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Original Article

Severity of individual obstruction events increases with age in patients with obstructive sleep apnea

Timo Leppänen [a, b, *], Juha Töyräs [b, c], Esa Mervaala [c, d], Thomas Penzel [e, f], Antti Kulkas [a, b]

[a] Department of Clinical Neurophysiology, Seinäjoki Central Hospital, Seinäjoki, Finland
[b] Department of Applied Physics, University of Eastern Finland, Kuopio, Finland
[c] Department of Clinical Neurophysiology, Diagnostic Imaging Center, Kuopio University Hospital, Kuopio, Finland
[d] Department of Clinical Neurophysiology, Institute of Clinical Medicine, Faculty of Health Sciences, University of Eastern Finland, Kuopio, Finland
[e] Interdisciplinary Sleep Center, Department of Cardiology, Charité – Universitätsmedizin Berlin, Berlin, Germany
[f] International Clinical Research Center, St Anne's University Hospital Brno, Brno, Czech Republic

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ABSTRACT

Background: Age is a risk factor of obstructive sleep apnea (OSA). It has been shown that OSA progresses over time, although conflicting results have been reported. However, the effect of age on the severity of OSA and individual obstruction events has not been investigated within different OSA severity categories by taking the most prominent confounding factors (i.e., body mass index, gender, smoking, daytime sleepiness, snoring, hypertension, heart failure, and proportion of supine sleep) into account.
Methods: Polygraphic data of 1090 patients with apnea–hypopnea index (AHI) ≥5 were retrospectively reanalyzed. The effect of age on the severity of OSA and obstruction events was investigated in general, within different OSA severity categories, and in different age groups (age <40, 40≤ age <50, 50≤ age <60, and age ≥60 years).
Results: In the whole population, AHI and durations of apneas, hypopneas, and desaturations increased with increasing age ($B \geq 0.108$, $p \leq 0.010$). In more detailed analysis, AHI increased with age only in the moderate OSA category ($B = 0.075$, $p = 0.022$), although durations of apneas increased in mild and severe OSA categories ($B \geq 0.076$, $p \leq 0.038$). Furthermore, durations of hypopneas increased with age in mild and moderate OSA categories ($B \geq 0.105$, $p \leq 0.038$), and durations of desaturations ($B \geq 0.120$, $p \leq 0.013$) in all OSA severity categories. AHI was not statistically significantly different between the age groups, although durations of obstruction events tended to increase towards older age groups.
Conclusion: As obstruction event severity was more strongly dependent on the age than it was dependent on AHI, considering the severity of obstruction events could be beneficial while estimating the long-term effects of the treatments and prognosticating the disease progression.

1. Introduction

Obstructive sleep apnea (OSA), in which a patient has frequent partial and complete breathing cessations during sleep, is a common problem, especially among middle- to old-aged men [1]. It has been estimated that 5.6–13.0% of individuals of 30–70 years of age have OSA [1] and it has been shown that age is positively related with the prevalence of OSA [2]. Peppard et al. demonstrated with four-year follow-up that apnea–hypopnea index (AHI) increases over time, although this increase was strongly related to weight gain [3]. Furthermore, Redline et al. reported that although long-term change in AHI varies non-uniformly with age, older male patients with higher body mass index (BMI) have the highest rate of increase in the number of apneas and hypopneas over time [4]. Moreover, Sahlman et al. showed that even mild OSA has a tendency to progress over time towards more severe OSA [5]. This increase parallels to an increase in age, occurrence of comorbid disorders, and obesity. In contrast, it has been shown that the prevalence of OSA increases with age until it starts to decline after the age of 60 years and that the severity of OSA decreases with increasing age [6]. This decrease might be related to increased mortality in patients with high AHI, so that fewer people with

* Corresponding author. Department of Clinical Neurophysiology, Seinäjoki Central Hospital, Hanneksenrinne 6, 60220 Seinäjoki, Finland. Fax: +358 6415 4037.
E-mail address: leppanen_timo@outlook.com (T. Leppänen).

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severe OSA survive. Hoch et al. reported that AHI did not differ statistically significantly between age groups (60–74 vs ≥75 years) and that AHI did not increase statistically significantly over time (3-year interval) in either of the age groups [7]. Furthermore, it has been shown in 18-year follow-up that changes in AHI were not associated statistically significantly with age [8].

Current AHI, which represents the number of obstruction events per hour of sleep, is lacking information on duration of individual obstruction events [9]. Previously, we have shown that the severity of individual obstruction events is dependent on, for example, weight change [10], sleeping position [11], and gender [12]. Furthermore, as the clinical severity estimation of OSA is improved when considering the information on individual obstruction event severity [13,14], it is important to be aware of the factors affecting the severity of individual obstruction events.

Even though the effect of age on AHI has been previously investigated (with conflicting results), there is no corresponding comprehensive information available about the effect of age on the severity of individual obstruction events. Therefore, we investigated the effect of age on the severity of OSA and individual obstruction events in general and within different OSA severity categories (mild-moderate-severe). Furthermore, it was explored whether these severities vary between different age groups. We hypothesized that increasing age leads to elevated severity of individual apneas, hypopneas, and desaturations with only a minor effect on event frequency.

2. Methods

This study was based on ambulatory polygraphic recordings of 2057 clinically suspected OSA patients conducted at Kuopio University Hospital. Recordings were conducted with custom-made four-channel (airflow, breathing movements of abdomen, oxygen saturation, and position) ambulatory devices [13,15,16]. The recordings were first analyzed during the years 1992–2003 and then manually reanalyzed between the years 2012 and 2015 using RemLogic software (Embla, Thornton, MA, USA). All recordings were manually reanalyzed based on the standard defined by American Academy of Sleep Medicine (AASM) in 2007 [17]. Hypopneas were scored using desaturation threshold level of 4% (rule 4A) [17]. The Research Ethics Committee of the Hospital District of Northern Savo, Kuopio, Finland gave favorable statements for the present study (decision numbers 127/2004 and 24/2013).

Inclusion criteria for the further analysis were AHI ≥5 events/h and age ≥18 years (893 male and 197 female patients met this criteria). First, patients were classified into OSA severity categories based on conventional AHI. In addition to AHI, the values of oxygen desaturation index (ODI), apnea index (AI), hypopnea index (HI), and obstruction severity parameter (ObsSev, Fig. 1, [15,18]) were calculated. Furthermore, the proportion of apneas from all breathing cessation events and severity of individual obstruction events (durations of apneas and hypopneas and areas, depths and durations of desaturations (Fig. 1, [15])) were calculated using custom-made MATLAB functions (Mathworks, Natick, MA, USA). Basic anthropometric data and information on smoking habits, heart failure, hypertension, snoring, and daytime sleepiness were collected from patients' medical records in Kuopio University Hospital. Second, patients were divided into four different age groups (age <40, 40≤ age <50, 50≤ age <60, and age ≥60 years) and AHI, proportion of apneas, and the severity of individual obstruction events were compared between these groups.

The effect of age on OSA severity parameters (i.e., AHI, ODI, AI, HI, and ObsSev) and the severity of individual obstruction events in general and within each OSA severity category were investigated by general linear model (GLM) univariate analysis adjusted for BMI, gender, smoking habits, snoring, daytime sleepiness, heart failure, hypertension, and proportion of supine sleep. Statistical significance of differences in AHI, proportion of apnea events, and the severity of individual obstruction events between the age groups were assessed using Mann–Whitney U-test. Statistical significance of differences in anthropometric data and background information between OSA severity categories and between age groups were evaluated using Mann–Whitney U-test and Chi-Squared test. Statistical analyses were performed using SPSS software (version 20.0, SPSS Inc., Chicago, IL, USA). A value of $p < 0.05$ was considered as the limit of statistical significance.

3. Results

From 1090 patients, 893 were men and 197 were women (Table 1). The age range was 20.7–84.1 years and the BMI range was 18.7–74.0 kg/m^2 (Table 1). In the whole population, AHI, ODI, ObsSev, and AI increased statistically significantly with age ($B \geq 0.133$, $p \leq 0.034$) (Table 2). Furthermore, proportion of apneas, duration of apneas, hypopneas and desaturations and areas of desaturations increased statistically significantly with increasing age ($B \geq 0.108$, $p \leq 0.012$) (Table 2). Depth of desaturation events did not increase statistically significantly with age ($B = 0.015$, $p = 0.131$) (Table 2). However, in more detailed analysis, when patients were divided into different OSA severity categories, AHI was found to increase statistically significantly only in the moderate OSA category ($B = 0.075$, $p = 0.022$) and no statistically significant association between ODI and age was seen (Table 3). AI increased statistically significantly with age in mild and moderate OSA categories ($B \geq 0.035$, $p = 0.004$) (Table 3). In all OSA severity categories, proportion of apneas and duration of desaturations increased with age ($B \geq 0.120$, $p \leq 0.027$) (Table 3). Furthermore, durations of apneas increased in mild and severe OSA categories, and durations of hypopneas in mild and moderate OSA severity categories with increasing age ($B \geq 0.076$, $p \leq 0.038$) (Table 3). No statistically significant change in depths of individual desaturation events was seen with increasing age in any OSA severity category (Table 3).

When patients were divided into different age groups (age <40, $N = 143$; 40≤ age <50, $N = 364$; 50≤ age <60, $N = 408$; and age ≥60 years, $N = 175$) younger patients tended to smoke more often than older counterparts, but hypertension was a more common finding in older patients (Table 4). No statistically significant difference between age groups was seen in snoring, daytime sleepiness, percentage of supine sleep or BMI (except that patients with age ≥60 years had statistically significantly lower BMI compared to patients of 50–60 years of age). AHI was not statistically significantly different between age groups, although the proportion of apneas was statistically significantly higher ($p < 0.05$) in age group 50–60 years than in age group 40–50 years and in age group >60 years than in age group 50–60 years (Table 5, Fig. 2). However, the severity of individual obstruction events tended to increase towards older age groups. Apnea events were longer ($p < 0.05$) and areas of desaturation events larger ($p < 0.05$) in age group 50–60 years compared to age group 40–50 years (Table 5, Fig. 2). In addition, hypopneas and desaturations were statistically significantly longer ($p < 0.05$) in age group 40–50 years than in age group <40 years and in age group 50–60 years than in age group 40–50 years (Table 5, Fig. 2).

4. Discussion

Based on the present results, increasing age, independently of BMI, gender, smoking, snoring, daytime sleepiness, hypertension, heart failure, and the proportion of supine sleep, increases both