

Biological parameters

Cholesterol (total, LDL and HDL), fasting glucose and HbA1c were measured to calculate the cardiovascular risk at inclusion (confirming the SCORE calculation) and after 6 months of treatment.

Sample size calculation

The hypothesis was that adherence after 6 months of CPAP treatment would be greater in the multimodal TM arm than in the UC arm. In the study of Sparrow *et al*²² there was a difference in adherence of 0.9 hours/night in favor of the TM arm. Owing to the high level of support given by healthcare providers to CPAP users in France, we expected a lower relative benefit of telemonitoring and thus a difference between groups of only 0.35 hours/night. In a previous study³⁵, we observed a standard deviation (SD) for CPAP adherence of 1.82 hours/night during a 4-month study. Therefore, with the assumption of a SD of 1.82 hours/nights, and 10% dropout, a sample size of 468 participants per group was required to detect a difference in adherence of at least 0.35 hours/night between groups, with 80% power.

Statistical Analysis

Continuous data are presented as mean \pm SD or median [interquartile] (IQR) and categorical data as frequency and percentage (%). Data were initially analyzed in intention-to-treat (ITT) including all randomized patients. In addition, a per-protocol (PP) analysis was done on all randomized subjects, excluding study dropouts. To replace missing data, multiple imputations were performed for the primary outcomes using a logistic and linear regression model for binary and continuous variables respectively. Fifty datasets were constituted, and Rubin's rules were observed for combining the results by using the SAS proc MIANALYZE.

A linear mixed effects model, with random effect by homecare provider was used to analyze the main and the secondary outcomes. We analyzed the difference between 6-month and baseline values by group (TM vs. UC) with adjustment on baseline values of the analyzed variable. For CPAP adherence, because there was no baseline value, only the random effect by homecare provider was introduced into the linear mixed model. When the conditions of use of the linear mixed model were not respected a Mann-Whitney test was performed.

Statistical Analysis Software SAS V9.4 software (SAS Institute Inc., Cary, NC, USA) was used for statistical analyzes. A p-value of < 0.05 was considered statistically significant.

Results

Study population

Study flow is presented in Figure 1 and baseline demographic and clinical characteristics are reported in Tables 1 and 2 and centers in Table E1. Patients were mostly middle aged 50.6 [42.1 ; 58.1], predominantly male (63%) and overweight or slightly obese (body mass index (BMI) of 30.6 [26.8 ; 35.1] kg/m² with a mean AHI 45.2 [34.0 ; 60.0] events/hour). By design, this population comprised severe symptomatic OSA patients frequently exhibiting sleepiness and fatigue. Owing to inclusion criteria studied patients did not present with cardiovascular comorbidities and office arterial blood pressure was in the normal range at inclusion.

Primary Outcome: CPAP adherence

After 6 months of CPAP treatment, in the ITT analysis, the mean nightly use of CPAP was similar in the two groups (4.73 ± 2.48 hours/night in the TM group and 5.08 ± 2.44 hours/night in the UC group, p = 0.30). In PP analysis, the mean use of CPAP was 5.15 ± 2.09 hours/night in the TM group and 5.30 ± 2.15 hours/night in the UC group (p = 0.65, Figure 2). Using adherence categories, the ITT analysis showed similar high CPAP adherence (over 4 hours usage/night, > 70% nights) in the two groups (64% in TM group versus 72% in the UC group, p = 0.24). This was also found in PP analysis (69% in TM versus 76% in UC, p = 0.38, Figure 3).

Finally, we analyzed adherence expressed as a percentage of subjective sleep duration and likewise, found no statistical difference (see table E2 in the online supplement).

Secondary outcomes

Functional status and quality of life

After 6 months of CPAP treatment, both groups exhibited substantial improvements in daily fatigue and excessive sleepiness, without significant differences between the groups (Table 2 A). There was an improvement in quality of life with CPAP treatment that was significant only in the SF-12 mental component in the TM group but without significant difference between groups (Figure 4).

Biological parameters

Lipid control and more specifically the total blood cholesterol improved significantly more in the TM group. This was mainly driven by a decrease in blood LDL cholesterol levels (Table 2B). However, there was no change in BMI (Table 2B).

Workload of care givers during follow-up

As expected, there was a much greater number of interventions in the TM group. In OSA patients with at least one intervention (Table 3), there was an overall 59% increase in the number of physician interventions and 54% in the number of homecare provider's interventions.

Discussion

In this multicenter randomized controlled trial conducted in 206 symptomatic and severe OSA patients who were free of severe comorbidities and had low cardiovascular risk, the implementation of multidisciplinary and coordinated follow-up based on telemonitoring did not give better CPAP adherence than UC. Lipid metabolism parameters improved significantly more in the TM group than with usual care, but with no change in BMI. Finally, in the TM group, there was a significant increase in the follow-up workload for both physicians and homecare providers.

One strength of our study was to have been conducted in a pre-specified and well-defined OSA phenotype. The longitudinal associations between OSA subtype, CPAP adherence and improvement in symptoms under CPAP have been recently deciphered.^{36,37} Reduced CPAP adherence was found in patients with concurrent insomnia and OSA, or in those with mild or minimally symptomatic OSA and comorbidities.⁶ We conducted a companion large randomized controlled trial (RCT), companion OPTISAS 2.³⁰ in another distinct OSA subtype with more comorbidities and relatively mild symptoms (see Table E3 online supplement). We showed that CPAP with multidisciplinary remote telemonitoring was not superior to usual CPAP care in reducing blood pressure but was nevertheless associated with better CPAP adherence and a greater improvement in patient centered outcomes than usual care.³⁰ In OPTISAS 2, CPAP adherence (secondary outcome) was 5.28 ± 2.23 hours/night in the TM group versus 4.75 ± 2.50 hours/night in the UC group.³⁰ That study suggested that in OSA patients with potentially poor lifestyle habits, more comorbidities and relatively mild to moderate symptoms, telemonitoring has a significant impact toward improving CPAP adherence.³⁰ In contrast, in the present study more highly symptomatic patients with fewer comorbidities did not benefit from telemonitoring in terms of better CPAP adherence. These data reinforce the concept that better CPAP adherence and treatment effectiveness can only be ensured by using distinctive tailored management strategies, with or without telemonitoring, according to the OSA phenotype.³⁸

Among studies evaluating telemonitoring as a tool for improving CPAP adherence (see for review: Pépin et al.¹⁷) only a minority have reported positive results. One RCT demonstrated a 6-month median increase in CPAP usage of 0.9 hours/night in the TM group and at one year 2.0 hours/night improvement in adherence.²² However, CPAP adherence was very low in the control group and the results more likely reflected the poor quality of UC than the efficacy of telemonitoring. More recent telemonitoring studies^{23,27} have more consistently shown similar adherence in the UC and the TM arms. The true interest of telemonitoring is probably its capability for the early identification of patients at risk of poor adherence. This would allow re-allocation of resources to low adherence subgroups with a concurrent reduction in the number of visits for those with good adherence who need only to be followed by regular nightly telemonitoring. The cost-effectiveness validation of such a strategy is essential because both our study and others highlighted the greater burden of

caregivers' interventions for both technical (masks, humidifiers, etc.) and medical (residual sleepiness, persistent high residual AHI) reasons.

In some OSA subgroups, telemonitoring has also been reported as enhancing self-perceived efficacy of CPAP treatment and/or improving biological parameters. It is often pre-supposed that any kind of support during CPAP treatment is favorable to improving patient's engagement both for CPAP adherence and the recovery of a healthy lifestyle. The use of automated feedback text messaging in association with CPAP + telemonitoring has been demonstrated as improving 90-day and one year adherence in patients with OSA¹⁵. Also, active patient engagement technology using smartphones along with telemonitoring led to about one hour increase in CPAP adherence.³⁹

Due to technical and funding issues, data allowing a complete cost analysis evaluation of the two different types of management were not collected. However, in view of the number of alerts that the TM system generated, one could hypothesize that an average of 30 minutes may have been necessary to respond to or to manage each alert. Therefore, the UC intervention might appear to be more efficient from a cost perspective.

The main limitation of this study was the failure to reach the estimated sample size. During the course of the study reimbursement of the cost of CPAP with telemonitoring by the national health insurance scheme was suspended in France by order of the high court "Conseil d'Etat". This decision was related to a request from several patients' associations concerned about data confidentiality. Consequently, the trial data monitoring committee recommended trial termination for pragmatic reasons. A post-hoc power analysis showed that for the small mean differences and the broad standard errors (0.34; IC 95% [-0.31 ; 0.99]) observed in this study between the UC group (5.08 ± 2.44 hours/night) and the TM group (4.73 ± 2.48 hours/night), a sample of 1646 patients would have been needed to reach a sufficient power of 0.8 to show a significant difference of 0.34 hour/night. However, future studies might determine sample sizes based on thresholds that are more clinically meaningful. For example, a threshold above 0.5h is often considered to be clinically meaningful. In this study, a sample size of 788 patients would have been needed to meet this threshold with a power of 0.80.

Compared to a previous report in high cardiovascular risk patients³⁰, the population in this study was younger, comprised more women, and reported less tobacco and alcohol consumption. A more detailed phenotyping of this population in terms of positional AHI,

ratio of apnea to hypopnea, sleep fragmentation, and periodic leg movement during sleep would enhance the description of OSA. As this data was not collected or present in our dataset, it represents another limitation of the study.

Another limitation that one might add to our study is that we did not select our population based on symptoms or on difficulties in treatment adherence during the first weeks of CPAP use. One could argue that in an unselected population it is difficult to improve on already high adherence. Therefore, telemonitoring might be more useful in specific populations (e.g. little symptomatic or poorly adherent patients). As a further insight for future research, we should also consider that a meaningful increase in CPAP adherence of less than 30 minutes is unlikely to be clinically significant. In our study the mean change in CPAP adherence was only 21 minutes and did not reach statistical significance.

Finally, we found an unexpected improvement in lipid profile without change in BMI in the TM group, which may be only a spurious finding.

Conclusions

OPTISAS 1, a RCT study of patients with low cardiovascular risk, demonstrated that the impact of telemonitoring in this population may be minimal. Whether an increase in adherence by combining TM with additional patient engagement tools remains to be seen and may be a focus of future research. When organizing the health management of sleep apnea care services, the likelihood of improved adherence with TM interventions will need to be balanced against the resources needed to implement the program and will require robust cost effectiveness evaluations.

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Guarantor statement: Renaud Tamisier takes responsibility for the content of the manuscript, including the data and analysis

Authors' contributions: JLP, RT contributed substantially to the study design, data collection and interpretation. , MS, YG, BS, JFM and HP included and followed up patients MB and SB performed the statistical analysis. ET, RT, MJF, and JLP wrote the article and PL, MS, YG, MB, SB BS, JFM and HP critically revised the manuscript.

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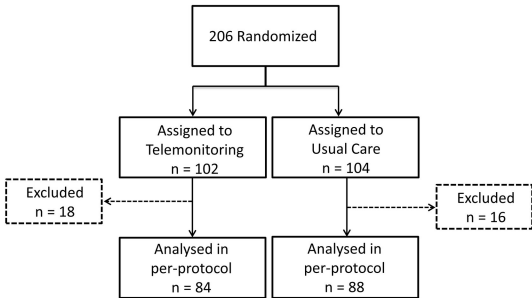
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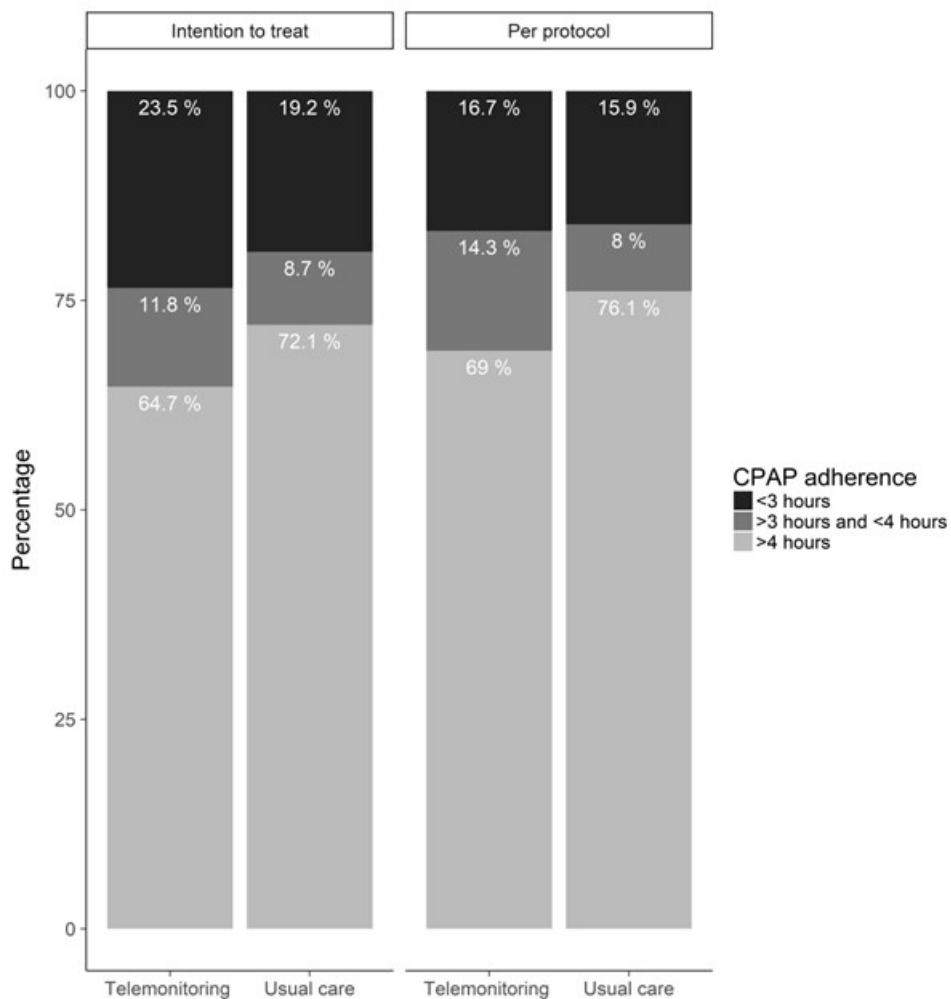
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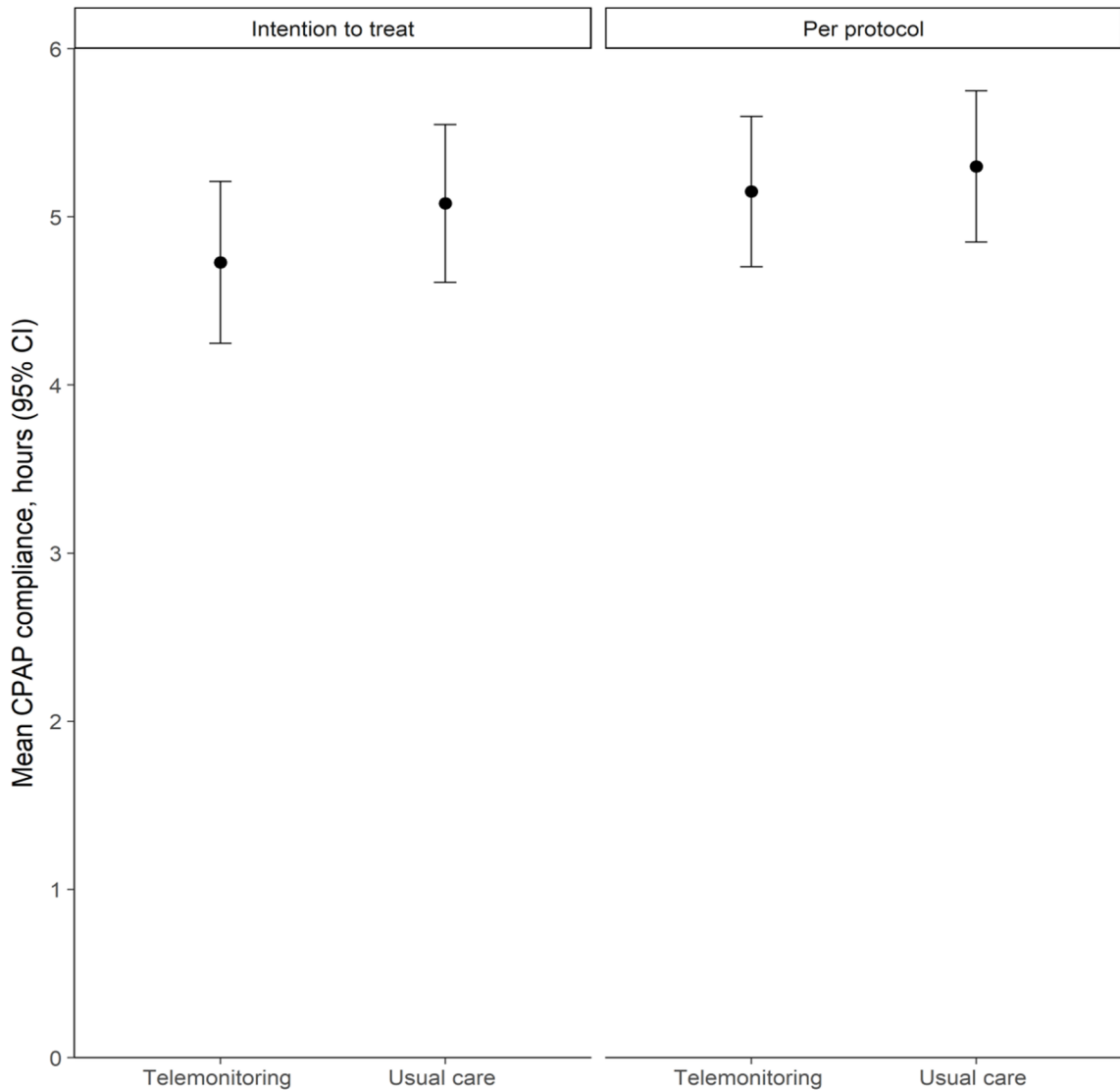
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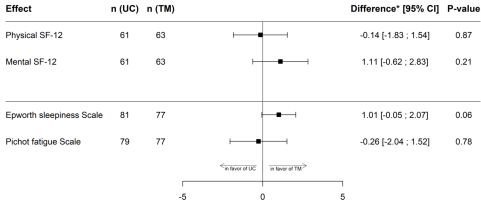


Table 1. Baseline demographic and clinical characteristics

Variables	Telemonitoring n=102	Usual Care n=104	Missing (%)
Demographics			
Age (year)	51.9 [44.8; 58.8]	49.4 [40; 57.9]	
Male gender (number (%))	60 (58.8)	71 (68.3)	
BMI (kg/m ²)	30.5 [27.5; 34.9]	31.3 [26.6; 35.2]	
Medical History			
Smoking (%)	45 (44.1)	42 (40.4)	
Alcohol (%)	6 (5.9)	5 (4.9)	1 (0.5)
Gastroesophageal reflux (%)	18 (17.6)	18 (17.3)	
Diabetes (%)	2 (2)	5 (4.8)	
Dyslipidemia (%)	14 (13.9)	19 (18.3)	1 (0.5)
Sedentariness (%)	17 (16.7)	14 (13.6)	1 (0.5)
Symptoms			
Snoring	96 (96)	99 (96.1)	3 (1.5)
Nocturia (%)	59 (57.8)	46 (44.2)	
Headache (%)	51 (50)	45 (43.3)	
Respiratory arrest (%)	55 (54.5)	49 (47.6)	2 (1)
Epworth	10.44 ± 5.05	9.65 ± 5.22	
Pichot tiredness	13.06 ± 7.01	11.66 ± 8.52	
Office Blood pressure			
Office SBP (mmHg)	130 [120; 135]	130 [120; 135.5]	
Office DBP (mmHg)	80 [70; 86]	80 [70; 80]	
Respiratory parameters			
AHI (events/hour)	45 [34 ; 58]	42.3 [33 ; 57.6]	
Mean SaO ₂ (%)	93 [91 ; 94.2]	93 [92 ; 94.9]	4 (1.9)
PaO ₂ (mmHg)	84 [75 ; 90]	83 [77 ; 90]	
PaCO ₂ (mmHg)	38 [35.3 ; 40]	39 [35.8 ; 40]	
pH	7.4 [7.4 ; 7.5]	7.4 [7.4 ; 7.4]	

BMI, Body Mass Index ; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; AHI, apnea hypopnea index; SaO₂, arterial oxygen saturation; PaO₂, arterial partial pressure of oxygen; PaCO₂, arterial partial pressure of carbon dioxide. Data are presented as number (%), mean ± standard deviation or median ± interquartile.

Table 2 A. Symptoms and Quality of life Biological parameters

Variables	Telemonitoring				Usual Care				
	n	Baseline	6 months	p value *	n	Baseline	6 months	p value *	P value †
Epworth	81	10.44 ± 5.05	4.51 ± 4.08	<0.0001	77	9.65 ± 5.22	5.19 ± 4.32	<0.0001	0.06
Pichot Tiredness	79	13.06 ± 7.01	6.05 ± 6.82	<0.0001	77	11.66 ± 8.52	5.20 ± 6.39	<0.0001	0.78
SF-12 physique	63	44.5 ± 5.8	45.7 ± 5.6	0.14	61	45 ± 5.6	46 ± 4.7	0.16	0.87
SF-12 mental	63	40.8 ± 6.4	43.9 ± 5.4	0.001	61	41.1 ± 5.6	42.9 ± 4.6	0.07	0.21

Data are presented as mean ± standard deviation or median ± interquartile range with 95% confidence interval (95% CI); * for comparison between baseline and after 6 months; † for comparison between the 2 groups.

Table 2 B. Clinical and Biological metabolism parameters

Variables	Telemonitoring				Usual Care				
	n	Baseline	6 months	p value *	n	Baseline	6 months	p value *	P value †
BMI (Kg/m²)	80	31.35 (27.68 ; 35.70)	31.29 (27.90 ; 35.78)	0.77	82	31.42 (26.45 ; 34.94)	31.28 (26.78 ; 35.27)	0.48	0.45
Glycemia (g/L)	63	1.02 (0.96 ; 1.21)	1.02 (0.92 ; 1.15)	0.47	67	0.99 (0.92 ; 1.08)	1.01 (0.94 ; 1.10)	0.07	0.12
Total cholesterol (g/L)	64	2.38 (2.11 ; 2.70)	2.19 (1.87 ; 2.59)	0.001	69	2.19 (1.89 ; 2.37)	2.16 (1.88 ; 2.39)	0.67	0.01
HDL cholesterol (g/L)	64	0.52 (0.44 ; 0.65)	0.52 (0.44 ; 0.63)	0.98	69	0.48 (0.41 ; 0.63)	0.52 (0.44 ; 0.66)	0.01	0.07
LDL cholesterol (g/L)	63	1.50 (1.29 ; 1.87)	1.36 (1.12 ; 1.60)	<0.0001	68	1.36 (1.13 ; 1.61)	1.31 (1.12 ; 1.51)	0.07	0.02
Triglycerides (g/L)	64	1.25 (0.98 ; 1.86)	1.30 (0.84 ; 1.64)	0.94	69	1.25 (0.88 ; 1.75)	1.18 (0.87 ; 1.63)	0.23	0.41

BMI, Body Mass Index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; IQR, interquartile range. Data are presented as mean ± standard deviation or median ± interquartile range with 95% confidence interval (95% CI); * for comparison between baseline and after 6 months; † for comparison between the 2 groups.

Table 3A. Number of alerts by subject in each group during the 6-month timeframe.

	Telemonitoring n=102	Usual care n=104
All alerts	13.31 ± 8.27	5.62 ± 2.71
Medical alerts	3.46 ± 4.08	0.04 ± 0.31
Protocol alerts	8.09 ± 4.54	5.09 ± 2.5
Technical alert	1.76 ± 2.16	0.49 ± 0.7
Mean ± standard deviation		

Table 3B. Alerts distribution during the 6-month timeframe.

Number of subjects with at least one alert (*) and number of alerts by subject having at least one alert (#) in each group (Telemonitoring and Usual care).

variables	Telemonitoring n=102		Usual care n=104	
	n* (%)	Mean# ± SD	n* (%)	Mean# ± SD
All alerts	97 (95)	14 ± 7.88	101 (97)	5.78 ± 2.57
Medical alerts	73 (72)	4.84 ± 4.07	2 (2)	2 ± 1.41
Protocol alerts	97 (95)	8.51 ± 4.26	101 (97)	5.24 ± 2.37
Technical alert	67 (66)	2.69 ± 2.15	41 (39)	1.24 ± 0.54

*: number of subjects with an alert, #: mean of number of alerts by subject with an alert