Sleep Apnea-Hypopnea Syndrome in the Elderly

Miguel Ángel Martínez-García, a,b,d,* Joaquín Durán-Cantolla, b,d and José María Montserrat c,d

a Unidad de Neumología, Hospital General de Requena, Valencia, Spain
b Unidad de Trastornos de Suelo, Hospital de Txagorritxu, Vitoria, Spain
c Unidad de Sueño Multidisciplinaria, Servei de Pneumología, Institut del Tórax, Hospital Clinic de Barcelona, Barcelona, Spain
d CIBER de enfermedades respiratorias, CIBERES, Spain

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The population pyramid is changing due to the increasing longevity of the population, making it a priority to have better knowledge of those diseases that have an increasingly major impact in advanced age. Sleep apnoea-hypopnea syndrome (SAHS) affects 15–20% of individuals over 65 years. Despite this high prevalence and the fact that one in four Spanish sleep studies are conducted on the elderly and that more 60% of these were treated with CPAP, there are few specific studies in this age group on the diagnosis and management of this syndrome. Over time, physiological increase in the number of sleep respiratory disorders may be the biggest obstacle when defining, diagnosing and treating SAHS in the elderly. In any case and while more solid scientific evidence is obtained, the Spanish SAHS Consensus, as well as the Guidelines on the diagnosis and treatment of SAHS, recommend that, within logical limits, age should not be an obstacle to offering the elderly diagnostic help and treatment similar to that offered to the rest of the population.

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E l s í n d r o m e d e a p n e a - h i p o p n e a s d u r a n t e e l s u e ñ o e n e d a s a v a n z a d a s

La pirámide de población está cambiando como consecuencia de la cada vez mayor longevidad de la población por lo que se hace prioritario conocer en profundidad aquellas enfermedades que impactan con mayor frecuencia en edades avanzadas. El síndrome de apneas-hipoapneas durante el sueño (SAHS) afecta al 15-20% de los individuos mayores de 65 años. Sin embargo, y a pesar de esta elevada prevalencia y que en nuestro país uno de 4 estudios de sueño se realiza en ancianos y que más del 60% de estos serán tratados con CPAP, apenas existen estudios específicos para este grupo de edad sobre el diagnóstico y manejo de esta enfermedad. Probablemente el incremento fisiológico con el paso del tiempo del número de trastornos respiratorios durante el sueño sea el mayor obstáculo a la hora de definir, diagnosticar y tratar el SAHS en los ancianos. En cualquier caso y mientras llegan evidencias científicas más sólidas tanto el Consenso Nacional de SAHS como las Normativas sobre el diagnóstico y tratamiento del SAHS recomiendan que, dentro de limites lógicos, la edad por sí misma no sea un obstáculo para ofrecer a los ancianos un trato diagnóstico y terapéutico semejante al ofrecido al resto de la población.

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Introduction

Undoubtedly, the population pyramid is changing. With the gradual advances in medical knowledge and improved social conditions, the population's longevity is on the rise. As a result, older people are beginning to play a central role in the health landscape, especially in the developed world. A recent study concluded that people born in the beginning of the twenty-first century in the industrialised world would have a life expectancy of over 100 years. Most importantly, in most cases, they would enjoy a good quality of life. In this context, which represents both the present and the future—and bearing in mind that due to the inexorable passage of time, the highest percentage of medical visits will continue to take place in the last quarter of a person's life—we are faced with a situation where an answer will need to be given to the growing demand of elderly patients, who justly require a diagnostic and therapeutic treatment similar to that provided for younger people. In this sense, Spain will face this situation early on, given that, after Japan, it has the second highest life expectancy in the world. In 2006, life expectancy in Spain was estimated at 77 years for men and 83.5 years for women, according to the National Statistics Institute. This means that it is 6 years more than the European Union average. It also implies that with 21% of the population over the age of 65, this figure will become greater than 35% in the coming decades. Logically, the most prevalent diseases among the population, with a particular impact on the elderly, or those for which our current knowledge is deficient, will be those with which we should mainly deal with to a greater extent. The sleep apnoea-hypopnoea syndrome (SAHS) is a clear example of this situation because it brings together both circumstances: its high prevalence and the widespread ignorance of its impact on advanced ages. If we accept that in Spain the current prevalence of SAHS is close to 20% in people over 65 years of age, and that this population has an increasing epidemiological importance, we can estimate that there are currently more than 1.7 million people over the age of 65 with SAHS, a figure that will double over the next three decades. The following article will review the current scientific evidence on SAHS in the elderly and will address the problems generated by a very common disease, which is relatively unknown by an increasingly ageing society.

Sleep Also Ages

Some epidemiological studies conclude that more than half of those over the age of 65 suffer from some form of chronic sleep disorder. Undoubtedly, the deterioration of physiological activities is inevitable over time, and sleep is no exception. In general, both the structure and duration of sleep change with age. According to the results taken from the sample of the Sleep Heart Health Study, in which over 2,500 people were studied, perhaps the most characteristic changes that occur in advanced ages are: increased shallow sleep and decreased deep sleep, with few changes in the percentage of REM sleep (decreases of less than 5%), but with an overall decrease in total sleep time and effectiveness; and increase in the number of awakenings “arousals”. These arousals can reach up to 15 episodes per hour of sleep, although with significant differences per gender, as changes in women generally do not seem too pronounced. It seems that these age-dependent changes in sleep quality and quantity respond to neurohormonal changes produced by alterations in both the endocrine secretion of the hypothalamic-pituitary-adrenal axis and the neural activity. From these, we should note the decrease in the concentration of growth hormone, variations in the hypocretin orexin system, changes in melatonin secretion, increase in night cortisol or in inflammatory cytokines, such as interleukin-6, involvement of serotonergic and GABAergic systems and the progressive inability to maintain homeostatic regulation, which sets the circadian rhythms of sleep-wakefulness in older people. In this sense, with older age, there is usually a phase advance which, according to some studies, does not depend only on endogenous changes but also on changes in lifestyle caused by age and external factors such as diet, physical activity or exposure to light, which take place over time. On the other hand, the presence of chronic comorbidities - especially insomnia, restless leg syndrome, joint diseases, the use of sleeping tablets or an increase in the number of sleep disordered breathing (SDB), which are more frequent in advanced ages - has a greater impact on sleep disruption in this age group. 

It is well known than the number of SDB increases with age in a physiological manner, because there is a greater tendency for the upper airway to collapse over time. Among the many factors that could explain this phenomenon, we highlight those listed in table 1. The final degree of collapse does not seem to depend exclusively on the role of only one of these factors. Instead, it appears as the end-result of the interaction of all of these factors. This would explain the great physiological heterogeneity observed for a particular age and the greatest difficulty for physicians when making a decision concerning an older patient with excessive SDB, i.e. the percentage of pathological events and physiological events and whether the situation should be treated. Thus, Bwille et al. suggested a heuristic model with two types of SAHS. On the one hand, the pathological type would appear in middle age and would correspond to patients who are usually diagnosed with SAHS in Sleep Units. The other type would appear after the age of 60, with some overlap between the two types. The ageing process and the increase in the resulting pharynx collapsibility would cause its physiological appearance. In any case, this dual model has not been suitably confirmed (fig. 1).

Table 1: Possible causes of increased collapsibility of the airway in older people

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased airway resistance during sleep</td>
<td></td>
</tr>
<tr>
<td>Decreased diameter of the pharynx due to the deposition of fat on the wall</td>
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<tr>
<td>Pharynx muscle dysfunction</td>
<td></td>
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<tr>
<td>Changes in the pharynx dilator reflexes</td>
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<tr>
<td>Altered sleep structure</td>
<td></td>
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<tr>
<td>Increased respiratory instability during sleep (central events)</td>
<td></td>
</tr>
<tr>
<td>Postmenopause in women</td>
<td></td>
</tr>
<tr>
<td>Tooth loss</td>
<td></td>
</tr>
<tr>
<td>Common comorbidities that are risk factors (stroke, heart failure, hypothyroidism, etc.)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Hypothesis that proposes two types of SAHS, one age-related and the other age-dependent, to explain the increase in the prevalence of SAHS among the elderly. SAHS indicates sleep apnoea-hypopnea syndrome.
Epidemiology of SAHS in Advanced Ages

In the General Population

Over time, the increased collapsibility of the airway caused by various factors associated physiologically with age, explains the increase in the number of SDB observed, which is associated or not with symptoms secondary to SDB.24-28 as shown in several population-based epidemiological studies conducted on older people (table 2). Young et al.29 found that the number of SDB increases according to age, to peak at the age of 60 and above, although this plateau phenomenon could not be observed by other authors. In Spain, there is a study by Duran et al.30 carried out on a sample of 428 people from the general population, aged 71-100 years. This study revealed that 67% of the men and 62% of the women had an AHI ≥ 10. If we accept the diagnosis of SAHS as the presence of an AHI ≥ 10 with compatible symptoms (daytime hypersomnia according to the Epworth score questionnaire > 10), 20% of the men and 15% of the women met the criteria for diagnosis. Although this study, and to the rest of the studies listed in table 2, shows a clear increase in the number of SDB with symptoms, it is important to clarify that the Epworth questionnaire, which is frequently used for all ages to subjectively assess the degree of hypersomnia, is not certified for use in advanced ages. There is also a significant increase in people with hypersomnia who are not dependent on the presence of SAHS (comorbidities, inactivity, obesity, taking psychotropic medication, cognitive impairment, etc.), and a cut-off point of 10 in the AHI is likely to fall within the physiological range for most people. Even so, Duran et al. observed that 26% of the men and 21% of the women had an AHI ≥ 30, a value that was probably within the pathological range even in older people. This makes us suspect that, in fact, SAHS presents a high prevalence in this age group, and that this prevalence tends to be equal between men and women in advanced ages. On the other hand, the increase in the number of SDB occurs both at the expense of obstructive and central events, especially the former, although certain authors note a particularly marked increase in the central-type events.34-37 Finally, Campos-Rodriguez et al. did not observe age being a factor in the development of obstructive SAHS located in the REM stage.28

Table 2

The most relevant population-based epidemiological studies on SAHS which were conducted on older people

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample (n)</th>
<th>Age</th>
<th>AHI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ancoli-Israel et al.26</td>
<td>427</td>
<td>65-99</td>
<td>AI ≥ 5: 28% M, 20% F</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AI ≥ 10: 11% M, 10% F</td>
</tr>
<tr>
<td>Zamarro et al.27</td>
<td>693</td>
<td>50-70</td>
<td>AI ≥ 20: 6% M, 2% F</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>RDI ≥ 5: 28.9%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>RDI ≥ 10: 15.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>RDI ≥ 20: 13.2%</td>
</tr>
<tr>
<td>Duran J et al.23</td>
<td>428</td>
<td>71-100</td>
<td>AI ≥ 5: 81% M, 79% F</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AI ≥ 10: 67% M, 62% F</td>
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<td></td>
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<td></td>
<td>AI ≥ 20: 44% M, 37% F</td>
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<td></td>
<td></td>
<td></td>
<td>AI ≥ 30: 26% M, 21% F</td>
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<td></td>
<td></td>
<td></td>
<td>AI ≥ 40: 24% M, 19% F</td>
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<td></td>
<td>AI ≥ 50: 20% M, 16% F</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AI ≥ 60: 13% M, 10% F</td>
</tr>
<tr>
<td>Bixler E et al.25</td>
<td>75</td>
<td>65-100</td>
<td>AI ≥ 5: 24.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AI ≥ 10: 23.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AI ≥ 20: 13.3%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AI ≥ 30: 45% M, 39% F</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AI ≥ 40: 32% M, 36% F</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AI ≥ 50: 15% M, 10% F</td>
</tr>
<tr>
<td>Young T et al.29</td>
<td>3,448</td>
<td>60-99</td>
<td>AI ≥ 5: 35% M, 18% F</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AI ≥ 10: 22% M, 5% F</td>
</tr>
</tbody>
</table>
| Hoch C et al.30 | 105        | 65-85 | AHI indicates apnoea-hypopnoea index; AI, apnoea index; F, female; M, male; RDI, respiratory disturbance index.

In Sleep Units

Some authors have observed that patients older than 65 who are referred to a sleep unit for suspected SAHS have an AHI similar to that of younger people, meaning that probably the clinical profile for which they are referred to the sleep units is also similar.35,39 Recently, a study was completed in Spain with data analysed from more than 50,000 sleep studies conducted between 2002 and 2008. These data came from 16 sleep units and show that one in four sleep studies (24.3%) are conducted on people over 65, preferably men (64.9%). Over 70% of them showed an AHI > 10 and, of those, approximately 70% were treated with CPAP. Since 2005, this percentage has gradually increased, especially in older men. Despite the lack of scientific evidence on the diagnosis, impact and treatment of SAHS in older people, these data confirm that health care in this age group is not only important but it has been growing in recent years.30

Do the Elderly Have Different SAHS Symptoms?

Similar to many other diseases, the clinical symptoms of SAHS in the elderly are probably different to those seen in young people. The way of living with, having or feeling the symptoms is shaped by the particular characteristics of the elderly, especially when many of the symptoms must be reported by bed partners, who sometimes are also elderly and suffer from neurosensory problems, or by the high percentage of elderly people who sleep alone. In this regard, Young et al.30 observed that after the age of 50, the number of people snoring not only decreases progressively, but also the percentage of women who do not know if they snore is greater than the percentage of women who know that they snore. On the other hand, in men this fact emerges after the age of 70, in which the percentage of men who do not know if they snore is 26%. We could therefore conclude the same with the identification of episodes of apnoea, another key symptom to determine the pretest probability of SAHS and to initiate the appropriate diagnostic and therapeutic algorithm. This phenomenon is probably due to the lack of medical consultation in this regard and, therefore, to the under-diagnosis of SAHS in the elderly.

Concerning hypersomnia, a key symptom to assess the severity of SAHS, there are significant difficulties in establishing its existence, particularly its relationship with possible SAHS in advanced ages. This is due to different reasons, including:

- **High prevalence of hypersomnia in the elderly.** Some authors have reported that up to 20% of the elderly have pathological hypersomnia during the day. In a group of more than 16,500 people between 20 and 100 years old from the general population, Bixler et al.31 observed that, regardless of other misleading factors, the prevalence of hypersomnia increased significantly from the age of 75.
- **Relationship with multiple factors.** Whitney et al.32 studied 4,578 people aged 65 and found that excessive hypersomnia was associated with multiple factors, including: age; obesity; chronic cardio-respiratory comorbidities and those causing physical pain, depression, use of psychotropics, sleep disruption, poorer quality of life, motor activity and symptoms related to SAHS (not closely related with the latter). Therefore, the presence of hypersomnia in the elderly is even less specific than in adults when suspecting SAHS.
- **Perception of hypersomnia as a “typical” symptom amongst the elderly.** Both patients and the medical team treating them often assume that the presence of excessive hypersomnia in the elderly is normal or that it is associated with physiological deterioration. This sometimes results in older patients not being referred by doctors to the sleep units, or the actual patient not reporting the situation to the doctor. Therefore, this is one of the causes of
under-diagnosis or of late diagnosis of SAHS in the elderly, especially women. Hypersomnia related with SAHS. However, some authors have observed that the degree of hypersomnia in the elderly referred to a sleep unit is similar to that of younger patients. This supports the fact that the elderly are referred to sleep units for similar causes as young people (typical symptoms). On the other hand, presenting “atypical” symptoms or few symptoms (in relation to hypersomnia) is very often in the elderly, with a suspected SAHS profile, who have more cardiovascular or neurocognitive problems. Measuring hypersomnia in the elderly. One more obstacle is the lack of widely used diagnostic tools that are specifically certified for the elderly for the subjective measurement of hypersomnia. In this sense, the Epworth questionnaire is not certified to be used in the elderly, in which some questions (such as those related to driving) would be meaningless in a high percentage of the elderly who no longer drive. Therefore, it should be used with caution. Many of the clinical and anthropometric data, such as chronic snoring, observed apnoea, presence of hypersomnia, body mass index, neck circumference and perimeter of the pelvic girdle, which are usually related to typical SAHS symptoms in middle-aged people, seem to have a more limited predictive value in the elderly due to the decrease in their specifications, the difficulty in their measurement or the presence of adaptive mechanisms with age. In return, the presence of SAHS in the elderly seems to better relate to a number of more specific clinical aspects of this age group - usually in the neurocognitive and cardiovascular field, particularly the former -. Since they can often be the expression of this disease, they should always be taken into account. In that regard, some authors have linked SAHS in the elderly with the onset or worsening of depressive symptoms, frequent falls, dementia, and excessive cardiovascular events. It is therefore likely that the concept of high, medium or low pretest probability, which is often used to classify patients referred to sleep units for suspected SAHS, is not valid in the elderly and should be reviewed for use in this age group.

Diagnosis of SAHS in the elderly

Today, polysomnography (PSG) is the gold standard for the diagnosis of SAHS in all ages. Due to the increasing frequency of patients referred to sleep units for suspected SAHS and the poor accessibility to some PSG centres, the enormous pressure put on health care in recent years has led to the proliferation of certain devices that omit neurophysiological variables. These technically simplify the test, with a loss of diagnostic efficacy assumable under certain circumstances. Despite the negativity of the simplified sleep test, in patients with a cardiopulmonary disease base, sleep instability, psychotropic treatment that can alter sleep structure, the possibility of alternative diagnoses to SAHS or suspected SAHS symptoms, carrying out a comprehensive PSG study is recommended. Often many of the circumstances that affect the sleep duration and structure converge in elderly patients. This means that, it is preferable to conduct a full PSG for the diagnosis of SAHS, whenever possible. On the other hand, the frequency of central events and the prevalence of restless legs syndrome in elderly patients are higher than in young people. This entails other disadvantages when using a simplified device, which is usually not certified for this type of events, or without the possibility of using tibial electromyograms. Nevertheless, due to logistical difficulties already discussed for the realisation of a PSG in many centres, the implementation of a simplified test would be acceptable in certain cases and circumstances, where there is a lack of accessibility for the less elderly with SAHS- suspected symptoms without significant cardiopulmonary comorbidities, or within epidemiological studies. If the decision is to use a simplified device, it is likely that home studies would have a special significance in advanced ages because they allow the patient to rest in their normal environment. On the other hand, the disadvantage is that the elderly have a lesser ability in managing the device and the frequent awakenings caused by nocturia or neurocognitive impairment. Therefore, this may result in an increased number of invalid studies. Although the night-to-night variability of the PSG results is higher in older people, it is accepted that, similar to young people, conducting one full valid PSG is sufficient to establish the diagnosis. Most studies that are based on diagnostic algorithms to make the decision (pretest probability and diagnostic tests) have been conducted based on studies in men aged 30-70. These were then extrapolated to the rest of the adult population (women and elderly). Consequently, the diagnosis of SAHS in the elderly, which usually has atypical symptoms, is another scientific challenge to be met over the coming years. Studies are needed to confirm the validity of simplified devices in this age range, under certain circumstances.

Impact of SAHS in the Elderly: A Continuing Dilemma

There are very few studies with a sufficient level of scientific evidence, which analyse the impact of excessive SDB or SAHS symptoms in the elderly. Most likely, the main problem is that we do not know the cut-off point in the AHI that can be considered as pathological, whether the AHI is the best form of identification of SAHS in the elderly, what percentage of SDB is due to age and does not have a negative impact on the elderly and what symptoms/clinical signs should we consider. Of these few studies, the conclusions drawn are misleading and often conflicting.

Impact on the Quality of Life

Some studies have shown that both the presence of excessive SDB and daytime hypersomnia, although less SAHS-specific in the elderly, can impair the patient’s quality of life. Stepnowsky et al. observed that the impact on the quality of life was evident from an AHI > 15, while Baldwin et al. showed that this impact was significant at a cut-off point above 30, using a quality of life questionnaire (SF-36) in the Sleep Heart Health Study, which was carried out on 6,440 people with an average age of more than 63 years (though not exclusively elderly). Similarly, these authors observed that the presence of daytime hypersomnia (Epworth > 11) was also associated with a decrease in all the sections of the questionnaire. In this regard, a recent study on 198 patients with suspected SAHS, and on those where this diagnosis was confirmed (98 of them over 65) using the Epworth questionnaire score (approximately 12 points) and AHI (between 37-40), revealed that the variables that significantly affected the quality of life of young people were: hypersomnia, age, BMI and AHI (in order of importance). Nevertheless, in the elderly the impact of comorbidities and age were far superior to the variables related to SAHS, leaving hypersomnia in fourth place, although significant decreases occurred mainly in the physical section of the quality of life questionnaire. Other studies however have shown no such relationship. Recently, in a study carried out in 2,849 male patients with a mean age of 76.4 years, Kezirian et al. observed no association between the values in the Pittsburgh questionnaire (PSQI) or the FOSQ questionnaire and AHI, after adjusting the results for total sleep time.

Cardiovascular Impact

Of the studies examining the impact of SAHS in the cardiovascular field, very few are conducted exclusively on elderly patients. From a
physiological point of view, Chung et al.\textsuperscript{40} observed that in people with SAHS over the age of 60, the AHI was correlated with C-reactive protein (CRP) levels, a known cardiovascular risk factor.\textsuperscript{61} Similarly, in a group of 851 patients (58.5% women) with a mean age of 68 years, Roche et al. recently observed a significant correlation between the CRP value and the presence of an oxyhaemoglobin desaturation index (ODI) > 10, but not with AHI. This finding supports the importance of intermittent hypoxaemia in this correlation.\textsuperscript{62} Moreover, in a large cohort of elderly patients (n = 1,037) aged 68-96 years that was drawn from the cohort of the Sleep Heart Health/ Cardiovascular Health Study, Nieto et al.\textsuperscript{40} observed that both the AHI and hypoxaemia, especially the latter, are associated with endothelial dysfunction, which was quantified by analysing the brachial artery flow, although this relationship was particularly strong in those under the age of 80. This shows that although there is some biological plausibility to explain a possible link between SAHS and excessive cardiovascular events among the elderly, it is possible that there is some protection or resistance factor in older people with regard to apnoea and hypoxaemia, as suggested by some authors attempting to explain the lower mortality caused by SAHS among the elderly\textsuperscript{44,65} and confirmed in animal studies.\textsuperscript{66} In the field of clinical studies conducted exclusively in elderly patients, some authors have observed that the presence of central SDB (but not obstructive) was associated with worse cardiac systolic function and atrial fibrillation, whereas obstructive events were associated with a greater intensity of night ventricular extrasystoles.\textsuperscript{72-74} Finally, in a study conducted on 70 people (57% women) with a mean age of 74.9 years, Endeshow et al. observed that the presence of an AHI > 15 was associated with an increase in the systolic and diastolic night blood pressure,\textsuperscript{18} after adjusting the AHI for various misleading variables. Some major studies examine the cardiovascular impact of SAHS and do not exclude elderly patients.\textsuperscript{60-71} In general, these studies show that there is an increase in cardiovascular risk even in patients with mild-moderate SAHS, although this risk is more pronounced in younger patients,\textsuperscript{33} as shown by a posteriori analysis of some of these studies. There are also studies examining the relationship between SAHS and stroke, as the latter occurs mainly in the elderly. Following a 6-year follow-up, Munoz et al.\textsuperscript{49} observed 394 people between 70-100 years old, noting that the presence of an AHI > 30 represented an adjusted stroke risk that was 2.5 times higher. The results are similar to those of cross-sectional and longitudinal studies that do not only exclude elderly patients, but in which the elderly constitute the predominant age range.\textsuperscript{45,46,34-76} However, other authors observe no significant relationship between excessive SDB or SAHS symptoms and a higher frequency of cardiovascular events or hypertension when analysing large cohorts of patients whose age is over 60.\textsuperscript{77,79}

Impact on Mortality

The overall mortality analysis is a key factor when assessing the impact of SAHS on the elderly. So far, however, the results offered by the literature are contradictory. As recent major studies on mortality in SAHS do not include patients older than 65,\textsuperscript{80,81} perhaps a more fundamental study is the one headed by Lavie et al.,\textsuperscript{64} which was conducted on 14,583 men between 20-95 years old, who were observed for more than 4.5 years. The authors found that the presence of an AHI > 30 (with respect to people with an AHI < 10) had an excess mortality that was identifiable in men under the age of 50, adjusted for age and BMI. A surprising fact in this study was that people over the age of 70 had a mortality rate that was even lower than that of age-matched people from the general population. The authors attribute these facts to the existence of a protective mechanism of the effects of apnoea in older people.\textsuperscript{64,65,71} However, we cannot rule out that the difference in mortality is due to various limitations in the methodology of the studies, i.e. bias with regards the severity of the condition, different levels of compliance with CPAP treatment or changes in the number of SDB over time, since people are observed for years as part of these studies and the value of AHI is taken at baseline to generate the conclusions after years of follow-ups. Other studies have found similar results, such as He et al. in their famous study on mortality, one of the pioneers on the subject. They observed an excess mortality among people with an AHI > 20, although this was age-dependent since it was only significant in people under the age of 50.\textsuperscript{83} More recent studies show that excess mortality was observed in people with excessive SDB.\textsuperscript{70,83,84} Nevertheless, a posteriori analysis suggests that this mortality was mainly found in younger people who did not follow CPAP treatment.\textsuperscript{70} Other authors have reached different conclusions, albeit with smaller-scale studies. For instance, in a study conducted on 426 people who were observed for 11 years, Ancoli-Israel et al.\textsuperscript{85} observed that those between 65-95 years (mean age at baseline was 72.5 years) with an AHI > 30, had a higher mortality rate – although the AHI was not a direct mortality factor, but probably the excessive cardiovascular disease that it induced, which was directly related to this excess mortality. Moreover, for five years, our working team observed a group of 223 patients who had suffered a stroke, with a mean age of over 73 years. We noted that patients with untreated SAHS (AHI > 20) had a mortality rate between 1.6-2.7 times higher than that of patients without SAHS or those with SAHS who received effective CPAP treatment.\textsuperscript{48} Similar results were found by Parra et al. who, during a period of two years, observed 161 patients, with a mean age of 72 years and who had suffered a stroke. They noticed that for each increase of 1 point in the AHI, there was a 5% increase in mortality.\textsuperscript{46}

In summary, current evidence suggests that while excessive SDB (especially an AHI > 30) implies an increase in general mortality (particularly cardiovascular), this effect is lower in older people, in whom the excess mortality disappears. While we cannot exclude methodological biases, especially with regards severity of the condition, some authors have pointed out that the explanation could be that the cardiovascular effects of SAHS predominantly affect young people, which could result in this excess mortality. Therefore, older people would survive with a lower mortality rate and would be somewhat resistant to the damaging action of apnoea, hypopnoea and sleep disruption caused by SAHS.

Neurocognitive Impact

Although the presence of SAHS has been shown to present adverse effects on different neurocognitive parameters in the general population, which improve following CPAP treatment (psychomotor follow-up, deficit in the degree of care, implementation of tasks, motor skills, construction skills and speed response to stimuli),\textsuperscript{57,88} the results of the literature are contradictory when studying the specific older age range. This is because both of the deterioration of these functions caused by age and the presence of neurocognitive diseases in the elderly are sometimes variables that cause insuperable confusion. Following a 3-year follow-up of 92 people over the age of 50, Phillips et al.\textsuperscript{85} observed that the presence of an AHI > 5 did not produce significant cognitive impairment, although the negative results of this study could be attributed to a poor follow-up time and a very low cut-off point in the AHI. On the other hand, Cohen-Zion et al.\textsuperscript{80} observed in 140 elderly people that the AHI was associated with cognitive impairment, which was objectified using the Mini-Mental questionnaire. Concerning cognitive impairment, we need to mention two diseases and their relationship with the elderly with excessive SDB: dementia (particularly Alzheimer’s disease) and depression. Both diseases are very common in the elderly because they can coexist in the same person.\textsuperscript{82,83} Furthermore, notwithstanding prevalence, some authors have found a relationship between both diseases - with a plausible pathophysiological basis discovered in
sleep fragmentation and intermittent nocturnal hypoxia. In this regard, some studies have noted a relationship between the severity of SAHS and the presence of Alzheimer’s disease, with a negative impact on memory, especially in patients carrying the APOE epsilon4 genotype. Finally, although in the elderly the diagnosis of depression or depressive symptoms has been associated with the presence of excessive SDB, to date there are no studies with a sufficient level of evidence to confirm this relationship. If we analyse together the results of the literature, the underlying idea could be that the relationship between the AHI and a negative impact on the neurocognitive area in elderly people may result from an AHI > 30, or an even a lower rate if it is accompanied by pathological hypersomnia.

Economic Impact

Regardless of the important questions concerning the impact of SAHS in elderly people, Tarasiuk et al. demonstrated that patients with SAHS incurred a pre-diagnosis health expenditure 1.8 times higher than those without SAHS. They did so by comparing 158 elderly people (67-89 years) with 1,166 younger control patients (40-64 years) at a 1:1 ratio of patients with and without SAHS during a 2-year follow-up. The study also showed that the elderly with SAHS incurred a cost that was 1.9 times greater than that of young people with SAHS. A multivariate analysis showed that much of the expenditure of the elderly with SAHS was associated with cardiovascular disease and taking psychotropic medication.

Treatment options

As previously mentioned, while generally any scientific evidence in the study of SAHS in the elderly is scant, it is of particular concern in relation to therapeutic aspects. Although the first CPAP treatment was prescribed more than twenty-five years ago – and the fact that in Spain, one in four sleep studies are performed in people over the age of 65, with more than 70% of them treated with CPAP – there is no clinical trial that demonstrates the effectiveness of this treatment on key aspects related to the symptoms or effect on sleep structure in elderly patients. Therefore, current decisions are based on evidence from the extrapolation of the results of clinical trials on the effectiveness of CPAP treatment in young adults or on studies in which the elderly are also involved, but without a specific analysis of this particular age group. Therefore, the Spanish SAHS Consensus, which was published in 2005, agrees that age should not be in itself an obstacle for CPAP treatment in elderly patients with SAHS. While no studies appear with a sufficient level of evidence to the contrary, this treatment should always be administered within reasonable limits.

Randomised Controlled Trials

For a detailed examination of the relevant information provided by the literature on the effect of CPAP treatment in older people, we carried out a search in the Medline database with the following terms: “CPAP or continuous positive airway pressure” in the manuscript title, thus restricting the search to randomised clinical trials involving, exclusively or partially, people of at least 65 years of age, with a subsequent manual selection of those relevant to this review. In general we noticed the lack of inclusion of people aged 60-70 in clinical trials. Within the group of studies that included this age range, there were a greater number of them studying the effect of CPAP on different aspects of cardiovascular disease over the last decade. On the other hand, the studies related to the effectiveness of CPAP treatment on symptoms related to SAHS dated back to a few years earlier. In the end, 38 relevant clinical trials were identified of which 8 used pills as the control group, 22 used sham-CPAP (at pressures below 2 cm H₂O), 7 compared CPAP with a conservative treatment and 1 included healthy subjects as the control group. The overall result could be that in relation to the effect on clinical variables and sleep structure, in general, CPAP treatment significantly decreased the number of SDB, resulting in a normalisation of the sleep structure with a decrease in phase 1 of shallow sleep and increased deep sleep stages. This led to an improvement in the symptoms related to SAHS, especially hypersomnia, except in people whose hypersomnia had not been assessed using objective evidence and in those with mild forms of the disease. The results concerning the effect of CPAP on neurocognitive variables are more controversial. Some studies show improvement with CPAP on variables, such as memory, executive functions, cognitive processes or attention span, while others do not. In this regard, we should note the study by Chong et al. who observed a significant improvement in hypersomnia after a 6-weeks CPAP treatment in 39 patients diagnosed with Alzheimer’s disease and with a mean age of 78 (7.04) years (range [53-91]). These patients also demonstrated good tolerance to the device for approximately 5 hours per night. Regarding the effect on the quality of life, the results are also inconsistent when using the SF-36 questionnaire, a questionnaire on the general quality of life, or the Functional Outcomes of Sleep Questionnaire (FOSQ), which is specific for the impact of hypersomnia, despite the fact that the effect of CPAP on the measurement of hypersomnia was generally positive.

In the analysis of the effect of CPAP on various cardiovascular aspects, there are only 2 studies that were conducted exclusively on patients over 60. Zhang et al. included patients with an age range of 60-74 years. They observed that those with SAHS (an AHI mean of 37 [9.6]) did not show a deterioration of the various analytical variables, among which were haematocrit, blood viscosity, platelet aggregation, blood coagulation and fibrinogen levels, compared with control healthy subjects. Furthermore, in a study conducted on 30 patients with stroke, with an age range of 65-81 years and with an AHI > 30, Hsu et al. found no effect of CPAP treatment on hypersomnia, quality of life and neurological recovery. The patients were randomised to receive CPAP or a conservative treatment for 8 weeks – although the patients’ compliance with the treatment was very poor (an average of 1.3 hours per night). Concerning the rest of the studies, which did not exclude the elderly, the results are uneven. Some studies show decrease in the figures for systolic and/or diastolic blood pressure with CPAP treatment, while others do not observe this effect. In this regard, three Spanish studies were recently completed on the effect of CPAP on various parameters, and they did not exclude elderly patients. Barbe et al. and Duran et al. observed a decrease of approximately 2mmHg in blood pressure, especially in people with good tolerance to CPAP, regardless of symptoms. On the other hand, in a study conducted on a large group of people with a mean age of 64.04 years (range: 34-80 years ) and in acute phase of stroke, Parra et al. observed no significant effect of CPAP treatment on functional recovery, quality of life and death at 2 years. In any case, we should note that the analysis of the distribution of patients by age would be necessary to assess the results properly, in particular those related to the effect of CPAP on hypertension and its impact on subsequent morbidity and mortality in the elderly.

Observational Studies

Similar to clinical trials, there are very few studies analysing the effect of CPAP, exclusively or almost exclusively, in elderly people using observational studies. Most of them refer to subgroups of people suffering from diseases that have an impact especially on the elderly, such as neurocognitive disorders or cerebrovascular diseases. In a small group of patients over 55 years old with SAHS (AHI > 10), Aloia et al. observed that the use of CPAP for 3 months produced an
improvement in some neuropsychological parameters, such as attention span and various psychomotor and verbal skills. On the other hand, Martínez-García et al. observed that despite the impact of SAHS on the quality of life in patients over the age of 65, this was lower than that in younger people. CPAP treatment significantly improved some aspects of the quality of life, mainly through an improvement in hypersonnia, in both older and younger people when compared with normal growth parameters obtained in the general population with the same age and gender. From a cardiovascular point of view, apart from an extensive study conducted by Marin et al. on the positive effect of CPAP treatment on the incidence of fatal and non-fatal cardiovascular events in patients with SAHS with tolerance to CPAP, we wish to mention two studies carried out on a cohort of patients who had suffered a stroke and who had been observed for 2 years and 5 years, respectively. These studies showed that CPAP treatment reduced both the incidence of new cardiovascular events (especially a second stroke) and mortality, reaching figures similar to those of patients without SAHS or with a mild form of the disease.

**CPAP Compliance**

An important aspect of CPAP treatment in the elderly is the level of compliance with the treatment. Elderly patients may present a number of characteristics that have been associated with worse compliance, such as living alone, minor symptoms (especially hypersonnia), fewer skills or alteration of cognitive abilities, comorbidities and neurological deficits. However, the studies conducted have shown that the degree of compliance with CPAP is not worse than that in younger people, even in patients with neurocognitive impairment. On the other hand, Kostikas et al. noted that the necessary blood pressure in older people is on average 2.5mmHg lower for a similar SAHS severity. This perhaps reflects the lower resistance of the expansion of the airway caused by external factors, a lower basic muscle tone or major lung distension. Despite the above-mentioned negative characteristics for compliance, this is probably the cause of compliance similar to that in young people.

**Conclusions**

While complex basic or applied research is admirable and necessary in both the SAHS disease and in other diseases, we should not give up the search for answers to basic issues that have a direct impact on our daily clinical practice. In this sense, discovering what this is and how we should manage the diagnosis and treatment of SAHS in the elderly is an excellent example. On the other hand, obtaining these answers is not particularly complex, because we have the raw material: high number of Spanish elderly people. Moreover, the variables to investigate are the same fundamental or basic variables as in any research study: impact, diagnosis and treatment effect. As recommended by both the Spanish SAHS Consensus and recent legislation on the diagnosis and treatment of SAHS, we should take into consideration some important aspects concerning SAHS in the elderly: always do an anamnesis that includes specific aspects of the patient; do not consider that hypersonnia is an inherent physiological symptom in the elderly, since excessive daytime hypersonnia is always abnormal regardless of the patient’s age; and, do not deny diagnostic or therapeutic methods to patients with suspected SAHS on reasons relating only to the patients’ age (table 3). We should leave the remainder to our common sense, until there is better scientific evidence.

**Conflict of Interest**

The authors affirm that they have no conflict of interests.

### Table 3

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Physiopathology</th>
<th>Higher airway collapsibility</th>
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<tbody>
<tr>
<td>Prevalence</td>
<td>Higher prevalence of respiratory events during sleep</td>
<td>Higher prevalence of SAHS</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Lesser specificity of the typical symptoms</td>
<td>Higher frequency of atypical symptoms</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Shortened methods in younger people without significant comorbidities</td>
<td>Preferable by full PSG</td>
</tr>
<tr>
<td>Impact</td>
<td>Greater neurocognitive impact</td>
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<tr>
<td>Treatment</td>
<td>Increased health costs</td>
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</tr>
<tr>
<td>Prognosis</td>
<td>Problems with alternative treatments</td>
<td>Good tolerance to CPAP</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Lesser impact on mortality</td>
<td>Problems with alternative treatments</td>
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</tbody>
</table>

PSG indicates polysomnography; SAHS, sleep apnoea-hypopnea syndrome.

### References


