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Diagnostic accuracy of overnight oximetry for the diagnosis of sleep-disordered breathing in atrial fibrillation patients

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ABSTRACT

Background: Sleep-disordered breathing (SDB) is highly prevalent in patients with atrial fibrillation (AF) and its treatment can improve rhythm control. Polysomnography (PSG) is the gold standard for the diagnosis of SDB but its high cost and limited availability constrain its role as a standard SDB screening tool. We sought to assess the diagnostic utility of overnight oximetry in predicting SDB in AF patients.
Methods: We analyzed prospectively collected data on 439 patients with documented AF (62% paroxysmal AF) who underwent PSG. Overnight oximetry was used to determine the oxygen desaturation index (ODI, number of desaturation/h) by a novel automated computer algorithm. ODI was validated against PSG derived apnea-hypopnea index (AHI).
Results: The sample consisted of 69% men with a mean age of 59.9 ± 11.3 years and body mass index of 30 ± 5 kg/m^2. The median AHI was 9.5 [3.6–21.0]/h and the prevalence of moderate (AHI 15–29/h) and severe SDB (AHI ≥ 30/h) was 17.3% and 16.6% respectively. The ODI was able to detect moderate-to-severe SDB (AHI ≥ 15/h; area under the receiver-operating-characteristic curve (AUC): 0.951, 95% CI: 0.929–0.972) and severe SDB (AHI ≥ 30/h; 0.932, 95% CI: 0.895–0.968) with high diagnostic accuracy. An ODI cut-off of 4.1/h resulted in a 91% sensitivity and 83% specificity in discriminating between patients with and without AHI ≥ 15/h. An ODI of 7.6/h yielded a sensitivity and specificity for AHI ≥ 30/h of 89% and 83%, respectively.
Conclusions: ODI derived from a simple and low-cost overnight oximetry can be used as an accessible and reliable screening tool, particularly to rule out SDB.

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1. Introduction

Sleep-disordered breathing (SDB), particularly obstructive sleep apnea, is highly prevalent in patients with atrial fibrillation (AF). It has been reported to be much higher (between 18% and 74%) compared to populations without AF (between 3% and 49%) [1–5]. SDB reduces the efficacy of catheter-based and pharmacological antiarrhythmic therapy [6,7]. Treatment of SDB by continuous positive airway pressure (CPAP) lowers the rate of AF recurrence after electrical cardioversion and improves catheter-ablation success rates in AF patients [8,9]. With accumulating evidence, the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation [10] as well as the guidelines for the management of atrial fibrillation of the 2016 European Society of Cardiology [11] mention SDB as a relevant modifiable risk factor for AF and recommend screening for SDB in patients with AF, including those who are being evaluated to undergo an AF ablation procedure.

The gold standard for the diagnosis of SDB is an overnight polysomnography (PSG). The presence and severity of SDB is determined using the apnea-hypopnea index (AHI) which represents the total number of apnea and hypopnea events per hour of sleep [12,13]. Limited access to PSG, its high cost, time commitment and variable

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patient compliance constrain PSG as effective tool for systematic SDB screening. In addition, the burgeoning prevalence of AF further limits the use of PSG as a means of screening for SDB.

Simpler and less expensive strategies such as overnight oximetry monitoring might be a good alternative to PSG to allow broad and systematic SDB screening in the large number of AF patients. While overnight oximetry is already considered as a screening tool for SDB in the general population [14–16], its diagnostic accuracy in AF patients is unknown. We sought to assess the diagnostic utility of different measures derived from overnight pulse oximetry in predicting SDB in AF patients when compared to the AHI which is derived from the gold-standard PSG.

2. Methods

Prospectively collected data on 439 consecutive patients with paroxysmal and persistent AF who were referred from the Centre for Heart Rhythm Disorders – University of Adelaide to undergo PSG between 2012 and 2017 as part of their clinical AF work-up irrespective of a suggestive SDB history or phenotype was analyzed. The study was approved by the Institutional Committee on Human Research at the University of Adelaide and all patients gave written informed consent before study enrolment.

2.1. Patient characteristics

The diagnosis of AF was confirmed with at least one available electrocardiogram (ECG) documentation. AF was defined as per the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation [10]. Paroxysmal AF was defined as self-terminating episodes of AF within 48 h (or cardioverted within 7 days). Persistent AF was defined as AF episodes that last over 7 days and longstanding persistent was defined as continuous AF lasting for ≥1 year [10].

The following clinical characteristics were collected: gender, age, body mass index (BMI), previous pulmonary vein isolation and prior electrical cardioversion. The presence of hypertension, diabetes, hyperlipidemia, a history of cerebrovascular disease (stroke or transient ischaemic attack) and the CHA2DS2-VASc score were extracted from patients' clinical records. In addition, pharmacological therapy at the time of PSG was recorded and included anticoagulants (vitamin K antagonist, VKA; new oral anticoagulants, NOACs), antihypertensives (ACE-inhibitors/Angiotensin receptor blocker, ARB; calcium channel blockers CCBs; diuretics), statins and beta-blockers, digoxin, flecainide, amiodarone and sotalol.

2.2. Assessment of daytime sleepiness

To assess the degree of subjective daytime sleepiness, the Epworth Sleepiness Scale (ESS) was administered to all participants the evening before polysomnography. The ESS is a validated questionnaire that requires subjects to rate their likelihood of falling asleep in several common situations [17]. Scores range from 0 (least sleepy) to 24 (sleepiest). Normal daytime sleepiness was defined as an ESS score between 0 and 10. Excessive daytime sleepiness was defined as a score of 11 or higher.

2.3. Polysomnography

AF patients underwent standard overnight polysomnography (Somte PSG, Compumedics) which included continuous recordings of electroencephalography (EEG), electro-oculography (EOG), and chin electromyography (EMG) for sleep staging. Nasal and oral thermistors were used to measure airflow and inductance plethysmography was used to measure rib cage and abdominal motion. The ECG and SpO_2 were also continuously monitored. A minimum of 4 h valid recording time was required. PSG data was scored by an experienced sleep specialist and reviewed and reported by a registered sleep physician according to methods described in the American Academy of Sleep Medicine manual for the scoring of sleep and associated events [18].

2.3.1. Scoring of the apnea-hypopnea index

Apnea was defined as a drop in peak nasal airflow by ≥90% of pre-event baseline of >10 s duration. Apnea was scored as obstructive if apnea criteria were met in association with continuation of, or increase in, inspiratory effort during the event. Central apnea was defined as apnea according to the above definition in the absence of associated inspiratory effort. Hypopnea was defined as a 30% reduction in the airflow signal or thoraco-abdominal movement compared to the baseline value of the immediately preceding breaths lasting >10 s accompanied by either a fall of ≥3% in saturation or an arousal. A desaturation was therefore not a requisite criterion if an arousal was present with reduction in airflow. Hypopneas were classified as obstructive if there was either snoring at the time of the event or an increase of inspiratory flattening of nasal airflow, or occurrence of associated thoracoabdominal paradox during, but not before, the event; central hypopnea was scored if none of the obstructive hypopnea criteria were met. The AHI was calculated as the total number of apneas plus hypopneas divided by the total sleep time. SDB-severity was determined according to categories of the PSG derived apnea-hypopnea index (AHI) (AHI 15–29/h, moderate SDB; AHI ≥ 15/h, moderate-to-severe SDB; AHI ≥ 30/h, severe SDB). SDB was classified according to the predominant type of apneas (>80% central events as predominant central sleep apnea; >80% obstructive events as predominant obstructive sleep apnea).

2.3.2. Scoring of oximetry derived measures

Digital oximetry signals of the complete recording time were extracted from the PSG for further processing by a novel fully automated MATLAB® based computer algorithm. Missing data were excluded by the algorithm. Acute desaturations were defined as episodic, monotonous drops in oxygen saturation levels by at least 4% that were followed by an onset of a resaturation to two-thirds of oxygen saturation level prior to desaturation within a period of 150 s. The requirement of a resaturation after a scored desaturation event is not implemented in the current AASM [18] scoring rules but allows the discrimination between episodic desaturation events and transient sustained drifts of baseline oxygen saturation as well as the determination of the onset and end of the desaturation event. In addition to mean nocturnal oxygen saturation (mean SpO_2) and time spent below 90% oxygen saturation (T90), the oxygen desaturation index (ODI) as count of desaturations per hour recording time was determined.

2.4. Statistical analysis

Descriptive statistics are presented as mean ± standard deviation or median and inter-quartile range (in square brackets) for non-normally distributed variables. An ANOVA was applied to normally distributed variables across the three groups (AHI < 15/h; AHI 15–29/h; AHI ≥ 30/h). The Kruskal-Wallis H compared ranked data for significantly skewed distributions. Categorical variables are presented as number and percentage and were analyzed with chi-square across the three groups. The main group effect p-value was reported for the between group comparison.

The primary objective of this study was to assess the diagnostic accuracy of oximetry derived parameters (T90, mean nocturnal oxygen saturation and ODI) and other demographic/clinical characteristics in the diagnosis of SDB as assessed via gold standard PSG. We ran two different prediction models for 1) the prediction of moderate-to-severe SDB (AHI ≥ 15/h) and 2) the prediction of severe SDB (AHI ≥ 30/h). Logistic regression was used to develop predictive models of either at moderate-to-severe (AHI ≥ 15/h) or severe (AHI ≥ 30/h) SDB. All parameters were assessed for their univariate relationships with SDB diagnosis and those with a relationship that resulted in a p value <0.10 were entered into a forward stepwise model. The final model was assessed for overall predictive value using receiver operating characteristic (ROC) analyses that allow assessment of sensitivity and specificity of all possible cut-offs of the predictor variable. The predictor cut-off with the best trade-off between sensitivity and specificity was calculated at the inflection point of the ROC curve.

All statistical analyses were performed using SPSS statistical software (Version 23; IBM Corp) and significance was set at $p < 0.05$.

3. Results

3.1. Patient characteristics

Patient characteristics are summarized in Table 1. The total sample of 439 subjects consisted of 69% men with 62, 35 and 3% having paroxysmal, persistent and long-standing persistent AF respectively. The mean age was 59.9 ± 11.3 yrs. The median AHI was 9.5 [3.6–21.0]/h and the prevalence of moderate and severe SDB was 17.3% ($n = 76$) and 16.6% ($n = 73$), respectively. Most AF patients with moderate ($n = 55$) and severe ($n = 67$) SDB showed predominant obstructive sleep apnea. 21 patients with moderate SDB and 6 patients with severe SDB showed predominant central sleep apnea. Mean SpO_2 was 93.9 ± 1.7%, and median ODI and T90 were 3.0 [0.8–8.2]/h and 0.5 [0.0–3.1] min, respectively.

3.2. Descriptive characteristics and their relationship to SDB severity

3.2.1. Age, gender and obesity

Age was not associated with the presence of moderate or severe sleep apnea ($p = 0.21$). However, male gender trended toward being over-represented in severe SDB ($p = 0.07$). 47% and 44% of the patients were overweight and obese, respectively. The presence of obesity was strongly related to severe SDB ($p < 0.001$) as was the presence of non-paroxysmal AF ($p < 0.037$) (Table 1).

3.2.2. SDB-related parameters

ODI and T90 both increased with more significant sleep apnea (all $p < 0.001$). Lower mean nocturnal SpO_2 was associated with a greater severity of sleep apnea ($p < 0.001$). The results showed a trend toward

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