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Version 3

At 68 yrs, unrecognized sleep apnea is associated with elevated ambulatory blood pressure

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Abstract :

Background: After 65 years old, the specific impact of unrecognized sleep-related breathing disorders (SRBD) on 24-hour blood pressure (BP) levels remains still debated. We tested the cross-sectional relationship between the severity of obstructive sleep apnoea/hypopnea (OSAH) and the increase of BP measured with an ambulatory BP monitoring in the PROOF-SYNAPSE cohort.

Methods: 470 subjects (age: 68 years) neither treated for hypertension nor diagnosed for SRBD were included. They all underwent ambulatory blood pressure monitoring, (ABP) and unattended at-home polygraphic studies. OSAH was defined by an apnea plus hypopnea index (AHI) above 15/hour. The severity of sleep apnea was also quantified as the index of dips in oxyhemoglobin saturation > 3% (ODI). Results are expressed in per- protocol analysis.

Results: Severe OSAH (AHI>30/h, 17% of subjects) was associated with a significant 5 mmHg increase in both diurnal and nocturnal Systolic BP, and with a nocturnal 3 mmHg increase in Diastolic BP. Systolic (mean SBP>135 mmHg) or diastolic (mean DBP>80 mmHg) hypertension were more frequently encountered in subjects suffering from moderate (AHI:15-30) or severe OSAH. After adjustment, the independant association between severe OSAH and 24-hour systolic hypertension remained significant (OR 2.42; CI[1.1-5.4]). The relationship was further reinforced when SRBD severity was expressed using ODI>10/h.

Conclusion: The impact of unrecognized SRBD on blood pressure levels also exists at 68 years old. The hypoxemic load appears the pathophysiological cornerstone for such a relationship.

Key words: obstructive sleep apnoea/hypopnea, hypertension, ambulatory blood pressure, elderly

Introduction

Obstructive sleep apnea/hypopnea (OSAH) syndrome is an independent risk factor for diurnal hypertension[1,2] and has now been implicated as a risk factor of first or recurrent[3] stroke occurence as well as post-stroke mortality.[4,5] The amount of oxygen desaturation (hypoxemic load) associated with apneas has been recognized as the pathophysiological cornerstone for the development of hypertension,[6] via enhanced peripheral chemosensitivity,[7] sympathetic overactivity and of the early atherogenesis process associated with chronic intermittent hypoxia exposure.[8] However, sleep fragmentation or increased respiratory effort could also by itselves precipitate sympathetically-mediated hypertension.[9]

Thus, sleep-related breathing disorders (SRBD) are now established as a potential cause of secondary and resistant hypertension in middle age subjects.[10] In the elderly, the Sleep and Heart Health Study (SHHS) failed to demonstrate any significant association between SRBD and hypertension according to classical casual blood pressure (BP) measurements.[11] This lack of relationship in elderly is supported by the limited impact of OSAH syndrome on mortality in the elderly population[12] but can also be explained by the use of office BP measurement in the study.

The better diagnostic and prognostic value of ambulatory blood pressure levels (ABPM) compared to casual measurements has now been firmly establish.[13-16] From an epidemiological point of view, such methodology allows a better and more objective evaluation of the influence of a medical or environmental stress on blood pressure control. Using ABPM, several studies have already reported the high prevalence of previously ignored, and thus untreated, hypertension in patients addressed at the sleep laboratory for suspicion of OSAH syndrome. Nocturnal and diastolic hypertension are the most frequently encountered abnormalities.[17,18]

Thus, on the one hand, SRBD remain undiagnosed and untreated in a large majority of patients [19] and it could be postulated that a significant proportion of essential hypertension is related to the presence of occult OSAH.[17] On the other hand, the impact of unrecognized sleep apnea on 24-hour blood pressure has never been assessed in older subjects. This appears to be important as it is now admitted that the ability to reduce blood pressure is associated with a mortality and morbidity reduction even in older subjects.[20] Continuous positive airway pressure (CPAP) is the first line treatment for OSAH. Its impact on arterial blood pressure control is well documented in hypertensives as well as in normotensives OSAH patients, more

particularly during night.[21] Then, this ventilator support is usable in the elderly [22] and could participate to control arterial blood pressure in this population.

The aim of the present study was then to evaluate, in a prospective cohort of homogenous elderly population, the impact of undiagnosed OSAH on blood pressure levels by assessing unattented sleep apnea or hypertension with a ventilatory polygraphy and a 24-hour ABPM.

Material and methods

Population

The present sample was issued from the prospective observational PROOF-SYNAPSE cohort of 1011 subjects, all aged 65 years at inclusion. The initial study was designed to assess the prognostic value of autonomic nervous system activity and its decline along the years and how this impacts on cardiovascular and cerebrovascular morbidity and mortality.[23] The population was selected from the electoral list of the 65 years old inhabitants of the town of Saint-Etienne, France, in the year 2001. Exclusion criteria were previous myocardial infarction or stroke, heart failure, insulin-dependant diabetes mellitus, atrial fibrillation or anti-arrhythmic treatment, and a severe disease limiting life expectancy to less than 5 years. All subjects were evaluated under standardised conditions, described in the protocol of the Proof study that has been previously published.[23] Demographic characteristics included gender, age, smoking (past or current), body mass index (BMI, kg/m^2), waist and hip circumference, alcohol intake, glycemia and blood pressure measurements. Daytime sleepiness was assessed with the Epworth Sleepiness Scale (ESS) score. Both the PROOF and SYNAPSE studies were approved by the University Hospital and the IRB-IEC committee (CCPRB Rhône-Alpes Loire) and all subjects gave their written informed consent before participating.

854 subjects were reevaluated three years after inclusion (subject age: 68 years). At this step, subjects of the cohort considered as normotensive according to the absence of self-reported history of hypertension and to the absence of prescription of antihypertensive drugs were complementary assessed by an at-home respiratory polygraphic sleep studies (Figure 1).

Examination procedure

The population study was examined in the Autonomic Nervous System consultation facilities at the University Hospital of Saint-Etienne, France. Casual blood pressure was systematically measured with a mercury sphygmomanometer at each visit, twice on a lying position after a 15-minute rest, then the measure was repeated immediately after orthostatic position.

The use of antihypertensive drugs (ACE inhibitors or ARB, betablockers, diuretics, calcium channel blockers, or others), history of hypertension and anthropometric data were assessed during a medical interview and examination.

Twenty-four-hour ambulatory blood pressure levels was assessed by ambulatory device recorders using auscultatory method (Diasys Integra, Novacor, Rueil-Malmaison, France), the measurements being programmed each fifteen minutes during the day period and each thirty minutes during the night period, with the cuff placed on the non-dominant arm. Average values of systolic and diastolic blood pressure were calculated for the different recording periods: day, night and 24-hour. Hypertensive status was defined with the level of 24-hour ABPM measures above 135/80 mm Hg, according to the recommended limits at the time of the study completion. [24] ABPM was realized after (the following day) at-home polygraphic monitoring to avoid discomfort or more awaken state due to automatic blood pressure measurements. A second ABPM was realized 1 week later (n=28) when blood pressure data were lacking for 30% or more BP measurements. At the end, ABPM were unavailable for technical problems in 18 subjects.

At-home respiratory polygraphic sleep studies

A ventilatory polygraphy system (HypnoPTT, Tyco Healthcare, Puritan Bennett) recorded ECG tracings (one lead), pulse oxymetry (sampling rate 1 Hz, minimal time duration to define an oxyhemogolbin desaturation event: 10 sec), rib cage excursions (transthoracic impedance), body position and nasal pressure for measurement of ventilation. Nasal pressure is now recommended both for adult and pediatric populations as the noninvasive reference method for assessing airflow. Unattended studies in a patient's home are reliable for the present age group.[25] All the recordings were made overnight at home on the night following the in-hospital clinical examination, during which an experienced technician instructed all participants how to place the sensors. A second night of monitoring was performed when reported sleep latency exceeded 2 h on the first night (n=5), or when one respiratory parameter was missing (n=23). A recording duration of at least five hours was required to validate the sleep study. All the recordings were validated visually and manually scored for apnea/hypopnea events and inspiratory flow limitation episodes by investigators blinded to the other parameters with an intrascorer reliability of 88%. To minimize potential overestimation of sleep duration, each subjects completed a sleep diary to exclude from the analysis the wakefulness before lights off. Apnea and hypopnea events were defined according to previously published guidelines[26] and an oxyhemoglobin desaturation threshold > 3% was chosen accordingly to recommendations. Hypopnea was defined as a 50% or more reduction in airflow from baseline value lasting at least 10 s and apneas were defined as the absence of airway on the nasal cannula lasting for 10 s or more. The apnea-hypopnea index

(number of apnea and/or hypopnea events per hour of time in bed, AHI), as well as the oxyhemoglobin desaturation index (number of desaturations per hour, ODI) were calculated. As indices of nocturnal hypoxemia we also considered the mean nocturnal SaO2, the % of recording time spent with a SaO2 below 90%, and the minimal value recorded during sleep (Nadir SaO2).

Pulse transit time (PTT) was continuously measured as the interval between the ECG R-wave and the subsequent arrival of the pulse wave at the finger (usually the point on the pulse waveform that is 50% the height of the maximal value). PTT is approximately 200 to 300 msec when using the finger probe and is measured with an accuracy of 2 msec. PTT values are available with every heartbeat and are typically oversampled at 5 Hz. Such an indicator of respiratory effort helps to qualify respiratory events as obstructive or central. The absence of rib cage movements associated with the absence of autonomic arousal defined a central respiratory event. Obstructive AHI and central AHI were calculated separately. Several groups have demonstrated, in both adults and children, that PTT is as accurate as esophageal pressure for measuring respiratory effort both in frank and subtle respiratory events.[27,28]

According to previously reported data, an obstructive AHI >15 was considered in the elderly as the diagnostic threshold for obstructive sleep apnea syndrome.[29,30] Cases were defined as mild or moderate for an AHI>15<or=30, or as severe with an AHI above 30. Increased hypoxemic load was also defined according an ODI>10/h.

Sleep study data were also presented according to interquartile comparisons.

Statistical analysis

The consistency of data was checked. When BP values or sleep study data differ of two standards errors or more from the mean value, they were checked individually by the medical doctor in the original subject file. If the value was considered inconsistent due to technical problem during the recordings, it was excluded from the analyses. Thus, we expressed our results in per-protocol and not in intention to treat analysis Casual systolic, diastolic as well as 24-hour Ambulatory BP was compared between the OSAH status, using ANOVA with one between-factor. We used Bonferroni method to adjust the level of significance for multiple comparisons. Analysis was adjusted for potential confounding factors when needed. Percentages of uncontroled ambulatory BP (systolic, diastolic or systolo-diastolic hypertension) was calulated according to the severity of unrecognized OSAH and comparisons made using chi-squared of Pearson.

To determine the independent association of hypertension and AHI, multiple logistic regressions analysis were built according to the presence of 24-hours systolic hypertension, or 24-hours diastolic hypertension. Hypertension and the severity of the OSAH (moderate or severe) relationship was assessed after adjustments for gender, BMI, presence of type 2 diabetes, dyslipidemia, and smoking status. Complementary, adjusted logistic regression analysis was also performed according to the presence of 24-hour systolic hypertension, or 24-hour diastolic hypertension and the severity of oxyhemoglobin desaturation index (>10/h).

Finally, using separate multiple logistic regression analysis, we compared the relationship of 24-hour systolic or 24-hour diastolic hypertensive status and AHI and ODI according to inter-quartiles comparisons. A value of $p<0.05$ was considered as statistically significant.

Results

The flow chart of the study is depicted in figure 1. A total of 488 normotensive subjects presented with a validated polygraphic data. Among them, 18 showed unvalidated ABPM unless a second ABPM had been realized one week later. The final dataset included a total of 470 subjects. Clinical, anthropometric and sleep study data are shown in table 1 according to the presence and the severity of OSAH. The subset of elderly (n=18) excluded from the analysis demonstrated anthropometric, sleep study data (table 1) as well as casual systolic and diastolic blood pressure values similar to the final (n=470) dataset (Sys. BP and Dia. BP respectively: 136.3±15.6 vs 135.2±15.7 mmHg, 84.5±8.1 vs 84.2±8.5 mmHg, p=ns).

In comparison to nonapneic subjects, severe OSAH (AHI>30/h, 17% of included subjects) was associated with a significant increase of 5mmHg or more in both diurnal and nocturnal ambulatory systolic BP and with a nocturnal increase of 3 mmHg in ambulatory diastolic BP (table 2). Presence of a moderate OSAH was associated with an elevation of 3 mm Hg of systolic BP during daytime and an increase of 5 mm Hg of systolic BP during the night period. A limited but significant increase of diastolic BP was also observed during the night period in this population of moderate OSAH. Interestingly, casual BP measurements did not differ according to the presence or not of an unrecognized SRBD and gender-stratified analysis confirmed significant relationships between AHI and BP-levels in men and women (table 2).

Table 3 is summarizing the respective rates of hypertension as defined by ABPM in non-apneic, moderate and severe OSAH subjects. Abnormal systolic (mean 24-hour ABP>135 mmHg) or diastolic (mean 24-hour ABP>80 mmHg) hypertension was more frequently encountered in subjects suffering from moderate or severe OSAH ($p<0.02$ and $p<0.03$, respectively) in comparaison to non-apneic patients. According to the presence of a moderate and a severe OSAH, the total prevalence of uncontrolled systolic or diastolic hypertension reaches respectively 22.6% and 29.6%.

Multiple logistic regression analysis showed, after adjustment on age, gender, BMI, diabetes, dyslipidemia, smoking status, and alcohol consumption, an independant association between severe OSAH (AHI>30) and 24-hour Systolic hypertension (OR: 2.42, CI[1.1-5.4]) but not with moderate OSAH (AHI 15-30). The increased risk of Systolic hypertension and of Diastolic hypertension (24-hour ABPM) was more pronounced when SRBD was expressed using an oxyhemoglobin desaturation index >10/h (OR: 2.43, CI[1.45-4.1] for 24-hour Systolic hypertension and OR: 2.52, CI[1.45-4.36] for 24-hour Diastolic hypertension).

Separate multiple logistic regression analysis were made using successively ODI, and AHI. When SRBD severity is presented according to interquartile comparisons for ODI parameters the analysis confirmed the significant relationship between OSAH and silent hypertension for systolic BP as well as for diastolic BP (Table 4). Such relationship was significant for AHI parameter and silent Systolic hypertension only.

Discussion

Our results showed that, in an elderly population, unrecognized severe sleep apnea is associated with a diurnal and nocturnal elevation of blood pressure equal or above 5 mmHg. The link between sleep apnea and elevated BP remained significant even after adjustment for age, gender, BMI, diabetes, dyslipidemia, smoking status, and alcohol consumption. Hypertension as defined by ABPM measurements reached a prevalence of nearly 30% in older people with unrecognized OSAHS. The oxyhemoglobin desaturation index > 10/h was the parameter demonstrating the stronger association with increases in blood pressure.

Hypertension in humans is a very common condition affecting over 1 billion people worldwide (www.who.int/en/index.html). The cause for hypertension is known in approximately 5% of cases, the other 95% being classified as 'essential hypertension'. OSAH syndrome is an independent risk factor for office hypertension.[2,10] The Wisconsin Sleep Cohort Study[1] prospectively investigated in middle age subjects the association between OSAH severity and incident hypertension at 4 years. Subjects with an apnoea/hypopnoea index (AHI) of >15 events per hour at initial evaluation had a threefold risk ratio for developing hypertension over the 4 year follow-up compared to those without any apnoea. In accordance with these results, it is now recommended both by European and American guidelines to seek at sleep apnea as an explaining factor for hypertension. [19,31]

The risk of hypertension in OSAS patients may be particularly pronounced in younger adult patients (<50 years) compared with older ones.[32] The SHHS study failed to found a significant association between SRBD and systolic/diastolic hypertension in subsets of elderly subjects. In this last study, analyses excluding participants treated for hypertension (49% of the population aged 60 yrs ore more) did not change the results. These results were in accordance with mortality studies of sleep apnea patients showing maximum risk of dying in younger patients and a pronounced age decline in relative mortality reaching non significant levels in patients older than 50 years.[12] A recent hypothesis is a pre-conditioning effect[33] due

to repeated intermittent hypoxia that may promote some degree of cardiovascular protection and a reduced risk of acute coronary heart disease owing to the development of coronary collaterals. Another recent experimental study in rats exposed to chronic intermittent hypoxia suggests an age-related resistance to oxidative stress in the myocardium.[34] The sympathetic burst in response to intermittent hypoxic events could be reduced and this could explain the relatively small secondary increases in blood pressure.

Actually, the major difference between the SHHS study and the PROOF-SYNAPSE studies were BP measurements methods for normotensive/hypertensive status determination. Ambulatory BP measurement has demonstrated its ability to detect subjects with normal clinic but high ambulatory BP (masked hypertension) and also to determine white-coat hypertension. The prevalence rate of masked hypertension in newly diagnosed middle age OSAH patients refered to Sleep Laboratory has been founded up to 30% by several authors.[17,18] To our best knowledge, the current study is the first one wich evaluates in an elderly population masked hypertension and its relationship with occult OSAH. According to our results, masked hypertension is also frequently associated to occult SRBD in elderly people, particularly in subjects suffering AHI>30/h or ODI>10/h. This dose-response relationship between OSAHS severity and hypertension was found more strictly for systolic hypertension than for diastolic hypertension.

While moderate, such increases in BP levels could have a direct or an indirect impact in atherogenesis development. Recent studies have shown abnormal vascular responses in patients with OSAHS even in patient without any over cardiovascular disease, and are similar to those occuring in patients with essential hypertension.[35-36] OSAH may be associated with increased vasoconstrictor sensitivity,[37] impaired endothelium-dependent vasodilatation to acetylcholine and bradykinin,[38,39] and decreased alpha- and beta 2-adrenergic vascular responses.[40] It has been shown that endothelial dysfunction, one of the factors underlying cardiovascular morbidity in SRBD, is clearly present in elderly OSAH patients and appears related to hypoxemia severity indices.[41] The high prevalence of masked hypertension that we have demonstrated in this study might be one of the underlying mechanisms.

The treatment of symptomatic OSA syndrome with CPAP clearly attenuates the cardiovascular consequences of this disease and reduces blood pressure levels in both hypertensive and normotensive patients with OSAH syndrome,[42,43] irrespective of sleepiness.[44] Such beneficial antihypertensive therapeutic effect has been most marked in those with the highest index of oxyhemoglobin desaturation/resaturations during sleep associated to the most frequent apnoeas and hypopnoeas occurences. Elderly symptomatic

SRBD patients tolerate CPAP as well as younger patients and should be effectively treated. The observance rate of nocturnal CPAP of an elderly asymptomatic or paucisymptomatic population would be expected to be low.[38]

Our study suffers limitations. Our cohort is homogeneous in age, and involves a low risk population since none of the subjects presented myocardial infarction, stroke, heart failure, atrial fibrillation at the time of inclusion**.** The performed a per protocol analysis. Since failure of ABPM is sometimes associated with severe hypertension or high variability of blood pressure, it could be speculated that subjects excluded from the protocol had a different BP level then the analyzed group. Actually, it was not the case as the clinical characteristics of the excluded subset (n=18) as well as their casual BP measurements were not statistically different from the 470 elderly in the study. A comparison between those subjects regarding the first ABPM they realized 20 months before in the PROOF study, showed no significant difference between included and excluded subjects (24h sys BP: 116.3±15.4 vs 114.7±10.8 mmHg; 24h dia BP: 75.1±8.3 vs 74.8±6.8 mmHg, p=ns). At the end we do not think that and intention to treat analysis would led to different conclusions. The results presented in this study are only cross sectional data and the percentage of masked hypertensives is relatively high in our population. To avoid altering sleep stability by repeated blood pressure measurements during night we realized ABPM procedure and sleep studies separately. This is a survival cohort study and the clinical impact of SRBD on hypertensive status as well as the independant effect of silent OSAH on cardiovascular and cerebrovascular morbilidy and/or mortality should be evaluated later. Some selection bias could account for our findings. First of all, despite a wide spectrum of SRBD was present in our population, mild cases were prevalent, the absence of severe cases reducing the relationship between diastolic BP and AHI especially in women. However, this finding is common in clinical and epidemiological studies, severe cases being more common in young patients. Another factor is that the examined healthy elderlies were non institutionalized subjects and therefore they may constitute a survivor group more resistant to vascular risk. This latter possibility could be suggested by the different clinical aspects of SRBD in elderly, in which neither sleepiness nor common predisposing factors appear strongly related to apnoea density.

In conclusion, unrecognized SRBD enhanced nocturnal as well as diurnal blood pressure in 68 years old subjects. The frequency of hypoxemia/reoxygenation cycles appears the pathophysiological cornerstone of such relationship in the present crosssectional analysis.

The impact of such findings on subsequent cardiovascular and cerebrovascular morbidity is still questionned.

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Table 1. Clinical and sleep study data. Significance *p<0.05 from subjects presenting an AHI<15.

	Excluded N=18	In the study N=470	AHI<15 N=234	AHI 15-30 N=155	AHI>30 N=81
Men, n (%)	8 (44.4)	197 (41.9)	70 (29.9%)	77 (49.7%)*	50 (61.7%)*
Age, ys	68.6±0.5	68.2±0.5	68.1±0.4	68.4±0.5	68.2±0.5
BMI, kg/m^2	24.7±4.2	24.6±3.3	24.3±3.3	24.6±3.0	25.8±3.5*
Diabetes, n (%)	0 (0%)	11 (2.3%)	6 (2.6%)	3 (1.9%)	2 (2.5%)
Current/past smoking, n (%)	4 (22.2%)	116 (23.8%)	49 (20.9%)	44 (28.4%)*	23 (28.4%)*
Dyslipidemia n (%)	7 (38.9%)	133 (27.3%)	62 (25.9%)	56 (35.8%)*	15 (17.2%)
Glycemia g/L	0.99±0.12	0.96±0.14	0.96±0.15	0.97±0.12	0.98±0.16
Total Cholesterol g/L	2.26±0.31	2.26±0.33	2.25±0.33	2.27±0.34	2.28±0.31
HDL-Chol. g/L	0.66±0.29	0.65±0.18	0.68±0.19	0.65±0.17	0.59±18*
LDL-Chol. g/L	1.39±0.26	1.40±0.31	1.37±0.30	1.41±0.32	1.46±0.29
Triglycerides g/L	1.08±0.51	1.05±0.54	1.02±0.55	1.01±0.51	1.18±0.55*
ESS Score	5.4±3.0	5.8±3.7	5.1±3.5	6.1±3.8	6.6±3.9
Obstructive AHI/h	19.9±22.3	18.5±14.0	7.0±3.6	20.4±4.5*	41.1±11.8*
Central AHI/h	1.8±3.7	1.8±3.2	0.7±1.0	1.6±1.6*	4.8±6.9*
ODI/h	10.8±15.9	7.8±8.2	3.3±3.1	7.9±5.1*	18.6±11.0*
Time SaO_2<90%, %	2.5±9.3	1.5±5.5	1.05±5.6	1.3±3.9	3.2±7.1*
Nadir SaO_2, %	89.8±5.4	90.1±4.0	91.5±2.8	89.5±4.2*	87.8±4.8*
Mean $Sa0_2$, %	94.9±1.5	95.4±1.8	95.6±2.1	95.4±1.4*	95.1±1.5*
ODI>10/h (%)	7 (38.9%)	136 (28.9%)	10 (4.3%)	50 (32.3%)	76 (93.8%)

Table 2. Casual and Ambulatory Blood Pressure data according to the presence of undiagnosed obstructive sleep apnea/hypopnea in all subjects (top), in women (middle) and in men (bottom). Significance *p<0.05 from subjects presenting an AHI<15. An adjustment was made for age, BMI, dyslipidemia, type 2diabetes, smoking status, and alcohol intake.

AHI total population		**<15**	**15-30**	**>30**
N	BP	*234*	*155*	*81*
Casual	Systolic	134.1±16.5	136.5±14.4	136.3±15.6
	Diastolic	83.7±7.9	85.5±8.6	85.2±7.6
Ambulatory, 24-hour	Systolic	114.2±12.8	117.9±12.7*	119.3±14.7*
	Diastolic	72.6±6.4	74.0±8.1	74.4±7.9
Ambulatory, diurnal	Systolic	118.4±13.6	121.9±13.5*	123.2±14.8*
	Diastolic	75.5±6.9	76.7±8.6	77.0±8.3
Ambulatory, nocturnal	Systolic	101.1±12.8	106.2±12.9*	107.6±14.2*
	Diastolic	63.7±7.6	66.1±8.3*	66.6±7.8*

AHI women		**<15**	**15-30**	**>30**
N	BP	*164*	*78*	*31*
Casual	Systolic	132.1±10.4	134.4±15.4	136.3±17.5
	Diastolic	82.4±6.0	83.3±8.9	85.0±9.0
Ambulatory, 24-hour	Systolic	113.0±11.0	116.9±13.7*	119.0±15.9*
	Diastolic	71.5±5.9	73.5±8.3	74.8±9.6
Ambulatory, diurnal	Systolic	119.3±11.6	121.3±16.5	123.9±16.2*
	Diastolic	74.6±4.5	75.9±8.5	77.3±11.0
Ambulatory, nocturnal	Systolic	101.6±10.8	106.2±13.9*	108.4±15.2*
	Diastolic	63.9±6.3	65.7±8.6	66.4±8.9*

AHI men		**<15**	**15-30**	**>30**
N	BP	*70*	*77*	*50*
Casual	Systolic	136.4±17.3	137.9±16.0	136.4±15.9
	Diastolic	83.7±7.9	85.5±8.6	85.2±7.6
Ambulatory, 24-hour	Systolic	115.2±13.8	118.7±12.9*	119.7±14.9*
	Diastolic	73.9±7.4	74.8±8.8	74.3±9.9
Ambulatory, diurnal	Systolic	117.8±14.6	122.9±14.5*	123.0±14.8*
	Diastolic	75.0±6.9	77.7±9.6	76.7±8.8
Ambulatory, nocturnal	Systolic	100.8±14.8	106.2±14.3*	107.1±15.2*
	Diastolic	63.6±9.8	67.1±9.1*	66.9±8.6*

Table 3. Contingency tables testing the association between unrecognized OSAH and rate of systolic or diastolic hypertension as defined by ABPM (%(n)). Significance *p<0.05.

ABPM	AHI	<15 (n=234)	15-30 (n=155)	>30 (n=81)	All (n=470)
Systolic hypertension		6.8% (16)	10.3% (16)*	18.5% (15)*	10.0% (47)
Diastolic hypertension		12.8% (30)	18.7% (29) *	23.5% (19)*	16.6% (78)
Sys. and/or Dias. hypertension		14.9% (35)	22.6% (35) *	29.6% (24)*	20.0% (94)

Table 4. Interquartile comparisons for trend of the frequency of systolic (upper pannel) and diastolic hypertension (lower pannel) according to the degree of SRBD severity defined using ODI and AHI. An adjustment was made for age, gender, BMI, dyslipidemia, diabetes, smoking status, and alcohol intake.

N=470		Quartiles (% of hypertensive)				Statistics		
Hypertension		Q1	Q2	Q3	Q4	R	OR	p
Systolic	ODI	6.1	6.5	9.7	25.6	0.191	4.94 [2.10-11.74]	0.0003
	AHI	4.3	8.8	8.8	20.2	0.116	2.61 [1.22-5.58]	0.01
Diastolic	ODI	10.6	12.2	15.7	33.7	0.178	4.31 [2.08-8.92]	0.0003
	AHI	11.3	13.6	21.1	22.3	0.050	1.83 [0.93-3.59]	0.08

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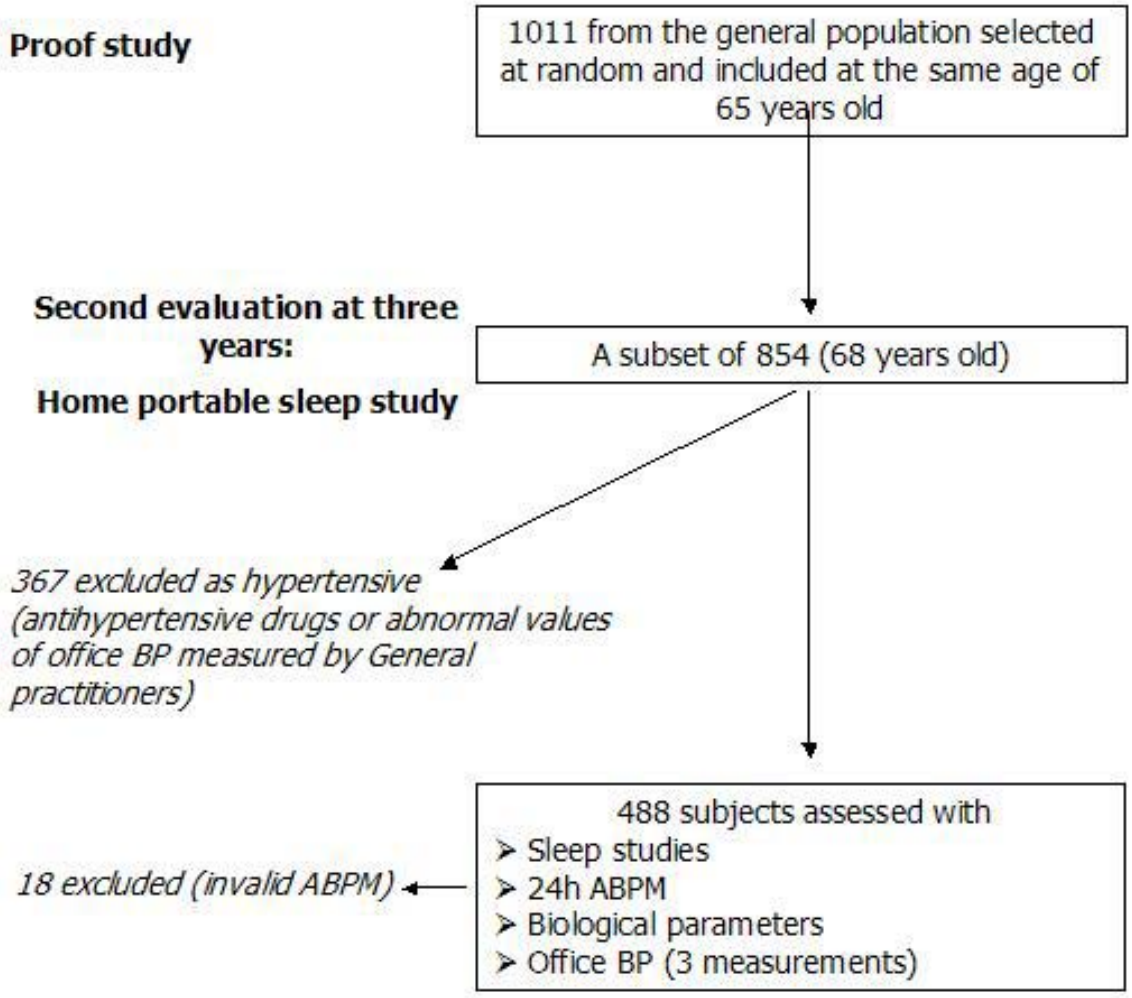
Proof study
1011 from the general population selected at random and included at the same age of 65 years old
Second evaluation at three years:
Home portable sleep study
A subset of 854 (68 years old)
367 excluded as hypertensive (antihypertensive drugs or abnormal values of office BP measured by General practitioners)
488 subjects assessed with
Sleep studies
24h ABPM
Biological parameters
Office BP (3 measurements)
18 excluded (invalid ABPM)