### IJC Heart & Vasculature 26 (2020) 100463

Contents lists available at ScienceDirect

## IJC Heart & Vasculature

journal homepage: www.journals.elsevier.com/ijc-heart-and-vasculature



# Sleep apnea in atrial fibrillation – Highly prevalent, highly relevant, but most patients are not somnolent!



Sleep apnoea (SA) is a common condition with a high prevalence in patients with atrial fibrillation (AF) [1]. The presence of SA negatively impacts AF-related outcomes, with evidence that treatment of SA with continuous positive airway pressure (CPAP) ameliorates this negative impact [2]. International AF management guidelines recommend screening for signs and symptoms of SA in AF patients, and that SA treatment is offered in order to improve the likelihood of maintaining sinus rhythm [3,4]. This is especially relevant for patients undergoing AF ablation in order to maximise the clinical benefit from a procedure that, while increasingly safe and effective, is not without potentially serious complications [5].

It is in this context that the study by Traaen and colleagues is timely and welcome [6]. The authors prospectively studied 579 paroxysmal AF patients, mostly from an ablation waiting list, and utilised home polygraphy for assessment of SA. Importantly, the Epworth Sleepiness Scale (ESS), STOP-Bang Questionnaire, and Berlin Questionnaire were also used to assess the degree of SA symptoms. The authors found a high prevalence of SA, with more than 4 out of 5 patients having an apnea-hypopnea index (AHI)  $\geq$  5/h, and nearly half of those patients meeting the moderate-to-severe SA criteria (AHI  $\geq$  15/h). The predominant type of SA found was obstructive and hypopneas accounted for over half of the events, followed by obstructive apneas (39%), central apneas (5.2%) then mixed apneas (4.6%). Age, body mass index (BMI), male gender, duration of AF, and habitual snoring were independently associated with moderate-to-severe SA. All the questionnaire-based tools performed poorly to detect SA, particularly moderate-to-severe SA. The STOP-bang questionnaire performed the best, with a sensitivity of 84% but a specificity of 45% for detecting those patients.

Dr Traaen and colleagues ought to be congratulated on their important study. The relatively large sample size from a representative cohort of paroxysmal AF patients help extrapolate their findings to every-day care. The study design is well-conceived, and the prospective enrolment allowed for detailed and consistent data collection. In addition to exhaustive anthropometric measures which included height, weight, neck and waist circumference, and bioelectrical impedance-based body composition, the authors also assessed the utility of patient-reported symptoms using various methods both for SA and AF. Of note, the authors found a gender-based difference in the perceived severity of AF, with a higher AF Symptoms Severity Scale scores reported by women, as well as lower overall quality of life as quantified using the SF-36 questionnaire. From a sleep medicine perspective, nearly half of the patients in this study would at least be considered candidates for CPAP therapy assessment by virtue of an AHI > 15 [7]. The fact that the majority of observed events were obstructive, is perhaps an indication that these patients may derive a good benefit from CPAP use.

The authors used home-based ambulatory polygraphy over two nights and observed no 'first night effect' in that the acquired results were comparable across the two nights - an interesting finding. A study by Linz et al which utilised an impedance-based respiratory disturbance index derived from pacemakers showed considerable night-to-night variability ranging 2-14 events per hour in any given patient [8]. Attended polysomnography (PSG) remains the gold-standard tool for SA assessment despite being time and resource intensive. PSG allows for the acquisition of many physiological parameters including brain waves and eye movements which enable more precise event scoring, particularly if hypopneas that otherwise would not account towards the total AHI had resulted in awakening. It also provides the ability to assess SA characteristics during rapid eye movement (REM) and non-REM sleep [9]. Additionally, factors such as alcohol consumption and physical activity, that can interact with SA severity and subsequently affect the yield of SA screening, were not reported in the study. While the relatively large sample size of this study and the consecutive recruitment nature is an advantage, the reader is reminded that all these patients had presented from the AF clinic, introducing a possible selection bias.

This study has an important clinical implication in further stressing the lack of utility of questionnaire-based tools in detecting SA in AF patients. There is an increasing body of evidence that patients with AF do not experience excessive daytime sleepiness in a similar way to the general population [10,11]. We recently reported the lack of correlation between self-reported daytime sleepiness and AHI on 442 consecutive paroxysmal or persistent AF patients, with ESS having little value over a coin toss to detect SA of any severity (AUC 0.48-0.56) [10]. The mechanisms behind this peculiar dissociation between SA severity and experienced sleepiness in the AF population are unclear. One could hypothesise that the excess baseline sympathetic drive experienced by AF patients may counteract the sleepiness [12]. Another potential explanation is that patients attribute their sleepiness from SA to fatigue from AF, with both fatigue and sleepiness being an often confused or similarly-perceived symptoms [13]. This is supported by the finding by Traaen et al that the correlation between AF

symptom severity and self-reported sleepiness improved when patients were also asked about daytime fatigue in addition to sleepiness, as part of the STOP-Bang questionnaire.

In AF patients, moderate-to-severe SA does not manifest in typical SA symptoms such as daytime sleepiness. Therefore, the lack of excessive daytime sleepiness, assessed by history taking or available questionnaires, should not preclude patients from being investigated for the potential presence of concomitant SA. This has important implications for comprehensive risk factor assessment and work-up of AF patients. We learn that interrogation of symptoms, as recommended by the current AF guidelines [3,4], is not sufficient to identify or rule out SA in AF patients. Instead, routine SA testing seems to be reasonable, particularly in AF patients scheduled for invasive or pharmacological rhythm control strategies. Simpler screening devices such as overnight oximetry or ECG-derived respiration monitoring included in Holter software [14,15] may allow more stream-lined implementation of SA management in AF Clinics as part of a comprehensive risk factor management approach [16–18]. Additionally, future studies should investigate the utility of risk scores including clinical features, rather than daytime sleepiness, to identify those patients who need a further and more detailed SA testing.

More research is required to identify the best way to test for SA in an AF clinic setting. Once identified as requiring SA assessment, it can prove challenging to access the right testing resource, motivate patients to undergo SA testing, or indeed to ensure patient compliance with treatment, especially CPAP. Given the large number of patients and the complexities involved in treatment of SA in AF patients, SA screening and management should ideally be organized in an integrated care model by a multidisciplinary team [19]. International AF management guidelines require updating to take the above-mentioned points into consideration, in order to facilitate management of SA in AF clinics and improve patient care.

#### Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2019.100463.

### References

- D. Linz, R.D. McEvoy, M.R. Cowie, V.K. Somers, S. Nattel, P. Levy, et al, Associations of obstructive sleep apnea with atrial fibrillation and continuous positive airway pressure treatment: a review, JAMA Cardiol. 3 (2018) 532–540.
- [2] A. Shukla, A. Aizer, D. Holmes, S. Fowler, D.S. Park, S. Bernstein, et al, Effect of obstructive sleep apnea treatment on atrial fibrillation recurrence: a metaanalysis, JACC Clin. Electrophysiol. 1 (2015) 41–51.
- [3] H. Calkins, G. Hindricks, R. Cappato, Y.H. Kim, E.B. Saad, L. Aguinaga, et al, 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation, Heart Rhythm. 14 (2017) e275–e444.
- [4] P. Kirchhof, S. Benussi, D. Kotecha, A. Ahlsson, D. Atar, B. Casadei, et al, 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS, Eur. Heart J. 37 (2016) 2893–2962.
- [5] E.P. Cheng, C.F. Liu, I. Yeo, S.M. Markowitz, G. Thomas, J.E. Ip, et al, Risk of mortality following catheter ablation of atrial fibrillation, J. Am. Coll. Cardiol. 74 (2019) 2254–2264.
- [6] G.M. Traaen, B. Øverland, L. Aakerøy, T.E. Hunt, C. Bendz, L. Sande, et al, Prevalence, risk factors, and type of sleep apnea in patients with paroxysmal atrial fibrillation, Int. J. Cardiol. Heart. Vasc. 26 (2020) 10447.

- [7] C.A. Kushida, M.R. Littner, M. Hirshkowitz, T.I. Morgenthaler, C.A. Alessi, D. Bailey, et al, Practice parameters for the use of continuous and bilevel positive airway pressure devices to treat adult patients with sleep-related breathing disorders, Sleep 29 (2006) 375–380.
- [8] D. Linz, A.G. Brooks, A.D. Elliott, C.J. Nalliah, J.M.L. Hendriks, M.E. Middeldorp, et al, Variability of sleep apnea severity and risk of atrial fibrillation: the VARIOSA-AF study, JACC Clin. Electrophysiol. 5 (2019) 692–701.
- [9] W.R. Ruehland, P.D. Rochford, F.J. O'Donoghue, R.J. Pierce, P. Singh, A.T. Thornton, The new AASM criteria for scoring hypopneas: impact on the apnea hypopnea index, Sleep 32 (2009) 150–157.
- [10] K. Kadhim, M.E. Middeldorp, A.D. Elliott, D. Jones, J.M.L. Hendriks, C. Gallagher, et al, Self-reported daytime sleepiness and sleep-disordered breathing in patients with atrial fibrillation: SNOozE-AF, Can. J. Cardiol. 35 (2019) 1457– 1464.
- [11] F.N. Albuquerque, A.D. Calvin, F.H. Sert Kuniyoshi, T. Konecny, F. Lopez-Jimenez, G.S. Pressman, et al, Sleep-disordered breathing and excessive daytime sleepiness in patients with atrial fibrillation, Chest. 141 (2012) 967–973.
- [12] S.L. Wasmund, J.M. Li, R.L. Page, J.A. Joglar, R.C. Kowal, M.L. Smith, et al, Effect of atrial fibrillation and an irregular ventricular response on sympathetic nerve activity in human subjects, Circulation 107 (2003) 2011–2015.
- [13] J. Shen, J. Barbera, C.M. Shapiro, Distinguishing sleepiness and fatigue: focus on definition and measurement, Sleep Med. Rev. 10 (2006) 63–76.
- [14] D. Linz, M. Baumert, L. Desteghe, K. Kadhim, K. Vernooy, J.M. Kalman, et al, Nightly sleep apnea severity in patients with atrial fibrillation: potential applications of long-term sleep apnea monitoring, Int. J. Cardiol. Heart Vasc. 24 (2019) 100424.
- [15] D. Linz, K. Kadhim, A.G. Brooks, A.D. Elliott, J.M.L. Hendriks, D.H. Lau, et al, Diagnostic accuracy of overnight oximetry for the diagnosis of sleepdisordered breathing in atrial fibrillation patients, Int. J. Cardiol. 272 (2018) 155–161.
- [16] M.E. Middeldorp, J. Ariyaratnam, D. Lau, P. Sanders, Lifestyle modifications for treatment of atrial fibrillation, Heart (British Cardiac Soc.) (2019).
- [17] D.H. Lau, S. Nattel, J.M. Kalman, P. Sanders, Modifiable risk factors and atrial fibrillation, Circulation 136 (2017) 583–596.
- [18] M.E. Middeldorp, R.K. Pathak, M. Meredith, A.B. Mehta, A.D. Elliott, R. Mahajan, et al, PREVEntion and regReSsive Effect of weight-loss and risk factor modification on Atrial Fibrillation: the REVERSE-AF study, Europace 20 (2018) 1929–1935.
- [19] L. Desteghe, J.M.L. Hendriks, R.D. McEvoy, C.L. Chai-Coetzer, P. Dendale, P. Sanders, et al, The why, when and how to test for obstructive sleep apnea in patients with atrial fibrillation, Clin. Res. Cardiol. 107 (2018) 617–631.

Kadhim Kadhim Dennis H. Lau

Prashanthan Sanders

Centre for Heart Rhythm Disorders, University of Adelaide and Royal Adelaide Hospital, Adelaide, Australia

Dominik Linz\*

Centre for Heart Rhythm Disorders, University of Adelaide and Royal Adelaide Hospital, Adelaide, Australia

Department of Cardiology, Maastricht University Medical Centre, Maastricht, the Netherlands

Department of Cardiology, Radboud University Medical Centre, Nijmegen, the Netherlands

\* Corresponding author at: Centre for Heart Rhythm Disorders, Department of Cardiology, Royal Adelaide Hospital, Adelaide 5000, Australia.

*E-mail address*: Dominik.Linz@adelaide.edu.au

Received 21 December 2019

Accepted 24 December 2019

Available online 6 January 2020