

Subjective tiredness does not correlate with the Apnoea-Hypopnoea Index

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ABSTRACT

INTRODUCTION: Sleepiness is a frequent complaint and might be a symptom of obstructive sleep apnoea. Our aim was to examine if patient-reported tiredness on either the Epworth Sleepiness Scale or on a visual analogue scale was associated with the Apnoea-Hypopnoea Index.

METHODS: We conducted a retrospective database study on 215 patients referred on suspicion of obstructive sleep apnoea. Before cardiorespiratory monitoring, all patients answered the Epworth Sleepiness Scale Questionnaire and rated their tiredness on a visual analogue scale.

RESULTS: No correlation was found between the Apnoea-Hypopnoea Index and the Epworth Sleepiness Scale (Spearman's $\rho = 0.02$) or the visual analogue scale of tiredness ($\rho = -0.04$). This also applied for a subgroup of patients with an Apnoea-Hypopnoea Index score > 15 .

CONCLUSIONS: Monosymptomatic patient-reported tiredness should not raise suspicion of obstructive sleep apnoea. Conversely, if obstructive sleep apnoea is suspected, a lack of tiredness should not postpone further evaluation.

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Due to increasing average BMI and age, obstructive sleep apnoea (OSA) is developing into an expanding global health threat. This article focuses on the important first steps of diagnosing the condition.

The pathophysiology of OSA is complex, and the underlying cause varies among patients [1]. Regardless of the cause, the end result is always the same; the upper airway collapses during sleep, denying a satisfactory airflow to the lungs which, in turn, causes the brain to arouse from deeper stages of sleep. The diagnosis is established by monitoring the patient's sleep, typically by cardiorespiratory monitoring (CRM) that expresses the severity of OSA as a numerical value: the Apnoea-Hypopnoea Index (AHI). Apnoea is defined as absence of breathing for a minimum of ten seconds. Hypopnoea is an event of at least 30% reduction in breathing amplitude with a minimum 3% oxygen desaturation. AHI is the average number of apnoeas, and hypopnoeas combined per hour during sleep.

Sleep fragmentation causes excessive daytime sleepiness in some patients, may affect concentration

and memory, and has been associated with a number of serious health consequences [2].

The Epworth Sleepiness Scale (ESS) questionnaire [3] is widely used to quantify patient-reported sleep propensity in cases of suspected OSA [4]. The questionnaire consists of eight questions in which the patient is presented to everyday situations and is asked to rate his or her propensity to fall asleep on a scale ranging 0-3. Hence, the final score on the scale ranges from 0 (would never doze in any of the situations) to a maximum of 24 (high chance of dozing in all eight situations). Both general physicians and sleep specialists use the ESS when examining patients with sleepiness, regardless of the underlying cause.

In recent decades, the ESS has been applied with varying cut-off values in both research and diagnostics of OSA patients [5]. A thorough sleep evaluation is both expensive and comprehensive. Compared with objective measurements such as the Multiple Sleep Latency Test, polysomnography (PSG) or CRM, the use of a questionnaire is a rapid and inexpensive alternative. However, a number of studies have indicated that the ESS has shortcomings when applied as a diagnostic tool [4, 6, 7].

Based on a retrospective analysis of all consecutive patients with suspected OSA referred through a four-year period, we evaluated and correlated both the ESS questionnaire and quantified on a visual analogue scale on tiredness (VAS-T) [8] to the AHI. A visual analogue scale (VAS) is a non-specific psychometric scale that provides a patient-reported estimate to subjective phenomena, which cannot easily be measured objectively. In this setting, it offers a subjective value of tiredness rather than the sleep propensity provided by the ESS. It is, in other words, a quantified reflection of what initially brings the patient to his/her general practitioner.

Due to the heterogeneity of the conditions causing sleepiness in general, our assumption was that patient-reported sleepiness alone is of little value when trying to identify OSA patients. Thus, the aim of the study was to assess the considered association between VAS-T/ESS and AHI when applied in a clinical setting.

METHODS

We conducted a retrospective database study including 284 consecutive patients referred from either an ear,

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nose and throat specialist or a general practitioner. The inclusion criteria were suspected or observed sleep apnoea. The patients were excluded if they had already been diagnosed with OSA or presented findings of central sleep apnoea only on CRM. A total of 69 patients were excluded due to incomplete datasets. Data were collected at a tertiary referral centre in the four-year period from 26 November 2012 to 1 July 2016. VAS, ESS, demographics and other general health data were logged in the electronic database directly by the patients (Table 1). Following a physical examination, the CRM monitoring was performed unattended. Data were assessed using the “Noxturnal software” and adjusted for any awake periods. A doctor registered the AHI in the database.

Statistics

Patient characteristics were summarised using descriptive statistics. The association between VAS-T/ESS and AHI was evaluated graphically by linear regression and Spearman’s rank correlation coefficient. Using a multiple linear regression model, we finally examined the effect of VAS-T/ESS on AHI, adjusting for pre-defined potential confounders (age, sex and BMI), based on literature studies. The regression model assumptions were assessed graphically, and model fit was evaluated by R-squared (which quantifies the proportion of variation that is explained by the included factors). We calculated two-sided p-values for either regression coefficients or correlation coefficients and considered $p < 0.05$ statistically significant. The statistical analyses were performed using Stata 14.2 (StataCorp, TX, USA).

Trial registration: not relevant.

TABLE 1

Patient and disease characteristics (N = 215).

| | |
|--|------------------|
| <i>Gender, n (%)</i> | |
| Male | 161 (75) |
| Female | 54 (25) |
| Age, median (interquartile range), yrs | 48 (37-59) |
| BMI, median (interquartile range), kg/m ² | 28.7 (25.5-33.9) |
| Hypertension, n (%) | 57 (27) |
| Diabetes, n (%) | 12 (6) |
| Medicated depression, n (%) | 26 (12) |
| Heart disease, n (%) | 17 (8) |
| VAS-T, median (interquartile range) | 61 (41-79) |
| AHI, median (interquartile range) | 11 (3-30) |
| ESS, median (interquartile range) | 9 (5-13) |

AHI = Apnoea-Hypopnoea Index: 0-100.

ESS = Epworth Sleepiness Scale: 0-24.

VAS-T = visual analogue scale of tiredness: 0-100.

RESULTS

Our results are in line with our initial thesis, as we found no correlation between VAS-T and AHI (regression coefficient = 0.029 (95% confidence interval (CI): -0.07-0.13)) or ESS and AHI (regression coefficient = 0.35 (95% CI: -0.18-0.88)), **Figure 1**. VAS-T showed a clear correlation with ESS (Spearman’s $\rho = 0.43$), although with considerable variation. As a consequence, the analysis of the association between AHI and VAS-T with respect to ESS was separated.

AHI was clearly correlated with BMI ($p < 0.001$), age ($p < 0.001$) and sex ($p = 0.001$). This remained unchanged in a multivariable analysis explaining 32% of the observed AHI variation. The remaining 68% was thus caused by other factors such as genetics, anatomy, smoking status, etc.

The analyses were repeated for the 90 patients with moderate OSA or above (AHI score > 15) and yielded similar results, although with broader confidence intervals due to the lower statistical power. Again, ESS and VAS-T were weakly correlated ($\rho = 0.40$; $p < 0.001$), and analyses were performed for both. Neither VAS-T (regression coefficient = 0.017 (95% CI: -0.15-0.18)) nor ESS (regression coefficient = -0.08 (95% CI: -0.96-0.80)) was correlated with AHI, **Figure 2**. As previously, the AHI and ESS were associated with BMI, age and sex. In a multivariable model, BMI was the most important factor explaining variation in AHI, accounting for 27% of the observed variation.

DISCUSSION

In this study we show that neither VAS-T nor ESS predicted a high AHI. Consequently, these measures were not useful in diagnosing obstructive sleep apnoea syndrome (OSAS). This also applied when adjusting for pre-defined potential confounders. The results were consistent with those of the subgroup of patients with an AHI score > 15 .

To our knowledge, this is the first study on the sensitivity of VAS-T as a parameter in a cohort of patients suspected for OSA. VAS scales [9] and Likert scales [10, 11] (on which the respondent specifies his/her level of agreement with a statement) have previously been used to report on instantaneous sleepiness. However, a specific association with AHI has not been studied.

Our results suggest that subjective tiredness as a stand-alone variable is an uncertain predictor of OSA. Our findings confirm that patients suffering from obstructive sleep apnoea are a heterogeneous group with symptoms ranging from profound to no tiredness. We are aware that our cohort is selected, but we have no reason to suspect that the findings in a background population would differ significantly from those presented herein. If no association between AHI and

VAS-T/ESS is found when professionals suspect OSA (even in patients with moderate or more severe OSA), an association seems unlikely in sleepy patients in general.

The study has some limitations. Patients might have reported higher scores on both the ESS questionnaire and the VAS-T-scale in order to receive treatment. This could, in some cases, have affected the validity of the answers. The opposite might also be the case. At the time when the questionnaire was answered, Danish law was quite strict with regards to OSA and confiscation of driver's licenses (AHI score > 15). This might have prompted some participants to report a falsely

low ESS and VAS-T. Retrospectively, we should have included information on the type of occupation and thereby the patients' dependency on having a driver's license. Also, we lacked information on smoking status, medication and alcohol consumption. These factors are all of relevance.

The gold standard for sleep monitoring is PSG. In addition to the parameters measured with CRM, PSG also records an electroencephalogram, eye movements and muscle activity. By measuring brain activity and airway obstruction simultaneously, PSG offers a much more detailed dataset that is indispensable in basic research of sleep disorders, including OSA. We acknow-

FIGURE 1

Correlation between visual analogue scale of tiredness (VAS-T) vs Apnoea-Hypopnoea Index (AHI) ($\rho = -0.04$; $p = 0.54$) (A) and Epworth Sleepiness Scale (ESS) vs AHI ($\rho = 0.02$; $p = 0.78$) (B).

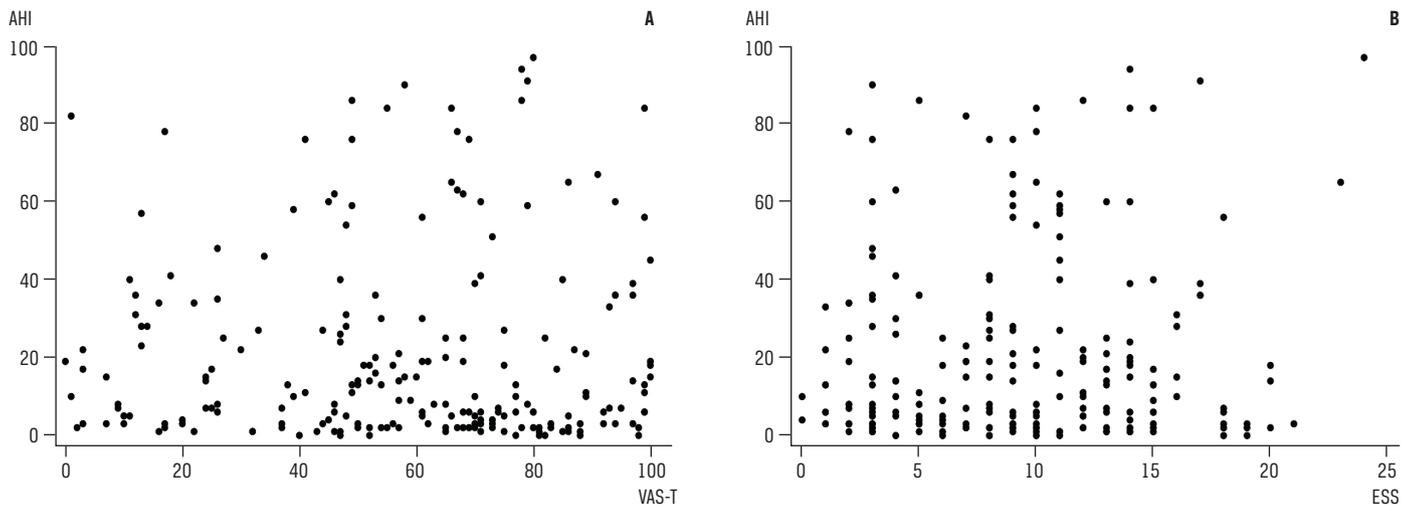
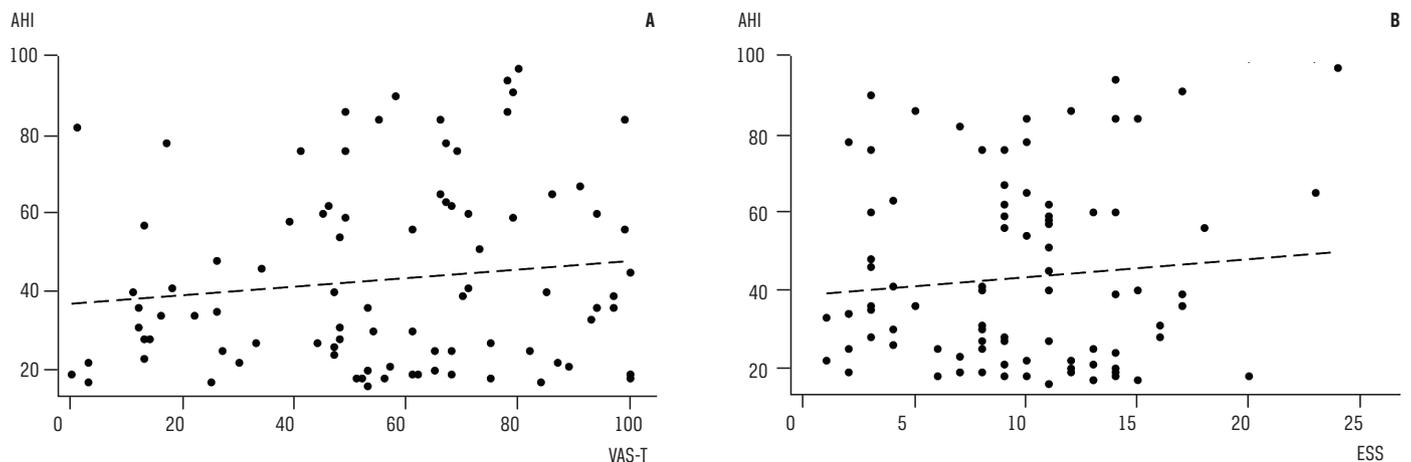


FIGURE 2

Correlation between visual analogue scale of tiredness (VAS-T) vs Apnoea-Hypopnoea Index (AHI) ($\rho = 0.10$; $p = 0.22$) (A) and Epworth Sleepiness Scale (ESS) vs AHI ($\rho = 0.01$; $p = 0.91$) (B) in patients with AHI score > 15.



ledge that sleep disorders other than OSA might be missed when relying only on CRM data only. In patients suffering from upper airway resistance syndrome, the AHI will be normal, but the sleep disorder leads to arousals that are spotted only on PSG. However, for the purpose of this study, we find that CRM is adequate as we focused on OSA only.

The largest study to date on this topic, the Sleep Heart Health Study, found a significant correlation between ESS and AHI as opposed to our findings [12]. However, as pointed out in an editorial of *Sleep Medicine* in 2003, the difference in ESS scores between patients with a healthy sleeping pattern and the worst apnoeic episode in the previous study was only two points, indicating that markedly higher scores might be caused by unknown factors [4]. This essentially supports our thesis that the pathogenesis of sleepiness is, indeed, multifactorial and that it cannot easily be assessed without objective measures.

Previous studies have found the ESS to be inferior to a number of questionnaires including the SACS, STOP BANG and the BERLIN questionnaire [13-15]. Miller & Berger found sleepiness-questionnaires in general to be both insensitive and unspecific in diagnosing OSA in a primary care setting [16]. Our data support this conclusion. However, the ESS is useful for other purposes, i.e. for evaluating whether or not driving should be avoided.

When it comes to selecting the next step in a work-up, having an easy tool to point the physician in the right direction is preferable, particularly with a symptom like sleepiness. However, it seems that there is no shortcut for either confirming or ruling out OSA.

CONCLUSIONS

Sleepiness is an unspecific symptom and should, in monosymptomatic cases, not necessarily lead to suspi-

cion of OSA. On the other hand, if a patient presents with observed apnoea or OSAS symptoms, the occasional absence of sleepiness should be considered irrelevant, and referral for CRM or even PSG might thus be indicated.

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