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Factors influencing the PAP-adherence of elderly European sleep apnoea patients in the ESADA cohort

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The population of the world is ageing and increasing age has been associated with increased prevalence of obstructive sleep apnoea (OSA) (1). However, guidelines concerning OSA rely on studies performed mainly on middle-aged people. Furthermore, information on the characteristics of OSA patients aged 80 or more, is almost non-existent.

Due to the demographic changes physicians are, however, confronted with a rapidly growing number of elderly OSA patients and decisions concerning their treatment and a need for further research on the field has been stated (2).

It has been suggested that the positive airway pressure (PAP) treatment of OSA may be able to result in fruitful patient-related outcomes and e.g. improve cognition, reduce depressive symptoms and improve physical performance in elderly patients (3). How to target PAP treatment in this elderly population is nevertheless not well known.

Multimorbid patients commonly take multiple prescriptions (polypharmacy), which further increase the complexity of the elderly populations best-practice treatment. Furthermore, the Baveno-classification which takes the level of OSA symptoms and severity of cardiovascular comorbidities into account, has been suggested as a way of defining those benefiting from active PAP treatment of OSA (4).

In light of all this, we aimed to study whether the very elderly OSA patients differ from patients aged 70-79 concerning the basic clinical characteristics and whether these, polypharmacy (reflecting multimorbidity), the Baveno-classification, the use of medications acting through the

central nervous system (CNS), or the general health status of the patient are associated with PAP adherence among elderly OSA patients.

The ESADA registry is a multicentre, prospective patient cohort collected in a network of 37 sleep centres in 20 countries in Europe and Israel. The methods of the study have been described earlier (5). Unselected patients (aged over 18 years) with suspected OSA are eligible for inclusion. Anthropometric characteristics, daytime symptoms and health-related lifestyle, blood tests, medical history, current medications and sleep data are verified at the initial visit. Daytime sleepiness is quantified by the Epworth Sleepiness Scale (ESS) (6). The severity of OSA is assessed by polysomnography or polygraphy according to the prevailing clinical routine at each participating sleep centre and analysed as described earlier by Escourrou and others (7). Corresponding follow-up data are collected when patients return according to local clinical routine. A central web-based platform is applied to record patient information. The research ethics committee at each participating centre approved the ESADA protocol, and informed written consent is obtained from all included patients.

The current analysis included patients assessed at baseline between 2007-2023, aged ≥ 70 years with an AHI ≥5 / hour, who were started on PAP therapy and had data from at least one follow-up visit available. Parameters for the Baveno-classification comprise symptoms and cardiometabolic comorbidities as described earlier (4). The patients are classified into four groups accordingly: Group A = minor symptoms and comorbidities, Group B = Severe symptoms and minor comorbidities, Group C = minor symptoms and severe comorbidities and Group D = severe symptoms and severe comorbidities. The use of ≥5 medications was considered polypharmacy,

as suggested by WHO (8). The Clinical Global Impression Scale -Severity (CGI-S) at initial visit was used to reflect the clinician's assessment of the patient's global functioning (9) using a 7-point scale with a higher score related to a poorer global functioning (Supplementary file 1). PAP-use was defined as the average use in all days (hours/day) measured by the in-built clock-counter of the device and read at the follow-up visit.

The data was split into two age-groups: those under 80 years old and those ≥ 80 years old. The distribution of continuous variables in these age-groups was assessed by the Kolmogorov-Smirnov test with the Lilliefors significance correction and further by assessing the skewness and its' standard deviation. Due to non-Gaussian distributions, the variables are presented as median and interquartile range (IQR). Categorical variables are expressed as absolute numbers and percentages. Mann-Whitney U test with the Monte Carlo method were used to compare differences between groups for parametric and non-parametric data, respectively. The Pearson Chi-square test was used to compare the categorical data between the age-groups.

The proportion of adherent patients at first control visit was calculated from the patient-group whose PAP-use was known. The change in ESS between the first visit and first follow-up visit was tested by the Wilcoxon Signed-Rank Test.

The association of BMI, AHI, ODI, mean SaO_2, initial ESS score, initial CGI-S, Baveno-classification, polypharmacy and the use of medications acting though the CNS on the odds of good (≥ 4hours/day) PAP-adherence was analysed using binomial logistic regression. Baveno-groups A, B

and C were evaluated in relation to group D, with most severe symptoms and comorbidities. The results are expressed as odds ratios (OR) and their 95% confidence intervals (CI).

The p-value <0.05 was considered statistically significant. The statistical analyses were performed using IBM SPSS Statistics 27.0 (Armonk, NY, USA: IBM Corp.).

There were 1057 70-79 years-old patients and 152 patients that were 80 years old older. The clinical characteristics of these patients in the two age-groups are shown in Supplementary table 1. The patients in the older age-group were slightly less obese than the patients in the younger age-group (median BMI 30.80, IQR 7.50 versus 31.57, IQR 8.30, p=0.045). Among the older patients, the time spent under oxygen saturation level 90% was longer (48.00 min, IQR 30.49 and 32.05 min, IQR 85.65, p=0.009). In both age-groups the change in ESS-value between the first visit and the follow-up visit was statistically significant (p<0.001). In the younger age-group the median initial ESS-value was 9 (IQR 7), and at first PAP-treatment control 6 (IQR 7), the values being 8.50 (IQR) and 7 (IQR 6) in the older age-group, respectively.

Of the tested variables, only baseline CGI-S had a significant effect on the probability of good PAP-adherence (Table 1). A higher CGI-S value was associated with lower odds of good PAP-adherence (OR 0.786, CI 0.665-0.930, p=0.005) when the other tested variables were kept constant.

To conclude, in this study we found that in elderly OSA patients, their global health status was related to adherence to PAP therapy. In contrast, symptoms as measured by the ESS, OSA

severity, the Baveno-classification, polypharmacy or the use of medications acting through the CNS were not indicators of CPAP-adherence. No clinically striking differences were found in the older age-group compared to the younger age-group. The very old OSA patients aged 80 years or more had a lower BMI and had a longer time under the oxygen saturation level of 90% during the night than the old patients aged 70-79, possibly reflecting frailty and the presence of more severe comorbidities in this older group. In a large French study, PAP compliance was peaking in the ages 55-80 and decreasing thereafter (10). In our study there was no significant difference in PAP adherence between the age-groups.

Our study has several strengths but also some limitations to be considered. The study is a multi-centric real-life study and includes unselected patients increasing the generalizability of our findings. This study comprised of a large cohort of elderly sleep apnoea patients. The number of patients aged 80 or more is limited but nevertheless large when considering the limited number of previous studies in this age-group. Furthermore, the data have been collected in the context of a standardized clinical protocol. However, the CGI-S is a subjective measure of functional status and no training for its' use was offered, possibly causing variability in the scoring. Furthermore, it is well established that the ESS is not as good a tool for the scoring of sleepiness among the elderly and not validated for the elderly (11). A further limitation is that the follow-up material is somewhat preselected to include follow-up visits in PAP-adherent patients.

Our results emphasize the importance of taking the elderly patients' functional status into account when considering OSA diagnostics and adherence to treatment. The CGI-S is,

however, a subjective measure of health and functioning status and there is a need for future OSA studies in the elderly to focus on more specific measures of functioning capacity e.g. the easy-to-use 7-point Clinical Frailty Scale (12) as predictors of treatment efficacy and adherence.

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Table 1. The effect of the clinical characteristics on the odds of good PAP-adherence in elderly OSA patients aged ≥ 70 years and the p-values for the odds ratios (OR).

	OR (95% CI)	p-value
Age	0.984 (0.936-1.035)	0.544
Gender	1.137 (0.725-1.784)	0.576
BMI	0.987 (0.953-1.022)	0.464
ESS	1.013 (0.949-1.081)	0.698
AHI	1.005 (0.995-1.016)	0.336
CGI-S	0.786 (0.665-0.930)	**0.005**
Baveno classification*		
A vs D	1.643 (0.646-4.175)	0.297
B vs D	0.591 (0.274-1.273)	0.179
C vs D	1.409 (0.634-1.695)	0.323
Polypharmacy	1.036 (0.634-1.695)	0.887
Use of CNS medications	0.706 (0.338-1.285)	0.255

* A = minor symptoms and minor comorbidities, B = severe symptoms, minor comorbidities C = minor symptoms, severe comorbidities, D = severe symptoms and severe comorbidities