The objective of this investigation was to assess the association between the presence of sleep disordered breathing (SDB) and daytime sleepiness, body mass index, hospitalisation, and survival. To this end, a prospective longitudinal study was conducted in the elderly population consisting of 80 patients of either sex over the age of 65 years admitted to a city hospital in Germany without any history of SDB. All patients met the following exclusion criteria: age <65 yr, heart failure, and chronic obstructive lung disease. Baseline anthropometric and cardiorespiratory (one-night portable polygraphic recording) data, and a standardized sleep and sleepiness-questionnaires (Epworth Sleepiness Scale, ESS) were obtained in 1999. A second screening was conducted in 2003. Thirty one women and 34 men completed the follow-up after 3 years. These patients were divided into two subgroups: (i) no clinically relevant SDB and (ii) SDB (apnea-hypopnea index, AHI, ≥5 plus excessive day time sleepiness, ESS, >9). Six men and 3 women fulfilled the criteria of SDB. Thirty three percent of patients with SDB and 20% of patients without SDB died during the follow-up period. Duration of hospital stay was 35 days for the SDB patients and 20 days for patients without it. Body weight and sleepiness did not change significant over the 3-year period between the two cohorts. We conclude that the presence of SDB was associated with a 1.5-fold higher mortality and longer hospital stay in elderly patients over a period of 3 years even in persons without previous history of SDB. Daytime sleepiness was a better predictor than AHI or BMI for death.

**Key words:** elderly, longitudinal cohort study, mortality, sleep-disordered breathing
INTRODUCTION

Obstructive sleep apnea (OSA) is a widespread disease with a strong male predominance characterized by repetitive sleep-induced collapse of the pharyngeal airway. This results in arousals and daytime sleepiness. Young et al (1) estimated that 2% of middle-aged women and 4% of middle-aged men meet the minimal diagnostic criteria for OSA (score of apnea-hypopnea index, AHI, ≥5 and daytime hypersomnolence). The prevalence of OSA in the elderly German population was found 2.5 times higher than that (2). The Cleveland family study (3) found a higher prevalence in patients over 60 years of age, which supports the notion that OSA in the elderly is 2-3 times more frequent than in middle-aged persons. However, a many of the old patient reports satisfactory sleep, which makes the clinical relevance of the disease uncertain, particularly that long-term sequelae in such patients have not been sufficiently analyzed.

In the past it was thought that hypoxemia and arousals from sleep contribute to increased cardiovascular mortality. It is now recognized that the mechanisms are more complex. On the one hand, sleep disordered breathing (SDB) and even heavy snoring, as partial obstruction of the upper airway (4), is a risk factor for cardiovascular and metabolic diseases, including hypertension, left ventricular hypertrophy, arteriosclerosis, endothelial dysfunction, stroke, heart failure, cardiac arrhythmias, sudden death, obesity, and the metabolic syndrome. On the other, SDB may occur as a result of several medical conditions (including obesity, chronic heart failure, and menopause) and then contributes to cardiovascular morbidity associated with these conditions. It is proven that SDB exerts significant effects on the autonomic nervous system, systemic hemodynamics, cardiac function, oxidative stress, endothelial function, inflammation, glycemic response, and coagulation (5). Nevertheless, it is unclear whether the relation between SDB and cardiovascular disease is independent of confounding risk factors such as hypertension, hyperlipidemia, overweight, diabetes mellitus, and smoking.

Many investigators consider SDB an independent cardiovascular risk factor, but it has yet to be scientifically proven. In general, the risk impact of SDB alone seems to be rather low. However, due to the high prevalence of SDB and its strong association with other coexisting risk factors, the syndrome has considerable implication for public health. Patients with known cardiovascular disease and coexisting SDB constitute a high risk population prone to excess mortality. This may be exemplified by a sleep study of Parra et al (6) who found in 161 elderly patients (mean age 72 ±9 yr) with first ever stroke that the number of SDB events is a powerful predictor of a 2-year mortality.

Sleep disturbances in elderly people are often thought to be normal consequences of old age and may be underdiagnosed and undertreated. It is still uncertain whether SDB is the same condition in both middle-aged and older populations. There is little information on the association of mild or asymptomatic SDB and hypersomnolence with clinically relevant outcome
parameters. Clinic-based epidemiologic studies are needed to get a closer look at older people with SDB and the importance of the disease for mortality.

Our current work describes a group of 40 elderly women and 40 men matched by age and weight who were originally studied in 1999 to assess gender differences. Due to the presence of SDB, the patients were followed-up for 3 years to observe the development of sleepiness, body mass index, hospitalisation, and survival. The patients underwent a cardiorespiratory polygraphy during one night. A standardized sleep and sleepiness-questionnaires was administered and anthropometric data were measured twice within three years.

MATERIAL AND METHODS

The study was conducted in accordance with the Declaration of Helsinki for Human Research and was approved by an institutional Ethics Committee.

Study subjects

The study was originally conducted using a matched-pair approach. The patient population consists of 80 aged participants: 40 women and 40 men admitted to the Department of Internal Medicine in a city hospital in Germany. They had no history of SDB. Patients had to be older than 65 years and they were balanced for age, sex, and body mass index. The group was quite heterogeneous in terms of presenting complaints. None of the patients were admitted because of snoring, day time sleepiness, observed periods of cessation of breathing, insomnia or suspected parasomnia. Most patients were admitted for treating diabetes. All patients met the following exclusion criteria: age <65 yr, heart failure, chronic obstructive lung disease. All 80 subjects completed the first part of the study in 1999.

Measurements

Anthropometric measurements were taken. The patients were studied with overnight polygraphy. Breathing was assessed by monitoring chest and abdominal wall movements using a strain gauge pneumograph. Nasal and oral flow were measured using thermistors. Arterial oxygen saturation was measured using a pulse oximeter. All variables were recorded simultaneously. Sleep recording was scored referring to standard criteria. SDB was quantified using the AHI. Indices of overnight desaturation were additionally taken. The exact definition of a relevant OSA is not easy; hence making robust estimates of OSA prevalence is difficult. A simple approach using the sleep study indices as the only definition criteria overestimates the clinically relevant events. Therefore, the AHI in conjunction with an index of sleepiness was used. The Epworth Sleepiness Scale (ESS) was utilized to assess excessive daytime sleepiness. A sleep questionnaire (7) was distributed to all participants.

Table 1. Demographic baseline characteristics at the beginning of the study in 1999.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>80</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Mean Age (yr)</td>
<td>74.1 ±6.3</td>
<td>73.3 ±4.8</td>
<td>74.9 ±7.5</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.8 ±4.6</td>
<td>26.8 ±4.7</td>
<td>26.8 ±4.5</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>6.9 ±2.4</td>
<td>6.5 ±2.1</td>
<td>7.3 ±2.8</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>22.9 ±11.3</td>
<td>23.0 ±1.7</td>
<td>22.8 ±20.8</td>
</tr>
</tbody>
</table>
Follow-up

The second examination was conducted 3 years later. Each patient was sent a follow-up questionnaire that included questions regarding the current state of health, hospitalizations, and treatment of sleep disorders and accompanying diseases since the baseline assessment. Sleep and sleepiness and other pertinent parameters were assessed in the manner described above. Attempts were made to telephone the patients who had not responded to the questionnaires sent. The exact date of death was recorded whenever possible.

Statistical analysis

We analyzed the association between sleep apnea and the development of sleepiness, BMI, hospitalization and death with univariate analysis, without any adjustment for confounding variables. The primary end point was death from any cause. Data are presented as mean ±SE. The Mann-Whitney U test and Wilcoxon signed rank test were used to assess differences in the two groups. P<0.05 was considered significant.

RESULTS

In 1999, a total of 34 from 80 patients (43%) (M/F 1/0.7) fulfilled the criteria for OSA. The group mean apnea index was 7.5 ±7.1 and the AHI dichotomized with respect to gender amounted to 4.8 ±3.9 in women and 10.2 ±11.4 in men (Table 2). The frequency and intensity of daytime hypersomnia (ESS Score) was 6.8 ±3.5 in men and 6.7 ±2.7 in women. Using the usual definition of OSA (AHI ≥5 and ESS >9) 11% of the participants (6 men and 3 women) fulfilled the criteria of a clinically relevant OSA (Fig. 1). BMI in patients with OSA did not differ significant from patients without it (Table 3).

Table 2. AHI in elderly men and women at the beginning of the study in 1999.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apnea index</td>
<td>1.7 ±2.5</td>
<td>0.6 ±1.4</td>
<td>2.8 ±4.1</td>
</tr>
<tr>
<td>AHI</td>
<td>7.5 ±7.1</td>
<td>4.8 ±3.9</td>
<td>10.2 ±11.4</td>
</tr>
<tr>
<td>AHI ≥5</td>
<td>34 (43%)</td>
<td>14 (35%)</td>
<td>20 (50%)</td>
</tr>
<tr>
<td>AHI ≥10</td>
<td>15 (18%)</td>
<td>3 (8%)</td>
<td>12 (30%)</td>
</tr>
</tbody>
</table>

Table 3. Demographic baseline characteristics of the patients with SDB and without SDB (controls) at the beginning of the study in 1999.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total</th>
<th>SDB Patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>64</td>
<td>8</td>
<td>56</td>
</tr>
<tr>
<td>Mean age (yr)</td>
<td>73.8 ±6.7</td>
<td>69.9 ±4.1</td>
<td>74.4 ±6.4</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>53.8</td>
<td>75.0</td>
<td>51.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.8 ±4.4</td>
<td>28.1 ±6.8</td>
<td>26.9 ±4.4</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>6.6 ±2.3</td>
<td>7.7 ±2.3</td>
<td>6.5 ±2.2</td>
</tr>
<tr>
<td>Sleep apnea (AHI)</td>
<td>7.5 ±9.1</td>
<td>24.8 ±10.7</td>
<td>5.1 ±5.4</td>
</tr>
<tr>
<td>Sleepiness (ESS)</td>
<td>5.2 ±3.3</td>
<td>8.4 ±2.3</td>
<td>4.8 ±3.2</td>
</tr>
</tbody>
</table>
Thirty one women and 33 men completed a follow-up and were evaluated after 3 years. The participants were divided into two subgroups: SDB ($AHI \geq 5 + ESS > 9$) and no clinically relevant SDB (controls) (Table 4). The two subgroups were similar in terms of sex and BMI. Patients with SDB were 7 years junior and had a higher HbA1c. As expected, the prevalence of hypertension and diabetes mellitus was higher in the subgroup with sleep apnea.

Thirty three percent of the patients with SDB and 19.6% without it died during a 3-year follow-up period. There was a total of 14 deaths during the follow-up, yielding an average yearly mortality rate of 11% in the subgroup with SDB and 6.5% in the controls.

Duration of hospital stays was 35 days in patients with SDB and 20 days in patients without it. Due to a high variability, the difference was insignificant. Body weight did not change over the follow-up in either subgroup. Day time sleepiness was significantly associated with SDB, but no change in sleepiness could be observed during the follow-up either in patients classified as having SDB or in the controls (Fig. 2). The presence of SDB was a predictor of neither weight gain nor progressive daytime sleepiness. On average, the AHI in patients who died was higher than that in those who survived. Moreover, daytime sleepiness was associated with increased mortality (Table 5). These differences were statistically significant.

**Table 4.** Results of the patients with and without SDB after a follow-up of three years.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total</th>
<th>SDB Patients</th>
<th>Controls</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>21.9%</td>
<td>37.5%</td>
<td>19.6%</td>
<td>0.26</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>21.4 ±20.4</td>
<td>35.6 ±26.6</td>
<td>19.8 ±19.0</td>
<td>0.11</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.5 ±4.5</td>
<td>26.5 ±3.7</td>
<td>27.6 ±4.5</td>
<td>0.60</td>
</tr>
<tr>
<td>Sleepiness (ESS)</td>
<td>5.2 ±3.2</td>
<td>8.4 ±2.3</td>
<td>4.8 ±3.2*</td>
<td>0.02</td>
</tr>
</tbody>
</table>

![Fig. 1. Elevated AHI and clinically relevant SDB in elderly men and women at the beginning of the follow up study in 1999.](image)
DISCUSSION

Epidemiological data show an increase in sleep disorders incidence in the elderly. Elderly patients are less likely to be symptomatic, but adverse cardiovascular consequences may be more serious in older patients. In this study we followed a clinic-based sample of elderly individuals without a history of SDB, heart failure, or chronic lung disease, who were originally studied in 1999 for mortality. Our results demonstrate that, despite a low rate of preexisting morbidity, SDB was associated with a 1.5-fold increase in the incidence of death from any cause. The difference did not achieve significance, due possibly to a small number of the subjects involved. Whether the association is independent of other cardiovascular and cerebrovascular risk factors, including hypertension, is unclear. The follow-up period may have not been sufficiently long to declare the elevated death rate, but many of our patients may have had a long history of untreated SDB.

Epidemiological studies of outcomes are particularly important in assessing the relevance of untreated SDB for the society as well as for the sufferer. Although findings are far from conclusive, population-based and clinic-based studies have linked SDB with cardiovascular and all cause morbidity. Some of these studies have provided support for a link between snoring or objectively measured SDB and myocardial infarction, angina, coronary heart disease, stroke,

Table 5. Relationship between death and baseline characteristics measured at the beginning of the study in 1999.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total</th>
<th>Dead</th>
<th>Alive</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>64</td>
<td>14</td>
<td>50</td>
<td>-</td>
</tr>
<tr>
<td>Mean age (yr)</td>
<td>77.8 ±6.7</td>
<td>82.9 ±7.3</td>
<td>76.7 ±6.0</td>
<td>-</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>53.8%</td>
<td>85.7%</td>
<td>45.1%</td>
<td>-</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.5 ±4.5</td>
<td>26.6 ±3.6</td>
<td>27.5 ±4.5</td>
<td>0.84</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>6.6 ±2.3</td>
<td>7.2 ±2.4</td>
<td>6.5 ±2.3</td>
<td>0.36</td>
</tr>
<tr>
<td>Sleep apnea (AHI)</td>
<td>7.5 ±9.1</td>
<td>14.3 ±12.6</td>
<td>5.7 ±6.7*</td>
<td>0.03</td>
</tr>
<tr>
<td>Daytime sleepiness (ESS)</td>
<td>5.2 ±3.3</td>
<td>7.9 ±3.7</td>
<td>5.2 ±3.3*</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Fig. 2. Results of the patients with and without SDB after a follow-up of three years.
and mortality, especially in younger SDB patients or those with a preexisting cardiovascular disease.

**Mortality in middle-aged patients with SDB**

In a prospective study of 1620 middle-aged patients from Lavie et al (8) age, body mass index, hypertension, and apnea index were all shown to be independent predictors of early deaths. Similarly, He et al (9) demonstrated in 385 male patients a decreased survival in patients with untreated OSA with an apnea index of >20/h. In another recent study, in an unadjusted analysis, OSA was significantly associated with stroke or death from any cause (hazard ratio 2.24) (10). After adjustment for age, sex, race, smoking status, alcohol-consumption status, BMI, and the presence or absence of diabetes mellitus, hyperlipidemia, atrial fibrillation, and hypertension, the syndrome retained a significant association with stroke or death. In a study of 62 patients suffering from coronary artery disease, univariate predictors of cardiovascular mortality were respiratory disturbance index (RDI) (P=0.007), OSA (P=0.014), age at baseline (P=0.028), hypertension at baseline (P=0.036), history of never smoking (P=0.031), and digoxin treatment during the follow-up period (P = 0.013). In a multiple conditional regression model, RDI still remained as an independent predictor of cardiovascular mortality (11).

Looking at the cause of death in untreated OSA patients, the majority of deaths were caused mainly by vascular disorders, which included coronary artery diseases and cerebrovascular events. Patients with a higher RDI, in general, have more cardiovascular risk factors than those with lower indexes (12). This may be one of the reasons why groups of elderly patients with a low medium AHI or RDI do not necessarily show differences compared with healthy controls.

**Mortality in elderly patients with SDB**

There is little information on the associations among mild or asymptomatic SDB, hypersomnolence, duration of hospital stay, and mortality, especially in the elderly. In our study we found an unexpectedly high mortality rate in the group with SDB, although the difference was insignificant. Our subjects were over 72 years old and AHI was rather low. Increased AHI at baseline was associated with increased mortality.

Mortality studies of sleep apnea patients showed a maximum risk of dying in younger patients and an age-decline in relative mortality often reaching nonsignificant levels in patients older than 50 years. Lavie and Lavie (13) hypothesized that the age-decline mortality risk in sleep apnea could be explained by cardiovascular and cerebrovascular protection due to ischemic preconditioning resulting from nocturnal cycles of hypoxia-reoxygenation. Comparison of mortality rates in 14589 males with sleep apnea with those in the general population revealed that only males aged below 50 showed an excess mortality rate. All-cause mortality rate was 5.55/1000 patient years, increasing with apnea
severity (14). Ancoli-Israel et al (15) showed in 233 elderly patients in nursing homes an association between OSA and decreased survival in elderly women but not in men. In a population-based probability sample, elderly individuals (n=426, mean age 72.5 years) were followed by the same investigators in 1996 for mortality (16). Those individuals with RDI ≥30 had significantly shorter survival, but the RDI was not an independent predictor of death.

Bliwise et al (17) found no difference in mortality in a group of treated and untreated elderly patients with OSA compared with control subjects. A four year follow-up of 163 non-demented retired old people found that the RDI was not a predictor of mortality in a group where the prevalence of high levels of RDI was low. Significant predictors of mortality were a history of hypertension, Parkinson's disease and cancer (18). In contrast, Parra et al (6) reported that SDB is an independent prognostic factor related to mortality after a first episode of stroke in elderly patients with preexisting cardiovascular disease. Ancoli-Israel et al (19) reported that survival in elderly patients with OSA and no heart failure is the same as that in those with neither disorder, but patients with heart failure have more severe sleep apnea than those with no heart disease. Taken together, data suggest that coexisting SDB increases the severity and rate of fatal and nonfatal cardiovascular events and hinders recovery, which is probably independent of age.

**Day time sleepiness and mortality**

SDB is associated with excessive sleepiness in middle-aged and older adults. Day time sleepiness is correlated with AHI, but not limited to those with clinically apparent sleep apnea (20). In our study, patients with SDB had a more than two-fold elevated sleepiness score, which may be an independent predictor of death, apart from age or AHI. The difference was significant. We found a good correlation between daytime sleepiness and SDB, diagnosed three years before.

In 5888 older men and women it was shown that daytime sleepiness was the only sleep symptom that was significantly associated with mortality in both men and women. Frequent awakenings, early morning awakening, and snoring were not associated with a significantly increased risk of mortality. RDI was not measured (21). Lindberg et al (22) provided additional prospective data on the mortality associated with snoring and daytime sleepiness, the two hallmark symptoms of SDB. In a 10-year follow-up of 3100 men, 213 died and 88 of the deaths were due to cardiovascular disease. Daytime sleepiness, but not snoring without excessive daytime sleepiness, was associated with an increased mortality rate (22). Also in the Honolulu Heart Program cohort study daytime sleepiness was assessed in 2905 older Japanese-American men and was associated with a higher prevalence of heart disease and with cognitive impairment and dementia, chronic obstructive pulmonary disease, and diabetes. Whether it also is an indicator for sleep apnea in this age group remains unclear, because polysomnography was not performed.
In a 7.5-year long study performed on 322 OSA patients, there was a significant difference between the alive and dead patient groups in the Maintenance of Wakefulness Test. The test results, adjusted for age, were shortened in dead patients (21 ±10 min vs. 28 ±11 min in alive patients) (24).

**Hospitalizations and costs**

Our results demonstrate the role of SDB in frequency and duration of hospital admissions. It was reported in a study of 1998 that OSA patients require more hospitalizations; they had 1118 or 6.2 nights per patient in hospital vs. 3.7 nights per non-OSA patient over a 10-year period (25). In 1996, Kryger et al (26) demonstrated that patients with OSA had 251 nights in hospital, compared with 90 nights for a control group over a 2-year period (26). In a comparable way, Tarasiuk et al (27) found that health-care utilization in OSA patients was 1.7-fold higher due to more hospitalization days, consultations, and cost for drugs, particularly those for the cardiovascular system (27). Undiagnosed sleep apnea leads to a roughly 2-fold increase in medical expenses (28). Treating the disease results in a decrease in these excess costs (29).

**Treatment**

Marti et al (30) found a rise in mortality in patients with untreated OSA compared with the general population, whereas mortality in those treated did not differ significantly from that in the general population. Patients <50 yr of age show a greater mortality rate (30). In a retrospective study, Partinen et al (31) reported decreased 5-year survival in 127 OSA patients treated with weight loss compared with 71 patients treated by tracheostomy. However, Gonzalez-Rothi et al (32) found no difference in mortality between treated and untreated patients with OSA and a group of control patients. Acceptance of and compliance with CPAP treatment in selected elderly patients can be as good as in younger patients, with remarkable effectiveness in terms of improvement in daytime sleepiness and cognitive function.

In conclusion, our study underscores that the presence of sleep disordered breathing is associated with a 1.5-fold higher mortality and longer hospital stay in elderly patients over a period of 3 years even in persons without any previous history of such disorders. Daytime sleepiness is a stronger predictor than AHI or BMI for death.

**REFERENCES**


32. Gonzalez-Rothi RJ, Faresman GE, Block AJ. Do patients with sleep apnea die in their sleep? *Chest* 1988; 94: 531-538.


Author’s address: C. Hader, Kliniken St. Antonius, Akademisches Lehrkrankenhaus der Heinrich-Heine-Universität Düsseldorf, Zentrum für Innere Medizin-Schwerpunkt Pneumologie, Carnapstrasse 48, D-42283 Wuppertal, Germany; e-mail: claus.hader@antonius.de