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EDITORIAL

Stroke and sleep-disordered breathing: A relationship under construction

Olga Parra, Adrià Arboix

Olga Parra, Service of Pneumology, Hospital Universitari del Sagrat Cor, University of Barcelona, E-08029 Barcelona, Spain

Adrià Arboix, Cerebrovascular Division, Service of Neurology, University of Barcelona, Hospital del Sagrat Cor, E-08029 Barcelona, Spain

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Correspondence to: Adrià Arboix, MD, PhD, Cerebrovascular Division, Service of Neurology, University of Barcelona, Hospital del Sagrat Cor, C/ Viladomat 288, E-08029 Barcelona, Spain. aarboix@hscor.com
Telephone: +34-93-4948940
Fax: +34-93-4948906

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Abstract

The association between sleep-disordered breathing (SDB) and cardiovascular risk has been the focus of attention in recent years. Sleep disorders are emerging risk factors for cardiovascular disease and have been related to the whole spectrum of stroke, including transient ischemic attack, ischemic cerebral infarction and intracerebral haemorrhage. It has been shown that lacunar stroke or lacunar infarctions affecting the internal capsule or the protuberance are associated with a higher frequency of SDB. Acute stroke patients with associated SDB have a worse prognosis and a higher mortality as compared to patients with first-ever stroke without SDB. Preliminary studies provide evidence of the usefulness of treatment with continuous positive airway pressure when SDB is present in stroke patients.

Key words: Apnea-hypopnea index; Cardiovascular risk factors; Continuous positive airway pressure; Ischemic stroke; Lacunar infarction; Sleep disordered

Core tip: Sleep disorders including obstructive sleep apnea are associated with an increased risk for a number of cardiovascular diseases, notably acute cerebrovascular events. A number of studies have shown a high prevalence of sleep-related breathing disorders in patients with stroke. A decrease in cerebral perfusion and increased coagulability related to metabolic, hematological and hemodynamic changes occuring in the presence of sleep-related breathing disorders are proposed as potential mechanisms in the pathogenesis of stroke. Early diagnosis and prompt therapeutic measures, including continuous positive airway pressure are necessary to reduce the stroke risk associated with sleep disorders. Sleep-related breating disorders should be considered modifiable risk factors for stroke, although they are frequenty underdiagnosed. The relationship between sleep breathing disorders and stroke should be further investigated for improving primary and secondary stroke prevention strategies and to contribute to reduce the global burden of stroke.

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INTRODUCTION

Sleep-disordered breathing (SDB) and stroke, a relationship story that from our point of view is a sort of story not yet ended, since as we shall see, is still under construction.

One of the first reports from the Sleep Heart Health Study[1] postulated an association of SDB with cardiovascular disease. A total of 6424 subjects were included in a cross-sectional study and underwent fully polysomnography at home. Sixteen percent reported at least one manifestation of cardiovascular disease, such as heart failure, angina, myocardial infarction, stroke or revascularization procedure. Considering upper *vs* lower apnea-hypopnea index (AHI) quartile, SDB was associated more strongly with heart failure (OR = 2.38, 95%CI: 1.22-4.62) and stroke (OR = 1.58, 95%CI: 1.02-2.46) than with coronary heart disease (OR = 1.27, 95%CI: 0.99-1.62). Therefore, this study shows that the effects of SDB were compatible with heterogeneous manifestations of cardiovascular disease, including stroke. Later on, other studies, among which the publication of Marin *et al*[2] has been probably one of the most cited, showed that the presence of SDB was related with an increase in cardiovascular morbidity and mortality especially when obstructive apnea was not treated with nasal continuous positive airway pressure (CPAP). Moreover, in a systematic review of the interaction of cardiovascular pathophysiology and obstructive sleep apnea, several of the mechanisms identified (sleep fragmentation, increased oxidative stress, metabolic dysregulation, increased sympathetic activation, increased platelet aggregability and vascular endothelial dysfunction) were described as possible explanations for implicating obstructive sleep apnea in the pathogenesis of hypertension and also as a contributing factor to stroke and cerebrovascular disease[3]. Much research has been done dealing with the association of SDB with hypertension and cardiac diseases, but there are fewer data regarding the relationship with stroke.

We here present an overview of salient findings regarding different aspects of the relationship between SDB and stroke, including SDB frequency, SDB types and clinical presentation, SDB as a risk factor for stroke and SDB as a prognostic factor for stroke, as well as treatment options in patients with SDB. Data here presented is based on a selective review of the literature of the most relevant publications that according to the author's criteria are of the interest of the readers. This information is presented together with data related to the experience of our group in the management of stroke patients with SDB.

A meta-analysis of the frequency of sleep apnea in patients with stroke and transient ischemic attack (TIA), which included 29 studies with 2343 patients, found that SDB was present in 71.4% of patients for AHI > 5 and in 14% for AHI > 40[4]. Also, the percentage of patients with AHI > 10 was higher among patients with recurrent stroke as compared to patients with first-ever stroke (73% *vs* 57%, P = 0.013) as well as in males than females (65% *vs* 48%, P = 0.001). Interestingly, patients with stroke of unknown cause (undetermined stroke) showed the highest incidence of SDB, confirming that SDB influences cerebrovascular events beyond its association with traditional cardiovascular risk factors. The findings of this meta-analysis support the need for screening for SDB in all TIA and stroke patients[4].

In a prospective study of 161 patients admitted to our stroke unit undergoing a portable respiratory recording study within 48-72 h after admission, AHI > 10 was recorded in 71.4% of cases and AHI > 30 in 28% (Table 1)[5]. In relation to the type of events and their clinical presentation, any types of respiratory events were observed, including obstructive, mixed and central apneas as well as Cheyne-Stokes (CS) breathing pattern. CS respiration was present in 26% of the patients. Differences in the percentage of patients with AHI > 10 and AHI > 30, which can be considered a severe sleep apnea, in relation to the different stroke subtypes (TIA, ischemic and hemorrhagic stroke) were not found. On the other hand, patients were neither obese nor had daytime somnolence according to results of the Epworth Sleepiness Scale. Three months after the acute phase of stroke, there was a reduction of SDB, mainly due to a decrease in central respiratory events. These results, in some way, led us to hypothesize that most obstructive apnea events were previous to stroke (perhaps acting as a risk factor) and that central obstructive events and CS respiration were secondary to stroke[5].

In this previous study, a correlation between the presence of SDB and the topography of stroke could not be established given that lesions were often too large and involved different cerebral areas. For this reason, we examined the occurrence of SDB in patients with lacunar stroke. Lacunar stroke is characterized by small, localized brain ischemic lesions with a maximum diameter smaller than 20 mm found in the blood supply of a penetrating arteriole, affecting different subcortical topographies[6,7]. In a clinical series of 68 patients with proven lacunar infarction, SDB was frequent, with 69% of patients showing AHI $\geqslant$ 10, 44% AHI $\geqslant$ 20, and 25% AHI $\geqslant$ 30. Variables independently associated with SDB were determined by logistic regression analysis. As shown in Table 2, smoking and topography of lacunes in the pons or the internal capsule were significant predictors of SDB. Body mass index was inversely associated with SDB. Therefore, smoker patients with capsular or pontine lacunar infarction should be screened for SDB[8]. Surprisingly, CS respiration was documented

Table 1 Sleep-related parameters in 161 consecutive patients with first-ever stroke included in the "Sagrat Cor Hospital of Barcelona Stroke Registry"[5]

Data	Transient ischemic attack (n = 39)	Ischemic stroke (n = 112)	Hemorrhagic stroke (n = 10)	Total (n = 161)
Age, yr, mean (SD)	67.9 (10.1)	72.5 (8.9)	73 (10.5)	72 (9)
Body mass index, kg/m^2, mean (SD)	27.3 (4.6)	26.2 (3.7)	26.7 (2.6)	26.6 (3.9)
Epworth sleepiness scale, score, mean (SD)	47 (3.3)	4.9 (3.3)	4.3 (2.1)	4.8 (3.3)
AHI, mean (SD)	19.4 (16.7)	21.5 (15.7)	25 (11.9)	21.2 (15.7)
OAI, mean (SD)	5.9 (10.2)	3.9 (7.8)	5.4 (6.7)	4.5 (8.4)
CAI, mean (SD)	3.32 (7.9)[a]	5.9 (10.1)	11.1 (15.1)[a]	5.6 (10.1)
Cheyne-Stokes breathing pattern, n (%)	8 (20.5)	31 (27.7)	3 (30)	42 (26.1)
AHI, n (%)				
> 10	24 (61.5)	83 (74.1)	9 (90)	116 (72)
> 30	10 (25.6)	31 (27.7)	4 (40)	45 (27.9)
CT90%, mean (SD)	8.2 (13.1)	8.1 (17.8)	5.7 (7.1)	7.8 (15.7)

CAI: Central apnea index; AHI: Apnea-hypopnea index; OAI: Obstructive apnea index; CT90%: Percentage of time below 90% arterial oxygen saturation; TIA: Transient ischemic attack. [a]P = 0.03 between CAI of TIA patients and CAI of patients with hemorrhagic stroke.

Table 2 Variables independently associated with different sleep-disordered breathing in a clinical series of 68 patients with first-ever lacunar infarction[8]

Model	β	SE (β)	OR (95%CI)	P value
AHI ⩾ 10				
Topography in the internal capsule or pons or smoking	1.153	0.576	3.17 (1.02-9.79)	0.045
AHI ⩾ 20				
Smoking and topography in the internal capsule or pons	2.225	1.111	9.25 (1.05-81.70)	0.045
AHI ⩾ 30				
Smoking	2.977	1.255	19.64 (1.68-229.85)	0.018
Body mass index	0.520	0.203	1.68 (1.13-2.50)	0.010

AHI: Apnea-hypopnea index; SE: Standard error.

in 20.6% of patients, which was in contrast with the previous idea that CS breathing pattern usually occurs in large strokes with unfavourable prognosis. Patients with CS respiration as compared with those without CS respiration showed higher AHI and central apnea index as well as higher scores of the Barthel index and the Canadian Neurological scale as a measure of stroke severity, and longer hospital stay[9].

But which are the evidences that we have about SDB being a risk factor for stroke? Two large cross-sectional studies, the Sleep Heart Health Study[1] and the Wisconsin Sleep Cohort Study[10] found an association between SDB and stroke, after adjusting for confounders and also a dose-response effect. Furthermore, longitudinal data of the Wisconsin Sleep Cohort showed a higher occurrence of stroke during a 4-year follow-up period in patients with high AHI, although statistical significance was not reached probably due to the low statistical power related to the sample size[10]. Further data from the Sleep Heart Health Study, with 5422 participants without a history of stroke at the baseline examination and untreated for sleep apnea followed for a median of 8.7 years, revealed that the adjusted hazard ratio increased with each one unit increase in obstructive AHI (OAHI). Patients with an AHI > 20 had a worse survival. In men, each one unit increase in OAHI was estimated to increase stroke risk by 6%[11]. In a meta-analysis of 17 prospective cohort studies to assess the effect of obstructive sleep apnea (OSA) on cardiovascular events, it was concluded that moderate to severe OSA increased significantly the risk of cardiovascular diseases, particularly stroke risk[12].

And what about SDB as a prognostic factor for stroke? In 1996, Good *et al*[13] already shown that arterial oxyhemoglobin desaturation (SaO_2) correlated with lower functional abilities as measured by the Barthel index at discharge and at 3 and 12 mo of follow-up. The study of Kaneko *et al*[14] in 2003, showed that patients with sleep apnea and stroke had lower functional capacity as compared to patients without sleep apnea, and also had longer periods of hospitalization and rehabilitation.

In our chort of 161 patients with TIA or a first-ever stroke followed over 2 years, AHI > 30 was an independent factor of poorer survival (Figure 1), with an implied 5% increase in mortality risk for each additional AHI unit[15]. Results of this study indicate that SDB may be considered an independent prognostic factor related to fatal outcome after a first stroke episode[15]. Similar results were obtained in other studies, in which the presence of OSA in stroke patients was associated with an increased risk of early death as compared to patients without OSA[16,17].

Most of the pathophysiological mechanisms described as being involved in the development of cardiovascular disease as a whole, could also be applied to stroke in

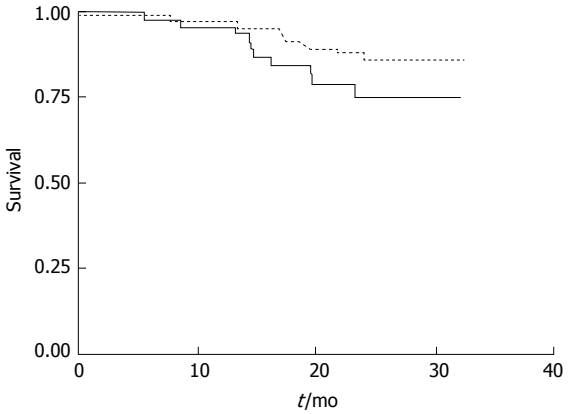

Figure 1 Kaplan-Meier survival estimates in patients with an apnea-hypopnea index < 30 (dash line) and in those with apnea-hypopnea index ⩾ 30 (solid line). Greater mortality in patients with an AHI above the cut-off value of 30. AHI: Apnea-hypopnea index.

particular. However, some more specific mechanisms have been identified in the cerebral circulation of patients with OSA. It has been shown that SDB could induce damage in the penumbra area (the area surrounding an ischemic event, which is at risk of progressing to infarction, but is still salvageable if re-perfused). Different mechanisms such as a decrease and variation in cerebral blood flow has been demonstrated using transcranial Doppler examination during apneas[18]. In this respect, Valipour *et al*[19] have observed decreases in cerebral oxygenation during apneas and hypopneas, which could also contribute to affect the penumbra area and impair prognosis.

The preceding paragraphs have shown that sleep disorders are more frequent in stroke, that they play a role as risk and prognostic factor in stroke patients, and that both disorders, SDB and stroke, are possibly linked by several underlying pathophysiological mechanisms. The next question to be answered is whether there is a rationale for treatment of SDB in stroke patients[20]. Nasal CPAP is an effective and safe method for OSA but its role in the management of SDB in stroke patients remains unclear. However, in relation to pathophysiological mechanisms, nasal CPAP has shown to be useful for decreasing platelet activation markers, soluble CD40 ligand (sCD40L) and soluble P-selectin (sP-selectin), in patients with moderate to severe OSA and silent brain infarction[21]. In another study, treatment with CPAP for 4 mo in patients with severe OSA who were free of comorbidities was associated with an improvement in early signs of atherosclerosis, with a reduction of carotid intima-media thickness, pulse-wave velocity, C-reactive protein and cetecholamines[22]. In addition, vascular response to hypoxia is diminished in patients with sleep apnea and can be also corrected with CPAP[23].

In a prospective observational study of ischemic stroke patients, those with an AHI ⩾ 20 who did not tolerate CPAP showed an increased risk of mortality compared to patients with moderate to severe OSA who tolerated CPAP[24]. However, no randomized controlled trials have been conducted to determine the value of CPAP treatment in stroke patients with SDB. For this reason, we designed a randomized controlled trial in which patients with ischemic stroke were assigned to early treatment with nasal CPAP (3-6 d after stroke onset) or conventional treatment[25]. The first learning from our study was that treating these patients with nasal CPAP in the acute stroke phase was feasible. The baseline characteristics of the 14 patients (19.7%) excluded from the study, because of refusal of nasal CPAP during hospitalisation were similar to those of the whole study population. The mean (SD) nasal CPAP use was 5.3 (1.9) h/night during a mean of 6.8 (0.6) nights/wk. The mean nasal CPAP pressure was 8.6 cm H_2O. A face mask was necessary in only four patients because of leaks, mainly due to facial palsy. The percentage of patients with neurological improvement 1 mo after stroke was significantly higher in the CPAP group than in controls (Rankin scale 90.9% *vs* 56.3%, OR = 5.8, $P < 0.01$; Canadian scale 88.2% *vs* 72.7%, OR = 2.8, $P < 0.05$). Early use of nasal CPAP seems to accelerate neurological recovery and to delay the appearance of cardiovascular events, although an improvement in patients' survival was not shown, perhaps because the follow-up period was not longer enough[25]. Therefore, the same group of patients was followed for a total of 5 years, and patients in the CPAP group had a higher survival free of cardiovascular events than controls[26]. Thus, we could suggest for the first time that early nasal CPAP therapy has some positive effect on long-term survival in patients with ischemic stroke and moderate-severe OSA[26].

The story of the relationship between SDB and stroke has not yet come to the end. There is sufficient evidence that this relationship makes sense and is going to be confirmed in future studies. However, for the present and future scenarios, pneumologists and neurologists especially those working in stroke units should work together to pursue in the establishment of a definitive relationship between sleep disorders and acute cerebrovascular events.

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REFERENCES

1 **Shahar E**, Whitney CW, Redline S, Lee ET, Newman AB, Nieto FJ, O'Connor GT, Boland LL, Schwartz JE, Samet JM. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. *Am J Respir Crit Care Med* 2001; **163**: 19-25 [PMID: 11208620 DOI: 10.1164/ajrccm.163.1.2001008]

2 **Marin JM**, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-

hypopnoea with or without treatment with continuous positive airway pressure: an observational study. *Lancet* 2005; **365**: 1046-1053 [PMID: 15781100 DOI: 10.1016/S0140-6736(05)71141-7]

3 **Shamsuzzaman AS**, Gersh BJ, Somers VK. Obstructive sleep apnea: implications for cardiac and vascular disease. *JAMA* 2003; **290**: 1906-1914 [PMID: 14532320 DOI: 10.1001/jama.290.14.1906]

4 **Johnson KG**, Johnson DC. Frequency of sleep apnea in stroke and TIA patients: a meta-analysis. *J Clin Sleep Med* 2010; **6**: 131-137 [PMID: 20411688]

5 **Parra O**, Arboix A, Bechich S, García-Eroles L, Montserrat JM, López JA, Ballester E, Guerra JM, Sopeña JJ. Time course of sleep-related breathing disorders in first-ever stroke or transient ischemic attack. *Am J Respir Crit Care Med* 2000; **161**: 375-380 [PMID: 10673174 DOI: 10.1164/ajrccm.161.2.9903139]

6 **Arboix A**, Martí-Vilalta JL. Lacunar stroke. *Expert Rev Neurother* 2009; **9**: 179-196 [PMID: 19210194 DOI: 10.1586/14737175.9.2.179]

7 **Arboix A**, Blanco-Rojas L, Martí-Vilalta JL. Advancements in understanding the mechanisms of symptomatic lacunar ischemic stroke: translation of knowledge to prevention strategies. *Expert Rev Neurother* 2014; **14**: 261-276 [PMID: 24490992 DOI: 10.1586/14737175.2014.884926]

8 **Bonnin-Vilaplana M**, Arboix A, Parra O, García-Eroles L, Montserrat JM, Massons J. Sleep-related breathing disorders in acute lacunar stroke. *J Neurol* 2009; **256**: 2036-2042 [PMID: 19629569 DOI: 10.1007/s00415-009-5236-x]

9 **Bonnin-Vilaplana M**, Arboix A, Parra O, García-Eroles L, Montserrat JM, Massons J. Cheyne-stokes respiration in patients with first-ever lacunar stroke. *Sleep Disord* 2012; **2012**: 257890 [PMID: 23471518 DOI: 10.1155/2012/257890]

10 **Arzt M**, Young T, Finn L, Skatrud JB, Bradley TD. Association of sleep-disordered breathing and the occurrence of stroke. *Am J Respir Crit Care Med* 2005; **172**: 1447-1451 [PMID: 16141444 DOI: 10.1164/rccm.200505-702OC]

11 **Redline S**, Yenokyan G, Gottlieb DJ, Shahar E, O'Connor GT, Resnick HE, Diener-West M, Sanders MH, Wolf PA, Geraghty EM, Ali T, Lebowitz M, Punjabi NM. Obstructive sleep apnea-hypopnea and incident stroke: the sleep heart health study. *Am J Respir Crit Care Med* 2010; **182**: 269-277 [PMID: 20339144 DOI: 10.1164/rccm.200911-1746OC]

12 **Dong JY**, Zhang YH, Qin LQ. Obstructive sleep apnea and cardiovascular risk: meta-analysis of prospective cohort studies. *Atherosclerosis* 2013; **229**: 489-495 [PMID: 23684511 DOI: 10.1016/j.atherosclerosis.2013.04.026]

13 **Good DC**, Henkle JQ, Gelber D, Welsh J, Verhulst S. Sleep-disordered breathing and poor functional outcome after stroke. *Stroke* 1996; **27**: 252-259 [PMID: 8571419]

14 **Kaneko Y**, Hajek VE, Zivanovic V, Raboud J, Bradley TD. Relationship of sleep apnea to functional capacity and length of hospitalization following stroke. *Sleep* 2003; **26**: 293-297 [PMID: 12749548]

15 **Parra O**, Arboix A, Montserrat JM, Quintó L, Bechich S, García-Eroles L. Sleep-related breathing disorders: impact on mortality of cerebrovascular disease. *Eur Respir J* 2004; **24**: 267-272 [PMID: 15332396 DOI: 10.1183/09031936.04.00061503]

16 **Yaggi HK**, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. *N Engl J Med* 2005; **353**: 2034-2041 [PMID: 16282178 DOI: 10.1056/NEJMoa043104]

17 **Sahlin C**, Sandberg O, Gustafson Y, Bucht G, Carlberg B, Stenlund H, Franklin KA. Obstructive sleep apnea is a risk factor for death in patients with stroke: a 10-year follow-up. *Arch Intern Med* 2008; **168**: 297-301 [PMID: 18268171 DOI: 10.1001/archinternmed.2007.70]

18 **Bålfors EM**, Franklin KA. Impairment of cerebral perfusion during obstructive sleep apneas. *Am J Respir Crit Care Med* 1994; **150**: 1587-1591 [PMID: 7952619 DOI: 10.1164/ajrccm.150.6.7952619]

19 **Valipour A**, McGown AD, Makker H, O'Sullivan C, Spiro SG. Some factors affecting cerebral tissue saturation during obstructive sleep apnoea. *Eur Respir J* 2002; **20**: 444-450 [PMID: 12212980 DOI: 10.1183/09031936.02.00265702]

20 **Parra O**. Sleep-disordered breathing and stroke: is there a rationale for treatment? *Eur Respir J* 2001; **18**: 619-622 [PMID: 11716164]

21 **Minoguchi K**, Yokoe T, Tazaki T, Minoguchi H, Oda N, Tanaka A, Yamamoto M, Ohta S, O'Donnell CP, Adachi M. Silent brain infarction and platelet activation in obstructive sleep apnea. *Am J Respir Crit Care Med* 2007; **175**: 612-617 [PMID: 17341649 DOI: 10.1164/rccm.200608-1141OC]

22 **Drager LF**, Bortolotto LA, Figueiredo AC, Krieger EM, Lorenzi GF. Effects of continuous positive airway pressure on early signs of atherosclerosis in obstructive sleep apnea. *Am J Respir Crit Care Med* 2007; **176**: 706-712 [PMID: 17556718 DOI: 10.1164/rccm.200703-500OC]

23 **Foster GE**, Hanly PJ, Ostrowski M, Poulin MJ. Effects of continuous positive airway pressure on cerebral vascular response to hypoxia in patients with obstructive sleep apnea. *Am J Respir Crit Care Med* 2007; **175**: 720-725 [PMID: 17218618 DOI: 10.1164/rccm.200609-1271OC]

24 **Martínez-García MA**, Soler-Cataluña JJ, Ejarque-Martínez L, Soriano Y, Román-Sánchez P, Illa FB, Canal JM, Durán-Cantolla J. Continuous positive airway pressure treatment reduces mortality in patients with ischemic stroke and obstructive sleep apnea: a 5-year follow-up study. *Am J Respir Crit Care Med* 2009; **180**: 36-41 [PMID: 19406983 DOI: 10.1164/rccm.200808-1341OC]

25 **Parra O**, Sánchez-Armengol A, Bonnin M, Arboix A, Campos-Rodríguez F, Pérez-Ronchel J, Durán-Cantolla J, de la Torre G, González Marcos JR, de la Peña M, Carmen Jiménez M, Masa F, Casado I, Luz Alonso M, Macarrón JL. Early treatment of obstructive apnoea and stroke outcome: a randomised controlled trial. *Eur Respir J* 2011; **37**: 1128-1136 [PMID: 20847081 DOI: 10.1183/09031936.00034410]

26 **Parra O**, Sánchez-Armengol Á, Capote F, Bonnin M, Arboix A, Campos-Rodríguez F, Pérez-Ronchel J, Durán-Cantolla J, Martínez-Null C, de la Peña M, Jiménez MC, Masa F, Casadon I, Alonso ML, Macarrón JL. Efficacy of continuous positive airway pressure 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 [PMID: 25040553 DOI: 10.1111/jsr.12181]

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