Benefits in quality of life following an obstructive sleep apnea screening and treatment program in patients with acute ischemic stroke

Ana Domínguez-Mayoral, Carmen Gutiérrez, Jesús Sánchez-Gómez, Soledad Pérez-Sánchez, Natalia Fouz, Patricia Guerrero-Zamora, Marta Ferrer, María Aguilar, Victoria Galiani, Carmen Albalá, José Moreno, Miguel Á. Gamero, Cristina García-Campos, Sara Banda, Joan Montaner

Introduction. Obstructive sleep apnea (OSA) has been proposed as a factor that worsens stroke prognosis. Our aim was to determine if an OSA intervention could improve quality of life (QOL, first objective) and modified Rankin score (mRS, second objective).

Patients and methods. The intervention group of this quasi-experimental study included patients with acute ischemic stroke <72 hours who underwent polygraphy and Continuous Positive Airway Pressure (CPAP) and hygienic-dietary measures if required. The control group followed routine clinical practice. The Short Form 36 Health Survey (SF-36) and mRS were applied at the sixth month after stroke in both groups.

Results. Fifty-five vs. sixty-two patients were included in the intervention and control group respectively. In the intervention group, 64.71% of patients accepted the proposed CPAP (16 cases with a good adherence). An improvement in SF-36 items was detected in the intervention group: physical functioning (p = 0.008), role physical (p = 0.002), bodily pain (p = 0.008), general health (p <0.001), vitality (p = 0.001) and role emotional (p = 0.015). In a per-protocol analysis, all these improvements were verified in the group of patients treated with good CPAP adherence (p < 0.05 in all the same SF-36 items). The percentage of patients with physical component summatory ≥ 50 was higher in the intervention group (p = 0.003). There were no differences in the median of mRS (p = 0.262).

Conclusions. Although more evidence is needed, a significant improvement in QOL was suggested after our OSA intervention, particularly in patients with good CPAP adherence.

Key words. Continuous positive airway pressure (CPAP). Quality of life. Screening. SF-36 score. Sleep apnea. Stroke.

Stroke Unit. Neurology Department (A. Domínguez-Mayoral, S. Pérez-Sánchez, V. Galiani, C. Albalá, J. Moreno, M.A. Gamero, C. García-Campos, S Banda, J. Montaner). Neurophysiology Department (C. Gutiérrez, M. Aguilar). Pneumology Department. Hospital Universitario Virgen Macarena (J. Sánchez-Gómez, N. Fouz, P. Guerrero-Zamora, M. Ferrer). Neurovascular Research Laboratory. Instituto de Biomedicina de Sevilla (IBiS). Seville, Spain (A. Domínguez-Mayoral, S. Pérez-Sánchez, V. Galiani, C. Albalá, J. Moreno, M.A. Gamero, C. García-Campos, S. Banda, J. Montaner).

Corresponding author:
Dra. Ana Domínguez Mayoral. Unidad de Ictus. Departamento de Neurología. Hospital Universitario Virgen Macarena. Avenida Dr. Fedriani, 3. E-41009 Sevilla.

E-mail:
anam.dominguez.mayoral.sspa@juntadeandalucia.es

Author contributions:
Conceptualization: Ana Domínguez-Mayoral and Joan Montaner. **Methodoloy:** Ana Domínguez-Mayoral, Carmen Gutiérrez and Jesús Sánchez Gómez. **Investigation:** Ana Domínguez-Mayoral and Soledad Pérez-Sánchez. **Data curation:** Carmen Gutiérrez, Jesús Sánchez Gómez, Marta Ferrer, María Aguilar, Patricia Guerrero Zamora, Victoria Galiani, Carmen Albalá, Miguel Ángel Gamero, Cristina García-Campos and Sara Banda. **Software and formal analysis:** José Moreno. **Writing:** Ana Domínguez-Mayoral, Natalia Fouz, Soledad Pérez-Sánchez and Joan Montaner.

Acknowledgments:
The authors wish to thank the invaluable help of staff members who also participated in the study: Eloy Ferrete, Reyes De Torres, Ana →

Introduction

The relationships between Obstructive Sleep Apnea (OSA) and stroke are a hot topic [1]. OSA is defined as Respiratory-Events Index (REI, including apneas and hypopneas) ≥ 5 per hour [2,3].

Stroke is a relevant problem in world health [1]. The prevalence of OSA among patients with acute ischemic stroke (IS) may reach up to 84.72% in some Spanish areas [1]. The factor that gives OSA the greatest relevance is its contribution to the progression of vascular disorders [4]. OSA triples the risk of IS in men [5]. Furthermore, OSA has a negative impact on quality of life (QOL) [6], although this issue has not been well studied in IS. In terms of rehabilitation, OSA may have a negative influence on recovery [7]. Emerging evidence suggests that Continuous Positive Airway Pressure (CPAP) treatment in post-stroke patients may lead to faster functional recovery and reduction in the hospital length of stay [8,9]. There are several studies that have linked functional recovery and QOL in patients with stroke [10,11]. Consequently, we hypothesize that an OSA intervention in patients with IS might improve QOL.

Quasi-experimental studies may help in the design of future randomized trials. Our main aim is to provide an estimation of the impact of our intervention in terms of QOL measured by the score Short Form 36 Health Survey (SF-36). As a secondary objective, we analyze the percentage of patients with modified Rankin Scale (mRS) ≤ 2 and the median of mRS at the sixth month after IS [12].

Barragán, Lidia Ruiz, Teresa Reviriego, Franscisco Álvarez, Julia Franco, Laura Ruiz, Montserrat Calado, Leandro Gila, Teresa Rodríguez, Manuel González, Concepción Navarrete, Asunción Herrero, Myriam Montblanc, Myriam Cabezali, Leandro Gila, Teresa Rodríguez, Inmaculada García, Antonia Carrión, Amparo Núñez, Rocío Lara, Berta Gallardo, Asunción Herrero, Eva Zaya, Natalia Delgado, Rafael Gómez, Ana María Hérnandez, Josefa Jiménez, Carmen Piña, Rosa Muñoz, Deborah Fernández, Silvia Sánchez (all of them of the Neurology Department), María Velarde (Pneumology Deparment) and Dolores Romero (Rehabilitation Department).

Funding:
This research received no external funding. We have received logistical support from the Neurovascular Research Group is part of the Cooperative Cerebrovascular Disease Research Network (INVICTUS+) (RD16/0019/0015).

Accepted:
25.01.23.

Conflict of interests:
The authors declare no conflict of interest.

Ethical aspects:
The study was conducted in accordance with the Declaration of Helsinki, and approved by our local ethics committee (ADM-SAS-2017/1773-N-17). Also, written informed consent has been obtained from the patient(s) to publish this paper.

How to cite this article:
Domínguez-Mayoral A, Gutiérrez C, Sánchez-Gómez J, Pérez-Sánchez S, Fouz N, Guerrero-Zamora P, et al. Benefits in quality of life following an obstructive sleep apnea screening and treatment program in patients with acute ischemic stroke. Rev Neurol 2023; 76: 117-25. doi: 10.33588/rn.7604.2022359.

Versión española disponible en www.neurologia.com

Patients and methods

Participants

This is a quasi-experimental study with time-series design. It was conducted at Virgen Macarena Stroke Unit during January 2018- June 2019. In the initial phase during 2018, an interventional study about OSA screening and treatment in patients with acute IS was made (intervention group). At the final phase of 2019, an observational study was made (control group).

We included consecutive patients with acute IS admitted to our Stroke Unit within < 72 hours of symptoms onset. Exclusion criteria were: baseline modified Rankin score (mRS) > 3, home oxygen therapy for any cause, upper airway tumours, significant neuromuscular and chest wall disorders, previous diagnosis of OSA, or need for high flow oxygen therapy owing to any disease. Another exclusion criteria were the presence of severe aphasia or cognitive impairment that, in the investigator's opinion, did not allow the administration of the SF-36 score to the patient. If there was severe agitation and the polygraphy was not possible, the patient was also excluded.

Losses during follow-up may be due to severe fatigue, revocation of informed consent, or patient death.

Stroke assessment at the acute phase

Diagnosis of stroke was confirmed by vascular neurologists based on a history of sudden onset of neurological deficit and a brain lesion on neuroimaging. The severity of stroke was assessed using a validated Spanish version of the National Institute of Health Stroke Scale (NIHSS) [13].

Study design and patient groups

Intervention group

Fifty-five consecutive cases of acute IS were included in this group. Each subject underwent polygraphy at the Stroke Unit made by trained staff and manually analyzed by specialized doctors. Polygraphy included recordings of airflow with a nasal cannula and thermistor, body position, snoring, oxygen saturation, heart rate, and respiratory effort [13]. Data were recorded with a validated multichannel digital polygraph (Sleep&Go, Sibelmed®, Spain). Only polygraphies with a total recording time > 4 hours were considered adequate [14]. Reasons of screening failure were: stroke mimic, clinical instability or agitation onset during sleep test, technical problems with polygraphy analysis software, or patient revocation.

Stroke patients with moderate and severe OSA were treated with CPAP. Mild OSA cases were treated with CPAP only if the patients had excessive daytime sleepiness or refractory hypertension [14,15]. Hoffstein's formula was used to calculate the initial CPAP pressure in each case [16]. Titration is only done in cases of residual symptoms or poor adaptation to CPAP [14,15]. Adherence was defined as a CPAP utilization for at least 4 h per night in more than 70% of the nights [14,15]. A chip inserted in the device registered the pressures, the residual REI, and the CPAP working time to assess adherence.

The hygienic-dietary measures applied in all OSA cases were: suspension of benzodiazepines drugs, weight and alcohol intake reduction and sleep in a lateral position.

Control group

Routine clinical practice was performed [17], so there was no intervention on OSA.

Clinical follow-up in both groups

The neurological follow-up at the sixth month after discharge was made by telephone interview in all cases. The degree of disability was classified by mRS score [12]. A validated Spanish version of SF-36 was used to assess the patient´s QOL [18]. Higher scores mean better quality of life [18]. Both scores have been validated by telephone administration [19,20].

The main endpoint was the results of the SF-36 at the sixth month after discharge. Secondary outcomes were the median of mRS and the percentage of patients with mRS ≤ 2 at the sixth month after discharge.

Statistical analysis

Mann-Whitney's U and Pearson's or Chi-Squared tests were performed to identify statistically significant differences between groups. Kruskal-Wallis rank test was used to determine if there are staticsally differences between two or more groups. A per-protocol and intention-to-treat analysis of the main end-point has been included. Binary logistic regression analysis was used to determine the influence of the clinical variables on the SF-36 score. All p values were 2-sided. A $p < 0.05$ was considered statistically significant. For a two-tailed hypothesis,

the recommended sample size was 55 in the intervention group and 62 in the control group. Results were presented as estimates with 95% confidence intervals. All statistical analyses were performed using the SPSS software package version 25.0 for Windows (IBM Corporation, Armonk, New York) and R 4.0.3.

Results

Study population

A total of 202 patients were invited to participate (Fig. 1). The causes of death in the intervention group were: a traffic accident due to drowsiness, an acute myocardial infarction and a pneumonia. All of these patients had severe OSA with poor adherence to CPAP. Deaths were not detected in the control group.

Due to the lack of funding for this study and the high care burden in our area, the sample size has been reduced. The baseline characteristics of both groups are similar (Table I).

In the intervention group, 89% of patients had OSA. Among OSA patients in the intervention group, the severe grade was observed in 47.8% and the rest of them have a mild or moderate grade. CPAP was indicated in 47 patients (85.5% of cases in the intervention group). CPAP was refused in 18 patients (38.3% of cases with indication) due to previous conceptions about the therapy discomfort despite the adequate medical information. A good CPAP adherence was achieved in 16 patients (34% of cases with indication).

The results of polygraphies in the intervention group were showed in figure 2.

Primary endpoint: quality of life (SF-36)

At the main endpoint, a significant difference (p < 0.05) was detected in 6 of 8 domains on the SF-36 scale (Fig. 3) at the sixth month after the IS.

All items´ results except social functioning and mental health were better in the patients of the intervention group than in the control cohort. The percentage of patients with physical component ≥ 50 was 38.18% in the intervention (Table II) vs. 14.5% in the control group (odds ratio 3.637; 95% confidence interval 1.491-8.873; p = 0.003).

An intention-to-treat and a per-protocol analysis of QOL results are represented in table II.

Differences between the intervention and control group in the physical and mental component summatory of the SF-36 score are illustrated in figure 4.

On the univariate analysis of the whole sample, age ≥ 70, male sex, and mRS ≤ 2 at the sixth month after the stroke was related to a good physical component QOL (p < 0.001 in all cases). An association between the percentage of patients with physical component ≥ 50 and male sex (90% vs. 55.2%, p = 0.005), age ≥ 70 years (30% vs. 67.8%, p = 0.006), and mRS ≤ 2 at the sixth month (96.7% vs. 63.2%,

Figure 1. Diagram of patient selection for the study.

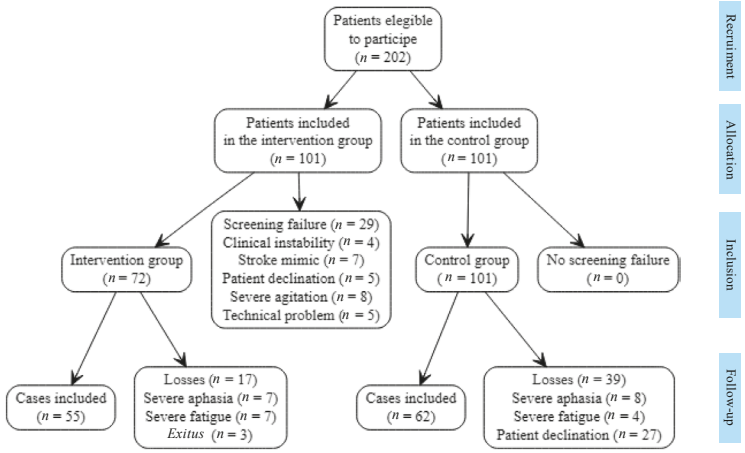
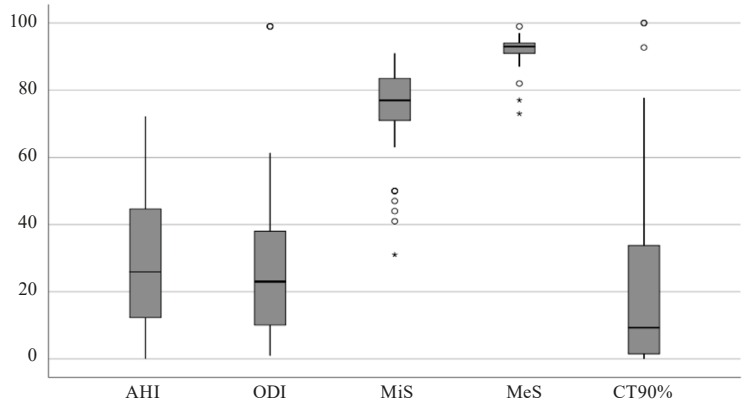


Figure 2. Box-and-whisker plot of sleep parameters in the intervention group. The box is drawn from Q1 (quartile) to Q3 with a horizontal line drawn in the middle to denote the median. All other observed points are plotted as outliers. Open circles represent individual outliers and asterisks denote far-out.



AHI: apnea-hypopnea index; CT90: the percentage of study time in which the patient remains with an oxygen saturation < 90%; MeS: mean oxygen saturation; MiS: minimum oxygen saturation; ODI: oxygen desaturation index –the average number of desaturation episodes (a decrease in the mean oxygen saturation of ≥3% that lasts for at least 10 seconds)–.

Table I. Baseline characteristics of the intervention and control group.

	Total 117 (100%)	Intervention 55 (47%)	Control 62 (53%)	df	χ^2	Z	U	*p*
Age, median IQR)	72 (14)	70 (14)	72 (15)			–0.265	1.656	0.791[b]
Female sex, *n* (%)	42 (35.9)	16 (29.1)	26 (41.9)	1	2.09			0.148[a]
Diabetes, *n* (%)	33 (28.2)	17 (30.9)	16 (25.8)	1	0.375			0.54[a]
Dyslipidemia, *n* (%)	38 (32.5)	16 (29.1)	22 (35.5)	1	0.543			0.461[a]
Hypertension, *n* (%)	82 (70.1)	36 (65.5)	46 (74.2)	1	1.062			0.33[a]
Basal atrial fibrillation, *n* (%)	17 (14.5)	7 (12.7)	10 (16.1)	1	0.272			0.62[a]
Ischemic cardiomyopathy, *n* (%)	15 (12.8)	8 (14.5)	7 (11.3)	1	0.276			0.599[a]
Limb arteriopathy, *n* (%)	7 (6.0)	4 (7.3)	3 (4.8)	1	0.307			0.75[a]
Previous stroke, *n* (%)	24 (20.5)	12 (21.8)	12 (19.4)	1	0.108			0.742[a]
Smokers, *n* (%)	24 (20.5)	14 (25.5)	10 (16.1)	1	1.555			0.212[a]
Benzodiazepines intake in the last three months, *n* (%)	21 (17.9)	13 (23.6)	8 (12.9)	1	2.28			0.131[a]
Opioids intake in the last three months, *n* (%)	9 (7.7)	8 (14.5)	1 (1.6)	1	6.865			0.012[a]
Facial palsy, *n* (%)	65 (55.6)	28 (50.9)	37 (59.7)	1	0.908			0.341[a]
Baseline NIHSS, median (IQR)		4 (4)	5 (5)			–0.746	1.569	0.456[b]
Large vessel occlusion, *n* (%)	34 (29.1)	16 (29.1)	18 (29)	1	0			0.994[a]
Hyperacute endovascular treatment, *n* (%)	21 (17.9)	8 (14.5)	13 (21)	1	0.816			0.366[a]
Thrombolysis, *n* (%)	18 (15.4)	10 (18.2)	8 (12.9)	1	0.624			0.43[a]

df: degrees of freedom; IQR: Interquartile range. [a] Chi-Squared test, [b] Mann-Whitney U test.

p = 0.014) was also verified on the multivariate analysis (Table III).

Secondary endpoint: disability (mRS)

The median of the mRS at the sixth month after discharge was 1 in the whole sample and differences among groups were not detected (p = 0.262).

Discussion

Many studies have suggested that OSA is associated with hypoxia and changes in cerebral hemodynamics, affecting QOL after stroke [6]. However, an improvement in QOL after an OSA intervention in stroke patients has not been verified until now [21].

Our study also found that the patients´ physical domain of QOL is significantly higher in the intervention group, particularly in patients who have good adherence to CPAP. However, the patient's mental QOL did not show significant improvement. This is consistent with previous reports [22].

Multivariate analysis of the whole sample suggests that male sex, younger ages, and mRS ≤ 2 at the sixth month after AIS are factors associated with good physical QOL. Previous reports observe that age is closely related to the improvement of QOL [10,11]. Functional status measured by mRS has also been established as an independent deter-

Table II. An Intention-to-treat and a per protocol analysis of quality of life results.

A per protocol analysis *n* (%)	Total 117 (100%)	A 16 (13.7%)	B 39 (33.3)	Control 62 (53%)	df	H	*p*
Physical functioning, median (IQR)	65 (50)	85 (37)	75 (40)	57.5 (50)	2	7.352	0.025
Role physical, median (IQR)	25 (100)	75 (94)	25 (75)	0 (75)	2	9.976	0.007
Bodily pain, median (IQR)	72 (44)	87 (24)	84 (29)	62 (49)	2	7.304	0.026
General health, median (IQR)	67 (34)	82 (28)	72 (37)	60 (32)	2	14.411	0.001
Vitality, median (IQR)	60 (35)	70 (24)	65 (25)	50 (31)	2	11.604	0.003
Social functioning, median (IQR)	75 (63)	87.5 (53.1)	75 (50)	81.2 (53)	2	2.086	0.352
Role emotional, median (IQR)	33.3 (100)	100 (91.6)	100 (100)	0 (100)	2	6.039	0.049
Mental health, median (IQR)	60 (17)	57.5 (10)	60 (10)	60 (32)	2	0.994	0.608
Physical component summatory, median (IQR)	42.9 (17.8)	49.4 (22.8)	47.2 (19.1)	37.8 (13.9)	2	16.935	0
Mental component summatory, median (IQR)	60 (22.8)	50.5 (14.2)	52.9 (21.1)	67.1 (21.9)	2	13.160	0.001
An intention to treat analysis *n* (%)	**Total** 117 (100%)	**A** 29 (24.8%)	**B** 26 (22.2)	**Control** 62 (53%)	**df**	**H**	***p***
Physical functioning, median (IQR)	65 (50)	29 (24.8)	26 (22.2)	57.5 (50)	2	8.894	0.012
Role physical, median (IQR)	25 (100)	85 (35)	65 (49)	0 (75)	2	9.781	0.008
Bodily pain, median (IQR)	72 (44)	25 (75)	50 (81)	62 (49)	2	7.129	0.028
General health, median (IQR)	67 (34)	90 (29)	82 (29)	60 (32)	2	15.513	0
Vitality, median (IQR)	60 (35)	77 (26)	72 (47)	50 (31)	2	11.589	0.003
Social functioning, median (IQR)	75 (63)	70 (30)	65 (22)	81.2 (53)	2	3.764	0.152
Role emotional, median (IQR)	33.3 (100)	87.5 (43.7)	56.2 (50)	0 (100)	2	5.902	0.052
Mental health, median (IQR)	60 (17)	100 (100)	100 (100)	60 (32)	2	0.709	0.702
Physical component summatory, median (IQR)	42.9 (17.8)	60 (10)	60 (10)	37.8 (13.9)	2	17.236	0
Mental component summatory, median (IQR)	60 (22.8)	48.9 (19.4)	47.1 (18.8)	67.1 (21.9)	2	13.07	0.001

A: patients of the intervention group treated with CPAP with a good adherence; B: patients of the intervention group treated with CPAP with a poor adherence + patients who refused CPAP + patients who had no indication of CPAP; C: patients of the interventiongroup treated with CPAP (good and bad adherence); D: patients of the intervention group who have refused CPAP + patients who had no indication for CPAP; df: degrees of freedom; IQR: interquartile range. Kruskall-Wallis H test.

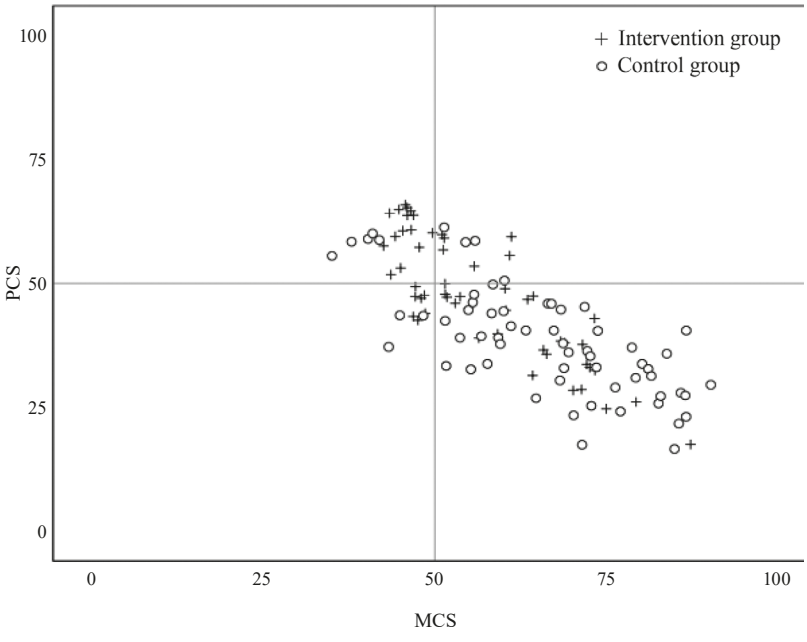
minant of poor QOL [10,11]. Some factors related to QOL including gender are described previously in IS [23].

The intention to treat analysis has shown that, in our study, patients treated with CPAP, particularly with good adherence, have a better QOL. These findings support our hypothesis about the potential benefits in QOL of an OSA intervention in IS. We consider that our results may even be underestimated. The main reasons would be the poor CPAP adherence in our area (34%) and the small sample size in this analysis. Similar rates of lower adher-

Figure 3. SF-36 quality of life score results among stroke patients according to whether they belong to the intervention or control group. Patients of the intervention group had higher scores in six of the eight SF-36 domains (p <0.05). The green squares represent the intervention group. The red circles represent the control group.

BP: bodily pain; ERF: emotional role functioning; GHP: general health perceptions; MH: mental health; PF: physical functioning; PRF: physical role functioning; SRF; social role functioning; VIT: vitality.

Figure 4. Differences between intervention and control group in the physical (PCS) and mental (MCS) component summatory of the SF-36 score.



ence to CPAP in socioeconomically disadvantaged areas and patients with comorbidities have been described [23]. The so-called Spanish stroke belt, where this study has been conducted, is one of these disadvantaged areas [24]. Despite the poor CPAP adherence of our patients, this treatment may have been sufficient to explain partially the improvement in QOL. The mechanisms by which CPAP may improve QOL and boost rehabilitation are not clear. CPAP-induced abolition of intermittent hypoxia and negative intrathoracic pressure swings should increase cerebral blood flow and oxygen delivery [25]. Morever, another OSA interventions such as suspension of benzodiazepines drugs, weight and alcohol intake reduction, and the advice to sleep in a lateral position, may also boost QOL improvements.

Regarding the secondary objective of our study, a relation between clinical recovery and an OSA intervention has not been observed. One explanation could be that mRS score, our secondary end-point, may not be sufficiently sensitive to detect small changes [12]. In fact, this scale has been questioned for the low sensitivity in minor strokes [12]. Morever, factors such as comorbidities and socioeconomic status could influence the mRS results [12]. In addition, the reduced sample size may also limit the study power. A randomized trial using another scores demonstrated that OSA treatment was associated with significant improvements in functional outcomes in IS [26]. Accordingly, improvements in the CPAP-treated group may have been attributable to an alleviation of the adverse cerebrovascular effects of OSA, possibly through enhanced neuroplasticity [25].

From a prognostic standpoint, there are controversial results about the relationships between OSA and stroke evolution. The most widespread hypothesis relates the presence of OSA with a poor prognosis [26-28]. Untreated OSA has been associated with incident and recurrent ischemic stroke and a higher long-term mortality [26-29]. By contrast, the minority hypothesis defends that the presence of OSA does not affect the stroke prognosis [30].

The effect of CPAP treatment on the incidence of vascular events is an issue that continues to arouse great controversy after the negative results of the last clinical trial [31]. However, these results are dependent on: the study methodology, the CPAP adherence, the type of vascular event, and the target population [32]. Many authors suggest the need to change the trial design [31]. A recent meta-analysis was designed to assess the effect of adequate CPAP treatment (at least 4 hours per day)

Table III. Factors associated with physical component and mental component summary (PCS and MC, respectively) results of the SF-36 score in the whole sample.

				Univariate analysis		Multivariate analysis	
n (%)	Total 117 (100%)	PCS ≥ 50 30 (25.6)	PCS < 50 87 (74.4)	OR (95% CI)	*p*	OR (95% CI)	*p*
Male sex, *n* (%)	75 (64.1)	27 (90)	48 (55.2)	7.3 (2-25.9)	0.001	6.4 (1.7-24.5)	**0.006**
Age ≥ 70, *n* (%)	67 (57.3)	9 (30)	58 (66.7)	0.2 (0.08-0.5)	0	0.2 (0.1-0.7)	**0.01**
Opioids intake, *n* (%)	9 (7.7)	3 (10)	6 (6.9)	1.5 (0.3-6.4)	0.692		
Baseline mRS ≤ 2, *n* (%)	110 (94)	29 (96.7)	81 (93.1)	2.1 (0.2-18.6)	0.676		
Baseline NIHSS ≤ 3, *n* (%)	48 (41)	13 (43.3)	35 (40.2)	1.1 (0.4-2.6)	0.766		
Thrombolysis, *n* (%)	18 (15.4)	4 (13.3)	14 (16.1)	0.8 (0.2-2.6)	0.781		
Hyperacute endovascular treatment, *n* (%)	21 (17.9)	5 (16.7)	16 (18.4)	0.8 (0.2-2.6)	0.832		
mRS 6m ≤ 2, *n* (%)	84 (71.8)	29 (96.7)	55 (63.2)	16.8 (2.1-129.8)	0	13.4 (1.6-108.6)	**0.015**
n (%)	Total 117 (100%)	MCS ≥ 50 87 (74.4)	MCS < 50 30 (25.6)	OR (95% CI)	*p*	OR (95% CI)	*p*
Male sex, *n* (%)	75 (64.1)	87 (74.4)	30 (25.6)	0.2 (0.09-0.7)	0.011	0.3 (0.1-0.9)	**0.044**
Age ≥ 70, *n* (%)	67 (57.3)	50 (57.5)	25 (83.3)	3.8 (1.5-9.1)	0.002	3 (1.2-7.5)	**0.019**
Opioids intake, *n* (%)	9 (7.7)	57 (65.5)	10 (33.3)	2.9 (0.3-24.5)	0.444		
Baseline mRS ≤ 2, *n* (%)	110 (94)	8 (9.2)	1 (3.3)	0.4 (0.05-4)	0.676		
Baseline NIHSS ≤ 3, *n* (%)	48 (41)	81 (93.1)	29 (96.7)	1.2 (0.5-3)	0.574		
Thrombolysis, *n* (%)	18 (15.4)	37 (42.5)	11 (36.7)	0.8 (0.2-2.7)	0.821		
Hyperacute endovascular treatment, *n* (%)	21 (17.9)	13 (14.9)	5 (16.7)	1.5 (0.4-5.1)	0.445		
mRS 6m ≤ 2, *n* (%)	84 (71.8)	17 (19.5)	4 (13.3)	0.2 (0.05-0.7)	0.01	0.2 (0.07-1.04)	0.058

CI: confidence interval; mRS 6 m: modified Rankin Score at the sixth month after the stroke; NIHSS: National Institute of Health Stroke Scale; OR: odds ratio.

on major adverse cerebrovascular and cardiovascular events based on per-protocol population of randomized control trials [33]. These results show for the first time that an adequate use of CPAP is associated with clinically meaningful improvements in major adverse vascular events [34]. This CPAP effect has a more significant impact on the cerebrovascular system than on cardiac consequences [34-35].

An improvement in survival in stroke patients treated with CPAP compared to usual care was found in a long-term follow-up study [36], so it would be interesting to analyze this endpoint in future trials.

Strengths and limitations

Using quasi-experimental designs minimizes threats to ecological validity as our real-life sample reflects. In fact, the representativeness of our sample is the greatest strength of the study.

There are some limitations. First, the level of evidence of this quasi-experimental study is limited by the single-center recruitment and the lack of a contemporaneous control group. Placebo CPAP was not performed because of ethical considerations. Second, the OSA prevalence could be underestimated in the intervention group because some patients with respiratory effort-related arousals may have false negative results of polygraphy. Third, benzodiazepines and opioids treatments were withdrawn after the study inclusion, so the interaction with the REI results in the intervention group could exist, but minimally, taking into account the half-life of these drugs. Fourth, there was a problem of missing data regarding the body mass index, so differences between the two groups could exist, but minimally, due to the homogeneity of the groups in the rest of the parameters. Fifth, the applicability of these interventions may be limited in those areas where the OSA prevalence is lower. Finally, the existence of another confounding factors, in addition of our intervention, that influence QOL cannot be ruled out.

Conclusions

This is the first real-life study in our country about the potential benefits in QOL of an OSA intervention in patients with IS. A new paradigm using more sensitive to change disability scores is needed.

References

1. Domínguez-Mayoral A, Sánchez-Gómez J, Guerrero P, Ferrer M, Gutiérrez C, Aguilar M, et al. High prevalence of obstructive sleep apnea syndrome in Spain's Stroke Belt. J Inl Med Res 2021; 49: 1-13.
2. Sateia MJ. International classification of sleep disorders-third edition highlights and modifications. Chest 2014; 146: 1387-94.
3. Berry RB, Brooks R, Gamaldo C, Harding SM, Lloyd RM, Quan SF, et al. American Academy of Sleep Medicine (AASM) scoring manual updates for 2017 (version 2.4). J Clin Sleep Med 2017; 13: 665-6.
4. Loke YK, Brown JWL, Kwok CS, Niruban A, Myint PK. Association of obstructive sleep apnea with risk of serious cardiovascular events: systematic review and meta-analysis. Circ Cardiovasc Qual Outcomes 2012; 5: 720-8.
5. Redline S, Yenokyan G, Gottlieb DJ, Shahar E, O'Connor GT, Resnick HE, et al. Obstructive sleep apnea-hypopnea and incident stroke: the sleep heart health study. Am J Respir Crit Care Med 2010; 182: 269.
6. Mediano O, Lorenzi-Filho G, García-Río F. Obstructive sleep apnea and cardiovascular risk: from evidence to experience in cardiology. Rev Esp Cardiol 2018; 71.5: 323-6.
7. Fulk GD, Boyne P, Hauger M, Ghosh R, Romano S, Thomas J, et al. The impact of sleep disorders on functional recovery and participation following stroke: a systematic review and meta-analysis. Neurorehab Neural Repair 2020; 34: 1050-61.
8. Brill AK, Horvath T, Seiler A, Camilo M, Haynes AG, Ott SR, et al. CPAP as treatment of sleep apnea after stroke. Neurology 2018; 90: e1222-30.
9. Stevens D, Martins RT, Mukherjee S, Vakulin A. Post-stroke sleep-disordered breathing: pathophysiology and therapy options. Front Surg 2018; 5: 9.
10. Wang R, Langhammer B. Predictors of quality of life for chronic stroke survivors in relation to cultural differences: a literature review. Scand J Caring Sci 2018; 32: 502-14.
11. Meckenzie AE, Chang AM. Predictors of quality of life following stroke. Disabil Rehabil 2002; 24: 259-65.
12. Banks JL, Marotta CA. Outcomes validity and reliability of the Modified Rankin Scale: implications for stroke clinical trials. Stroke 2007; 38: 1091-6.
13. Montaner J, Álvarez-Sabín J. La escala de ictus del National Institute of Health (NIHSS) y su adaptación al español. Neurologia 2006; 21: 192-202.
14. Alcázar JD, Bujalance J, Campos-Rodríguez F, Capote F, Carmona C, Cordero P, et al. Documento de consenso sobre el síndrome de apneas-hipopneas del sueño en Andalucía. Rev Esp Patol Torac 2012; 24: 214-54.
15. Lloberes P, Durán-Cantolla J, Martínez-García MÁ, Marín JM, Ferrer A, Corral J, et al. Diagnosis and treatment of sleep apnea-hypopnea syndrome. Arch Bronconeumol 2011; 47: 143-56.
16. Hoffstein V, Mateika S. Predicting nasal continuous positive airway pressure. Am J Respir Crit Care Med 2011; 150: 486-8.
17. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2019; 50: e344-418.
18. Alonso J, Prieto L, Anto JM. La versión española del SF-36 Health Survey (Cuestionario de Salud SF-36): un instrumento para la medida de los resultados clínicos. Med Clin (Barc) 1995; 104: 771-6.
19. Watson EK, Firman DW, Baade PD, Ring I. Telephone administration of the SF-36 health survey: validation studies and population norms for adults in Queensland. Aust N Z J Public Health 1996; 20: 359-63.
20. Savio K, Della Pietra GL, Oddone E, Reggiani M, Leone MA. Reliability of the Modified Rankin Scale Applied by telephone. Neurol Int 2013; 5: 6-7.
21. Parra O, Sánchez-Armengol A, Bonnin M, Arboix A, Campos-Rodríguez F, Pérez-Ronchel J, et al. Early treatment of obstructive apnoea and stroke outcome: a randomized controlled trial. Eur Respir J 2011; 37: 1128-36.
22. Chen Q, Cao C, Gong L, Zhang Y. Health related quality of life in stroke patients and risk factors associated with patients for return to work. Medicine (Baltimore). 2019; 98: e15130.
23. Wickwire EM, Jobe SL, Oldstone LM, Sharf SM, Jhonson AM, Albrecht JS. Lower socioeconomic status and co-morbid contidions are associated with reduce CPAP aderehence use among older adult Medicare beneficiaries with obstructive sleep apnea. Sleep 2020; 43: zsaa122.
24. Cayuela A, Cayuela L, Rodríguez-Domínguez S, González A, Moniche F. Analysis of cerebrovascular disease mortality trends in Andalusia (1980-2014). Neurologia 2019; 34: 309-17.
25. Ryan CM, Bayley M, Green R, Murray BJ, Bradley TD. Influence of continuous positive airway pressure on outcomes of rehabilitation in stroke patients with obstructive sleep apnea. Stroke 2011; 42: 1062-7.
26. Brown DL, Shafie-Khorassani F, Kim S, Chervin RD, Case E, Morgenstern LB, et al. Sleep-disordered breathing is associated with recurrent ischemic stroke. Stroke. 2019; 50: 571-6.
27. Menon D, Sukumaran S, Varma R, Radhakrishnan A. Impact of obstructive sleep apnea on neurological recovery after ischemic stroke: A prospective study. Acta Neurol Scand 2017; 136: 419-6.

28. Parra O, Arboix A, Bechich S, García-Eroles L, Montserrat JM, López JA, et al. Time course of sleep-related breathing disorders in first-ever stroke or transient ischemic attack. Am J Respir Crit Care Med. 2000; 161: 375-80.
29. Catalan-Serra P, Campos-Rodriguez F, Reyes-Nuñez N, Selma-Ferrer MJ, Navarro-Soriano C, Ballester-Canelles M, et al. Increased incidence of stroke, but not coronary heart disease, in elderly patients with sleep apnea: Role of continuous positive airway pressure treatment. Stroke 2019; 50: 491-4.
30. Lefevre-Dognin C, Stana L, Jousse M, Lucas C, Sportouch P, Bradai N, et al. Lack of repercussions of sleep apnea syndrome on recovery and attention disorders at the subacute stage after stroke: a study of 45 patients. Ann Phys Rehabil Med 2014; 57: 618-28.
31. McEvoy RD, Antic NA, Heeley E, Luo Y, Ou Q, Zhang X, et al. CPAP for prevention of cardiovascular events in obstructive sleep apnea. N Engl J Med 2016; 375: 919-31.
32. Navarro-Soriano C, Martínez-García MA, Torres F, Barbé F, Sánchez-de-la-Torre M, Caballero-Eraso C, et al. Long-term effect of CPAP treatment on cardiovascular events in patients with resistant hypertension and sleep apnea. Data from the HIPARCO-2 study. Arch Bronconeumol 2020; 56: 1-7.
33. Javaheri S, Martinez-Garcia MA, Campos-Rodriguez F. CPAP treatment and cardiovascular prevention: we need to change our trial designs and implementation. Chest 2019; 156: 431-7.
34. Javaheri S, Martinez-Garcia MA, Campos-Rodriguez F, Muriel A, Peker Y. Continuous positive airway pressure adherence for prevention of major adverse cerebrovascular and cardiovascular events in obstructive sleep apnea. Am J Respir Crit Care Med 2020; 201: 607-10.
35. Navarro-Soriano C, Martínez-García MA, Torres F, Barbé F, Sánchez-de-la-Torre M, Caballero-Eraso C, et al. Long-term effect of CPAP treatment on cardiovascular events in patients with resistant hypertension and sleep apnea. Data From the HIPARCO-2 Study. Arch Bronconeumol 2021; 57: 165-71.
36. Parra O, Sánchez-Armengol Á, Capote F, Bonnin M, Arboix A, Campos-Rodríguez F, et al. Efficacy of continuous positive airwaypressure treatment on 5-year survival in patients with ischaemic stroke and obstructive sleep apnea: a randomized controlled trial. J Sleep Res 2015; 24: 47-53.

Beneficios en la calidad de vida de un programa de cribado y tratamiento de apnea obstructiva del sueño en pacientes con ictus isquémico agudo

Introducción. La apnea obstructiva del sueño (AOS) se ha propuesto como un factor de mal pronóstico en el ictus. Pretendemos determinar si una intervención sobre la AOS puede mejorar las escalas de calidad de vida (primer objetivo) y de discapacidad (segundo objetivo).

Pacientes y métodos. El grupo de intervención de este estudio cuasi experimental incluye a pacientes con ictus isquémico agudo < 72 horas de evolución a quienes se les realizó poligrafía, así como presión positiva continua en las vías aéreas (CPAP) y medidas higienicodietéticas si se requerían. En el grupo de control se siguió la práctica clínica habitual. Se aplicaron las escalas *Short Form 36 Health Survey* (SF-36) y *modified Rankin Score* (mRS) en el sexto mes del ictus en ambos grupos.

Resultados. Se incluyó a 55 y a 62 pacientes en el grupo de intervención y en el de control, respectivamente. En el grupo de intervención, el 64,71% de los pacientes aceptó la CPAP indicada (16 casos con buena adhesión). Se detectó una mejoría en los ítems de la escala SF-36 en el grupo de intervención: funcionamiento físico (p = 0,008), rol físico (p = 0,002), dolor corporal (p = 0,008), salud general (p < 0,001), vitalidad (p = 0,001) y rol emocional (p = 0,015). En un análisis por protocolo, todas estas mejorías se comprobaron en el grupo de pacientes tratados con CPAP con buena adhesión (p < 0,05 en todos los ítems de la SF-36). El porcentaje de pacientes con el sumatorio del componente físico ≥ 50 fue más alto en el grupo de intervención (p = 0,003). No había diferencias en la mediana de la mRS (p = 0,262).

Conclusiones. Aunque se necesitan más evidencias, nuestro estudio sugiere una mejoría significativa de la calidad de vida tras nuestra intervención en la AOS, especialmente en pacientes con buena adhesión a la CPAP.

Palabras clave. Apnea del sueño. Calidad de vida. Cribado. Escala SF-36. Ictus. Presión positiva continua en las vías aéreas (CPAP).