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Original Article

Sleep disordered breathing in community dwelling elderly: Associations with cardiovascular disease, impaired systolic function, and mortality after a six-year follow-up

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ABSTRACT

Introduction: Sleep disordered breathing (SDB), cardiovascular disease (CVD) and impaired cardiac function are common in elderly people. We investigated the association of SDB and mortality in a community dwelling elderly population, considering CVD and objectively measured impaired cardiac function have been poorly studied thus far.
Aim: To investigate whether SDB is a factor that affects mortality in elderly people, with a focus on those with CVD and/or signs of impaired cardiac function.
Methods: A prospective cohort design was used and 331 community dwelling elderly aged 71–87 years underwent one-night polygraphic recordings in the subjects' homes. CVD and systolic function were objectively established. Mortality data were collected after 6 years.
Results: In the total population there were no significant associations between mortality and SDB. In those with CVD and impaired systolic function, as measured by NT-proBNP, oxygen desaturation index (ODI) $\geqslant$10 was associated with mortality. The hazard ratio of 3.0 (CI 95% 1.1–8.6, $p = 0.03$) remained statistically significant after adjustments for age, gender, diabetes and plasma values of NT-proBNP.
Conclusion: SDB in community dwelling elderly has no overall association to mortality irrespective of degree of SDB. However, hypoxic events (i.e., ODI $\geqslant$10) were associated with mortality in the group who had CVD in combination with impaired systolic function.

1. Introduction

Sleep disordered breathing (SDB), characterized by repeated cessations in breathing during sleep, affects approximately 9% and 4% of middle-aged men and women, respectively, and 25% of persons older than 65 years [1–3]. SDB may cause nightly decreases in oxygen saturation (i.e., intermittent hypoxia) and increased sympathetic activity, which might contribute to cardiovascular stress [4,5]. Large-scaled epidemiological studies have shown SDB to be independently associated with hypertension [6–8], as well as to heart failure (HF) and stroke [9]. A number of studies with samples recruited at sleep clinics or hospitals have also shown SDB to be an independent predictor of mortality [10–14]. The importance of SDB cannot be generalized to the general population based on these studies. However, two recent community based studies, including only middle aged men and women, showed that SDB was independently associated with mortality [15,16]. Despite the high prevalence of SDB in the elderly its association with mortality has not been well studied. Mant et al. followed 163 non-demented elderly village residents for 4 years [17]. Their data could not establish SDB to be independently associated with all-cause mortality. However, the study reported that deaths were more frequent in people with moderate/severe SDB and a history of hypertension, but due to the small sample size they could not test this interaction effect. Ancoli-Israel et al. followed 426 elderly community residents for almost 10 years [18]. Those with severe SDB had shorter survival, but the effect on mortality was not independent. CVD combined with higher age

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and pulmonary disease were independent predictors of death in a Cox proportional hazards analysis. Data regarding CVD were collected by patient interviews but not objectively verified [18].

SDB is known to be common among people with impaired systolic function and heart failure [3]. But to diagnose heart failure is difficult, so when evaluating the association of SDB to mortality in the elderly it is important to have objective data (e.g., Doppler echocardiography or natriuretic peptides) regarding cardiac function besides subjective symptoms/signs of the patient. To our knowledge no such studies have been performed in an elderly community-dwelling population. The aim of this study was therefore to investigate whether SDB is a factor that affects prognosis in elderly people, with special focus on those with a CVD and/or signs of impaired cardiac function.

2. Methods

2.1. Sample

The patient population was derived from the CoroKind study and has been described previously [3,19]. In brief, the major aim was to evaluate the prevalence of HF among community dwelling elderly. The study took place from year 1998 to year 2000. All included subjects were aged 65–82 years and lived in a rural community with 10,300 inhabitants in southeast Sweden. All inhabitants in the age span mentioned above were invited to clinical and echocardiographic examinations. Of 1130 individuals, 876 agreed to participate (participation rate 78%). From January 2003 to June 2005 the cohort was again contacted and invited to renewed clinical and echocardiographic examinations. A total of 675 subjects agreed to participate. The reasons for not participating were death (12%), having moved to nursing homes or other parts of Sweden (3%), declination (7%) or not showing up (1%). Out of the 675 participants investigated a total of 346 subjects (participation rate 51%) also agreed to have their breathing pattern during sleep recorded. The data in the present study are from those 346 participants who had both their systolic cardiac function as well as their sleep respiratory patterns investigated. Those participating in the sleep study did not differ regarding gender, CVD, diabetes, body mass index (BMI), smoking, and plasma values of N-terminal fragment of proBNP (NT-proBNP) from those who did not. But sleep study participants had more respiratory disease (asthma or chronic obstructive pulmonary disease) (17% vs. 12%, $p = 0.04$), less hypertension (73% vs. 82%, $p = 0.007$) and less left ventricular ejection fraction (LVEF) <50% (17% vs. 27%, $p = 0.002$) compared to non-participants.

2.2. Baseline assessment

Every participant was examined by an experienced cardiologist (UA), who took the patient's history and performed a clinical examination. The examination included electrocardiogram, measurement of blood pressure, body mass index, and auscultation of the heart. Doppler echocardiographic (Accuson XP-128c) examinations were performed with the patient in the left-supine position. LVEF was determined semiquantitatively and LVEF $\geqslant$50% corresponded to normal systolic function, whereas LVEF <50% corresponded to an impaired systolic function. Hypertension was defined as a previous diagnosis or a blood pressure of more than 140/90 mm Hg. Ischemic heart disease (IHD) was defined if the participants had a history of angina pectoris, previous myocardial infarction or coronary artery by-pass surgery. TIA/stroke was defined if the participants had a diagnosis of TIA or stroke. Diabetes mellitus was defined as ongoing treatment for diabetes or a fasting blood glucose concentration $\geqslant$7 mmol/L. A respiratory disease was established if the participant had a diagnosis or was undergoing treatment for chronic pulmonary disease or asthma. Blood sampling of the NT-proBNP was drawn while the patients were fasting, sitting, and after resting for 30 min. NT-proBNP was measured using an electrochemiluminescence immunoassay (Elecsys 2010, Roche Diagnostics, Mannheim, Germany).

Sleep respiratory recordings were performed unattended for one night in the participants' home using the Embletta Portable Diagnostic System (ResMed Trollhättan, Sweden) [20,21]. Recordings included nasal air flow pressure, posture and body position, abdominal and thoracic movements, pulse, and oxygen saturation (SaO_2). Apneas, hypopneas and SDB severity were scored manually according to American Academy of Sleep Medicine Task Force guidelines [22]. A hypopnoea was defined as $\geqslant$50% in reduction airflow for $\geqslant$10 s accompanied by $\geqslant$4% desaturation. Absence of SDB was defined as an apnea–hypopnea index (AHI) <5; mild SDB was defined as an AHI 5–15; moderate SDB as AHI 15–30; and severe SDB as AHI >30. Onset and end of the probable sleep period were determined with the combination of the recorded breathing pattern, posture, movements, and information about the subject's self-estimated sleep onset and morning awakening. All recordings were scored by the main researcher (PJ). The study protocol was approved by the ethics committee at the faculty of health sciences, University of Linköping, Sweden, in accordance with the provisions of the Helsinki declaration.

2.3. Mortality follow-up

Death certificates were collected from the National Board of Health and Welfare, Stockholm, Sweden. No patient was lost during follow-up.

2.4. Data analysis

Categorical variables are presented as numbers and percentages and were analyzed using the Chi-square test or Spearman rank correlations. Continuous variables were analyzed using the Student's *t*-test, and data are presented as mean and SD or median and 25th–75th quartiles. Binary logistic regression analysis was used to calculate univariate odds ratios for mortality. The association between SDB and mortality was analyzed according to the standard cut-off points of SDB severity. When associations of SDB to mortality in people with different types of CVD and measures of systolic function were evaluated the following variables were used: hypertension, IHD, TIA/Stroke, LVEF <50%, plasma values of NT-proBNP > median. In these analyses presence of SDB was defined according to the dichotomized variables, AHI $\geqslant$15, or oxygen desaturation index $\geqslant$10 (ODI). ODI was used as a complement to AHI since studies have shown stronger associations with hemodynamic stress and inflammation for ODI [23,24]. Since no established cut-off for ODI exists ODI $\geqslant$10 was used. In the next step analyses were made to evaluate if SDB was associated with morality in those with CVD alone.

Since IHD and/or TIA/Stroke both were associated with mortality and in order to increase the power in these analyses the participants with IHD and/or TIA/Stroke were amalgamated into one group, labeled the CVD. The CVD group was divided into two different groups in relation to the presence of the respective measure of impaired systolic function (i.e., CVD and LVEF <50%; CVD and plasma values of NT-proBNP > median). Mortality rates in these groups were evaluated in relation to the presence of SDB, as measured by AHI $\geqslant$15 or ODI $\geqslant$10. Cox proportional hazard regression analyses were used to analyse if SDB independently was associated with mortality in those with CVD and impaired systolic function. SPSS version 18.0 (SPSS Inc., Chicago, Illinois, USA) was used for statistical computing.