Ambulatory ECG predictors of atrial fibrillation are ineffective in severe sleep apnea

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ABSTRACT

Background: Obstructive sleep apnea (OSA) is strongly associated with atrial fibrillation (AF). Long-term ECG monitoring with implantable loop recorders facilitates the identification of undiagnosed AF in 20% of severe OSA cases. However, ambulatory ECG (AECG) monitoring is less resource intensive, and various parameters have been shown to predict AF. The aim of this study was to assess the efficacy of such AECG-based AF predictors in identifying patients with severe OSA most at risk.
Methods: Prospective observational study including patients with severe OSA and no history of AF. Patients had two 24-h AECG recordings, and if no AF was detected, implanted with a loop recorder (maximum 3 years).
Results: Of 25 patients implanted, AF ≥ 10 s was detected in 5 patients. None of the parameters from the AECG recordings were significantly different between patients who did and did not develop AF.
Conclusions: AECG-based parameters were not effective for the prediction of AF in this severe OSA cohort.

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Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia, affecting 1–4% of the general population [1] and increases the risk of stroke five-fold [2]. Obstructive sleep apnea (OSA) is prevalent in approximately one-third of AF patients [3]. OSA causes hypoxemia, hypercapnia, sympathetic arousal, intrathoracic pressure changes, endothelial dysfunction, and the activation of pro-inflammatory substances [4,5]. These factors contribute to electrical atrial remodeling, which, if uncorrected, produces fibrosis, resulting in permanent changes in the atria and a definitive pro-arrhythmic substrate.

It has recently been demonstrated that long-term ECG monitoring with implantable loop recorders (ILRs) detects undiagnosed AF in 20% of those with severe OSA [6]. However, short-term monitoring is less resource-intensive and may be useful in identifying patients most at risk. Various ambulatory ECG (AECG) parameters such as ectopic burden [7], supra-ventricular arrhythmias [8], and heart rate trends [9] have been purported as predictors of AF. The aim of this study was to assess the value of AECG-based AF predictors in a cohort of patients with severe OSA and no known history of AF.

Materials and methods

This study is a sub-analysis of the Reveal XT-SA study [6]. The Reveal XT-SA study was a prospective observational single-center study that included patients with severe OSA (diagnosed based on polysomnography, Apnea-Hypopnea Index ≥30), age ≥ 18 years, and no history of AF, with the primary outcome of detection of AF lasting ≥10 s. Exclusion criteria included prior history of AF, congestive cardiac failure, or any cardiac devices. Patients underwent two 24-h AECG (Holter) recordings, one month apart, to assess for the presence of AF. If no AF was detected on the AECGs, the patient received a Medtronic Reveal XT implantable loop recorder and had follow-up appointments at 6, 12, 18, 24, 30, and 36 months post-implantation. The loop recorder was explanted if AF was detected or the battery was depleted (estimate 3 years). In this study, analysis of the AECG data was performed to investigate the value of AF predictors in this cohort. Recorded variables included heart rate parameters, supra-ventricular and ventricular ectopics (isolated, couplets, bigeminal cycles, and percentage of total beats), tachyarrhythmias, and pauses.

The study was approved by the Research Ethics Board at Queen's University and conforms to the provisions of the Declaration of Helsinki, 2013. The study is registered on ClinicalTrials.gov (identifier: NCT01058551). All patients gave written informed consent prior to enrolment.

Standard statistical methods were used to analyze the baseline AECG data from patients who did and did not develop AF, including Fisher's

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exact test for binary variables and the independent samples *t*-test with Welch's correction for continuous variables.

Results

Of 31 patients screened, five patients withdrew themselves from the study prior to completion of the two AECG recordings, and one patient withdrew themself prior to the ILR implantation. None of the patients screened had AF detected on any AECG recording.

Of the 25 patients implanted with an ILR (mean age 57.5 ± 9.6 years, mean body mass index 34.9 ± 5.7; 52% male), AF ≥ 10 s was detected in 5 patients (20%). As previously published, the mean duration of AF was 4.8 h, and the mean time to diagnosis was 11 ± 7 months [6]. None of the parameters investigated from the AECGs were significantly different between the patients who did and did not develop AF (Table 1). All patients had premature atrial contractions in at least one 24-h AECG. Of the patients who developed AF during the follow-up, 3 (60%) had supraventricular couplets versus 11 (55%) in patients who did not develop AF (*p* = NS). Patients presenting with ventricular couplets exhibited a similar trend (*p* = 0.60). Likewise, the presence (or duration) of supraventricular runs did not differentiate the populations either. Sinus pauses were similar in both groups.

Of the patients who developed AF, two (40%) reported symptoms; of the patients who did not develop AF, four (20%) reported symptoms (Table 2).

Discussion

Various AECG parameters are associated with an increased incidence of AF. The burden of atrial ectopics was demonstrated to have strong dose dependent relationship [7,10]. Other variables include non-sustained supraventricular arrhythmias [8] and heart rate trends [9]. However, in our cohort of patients with severe OSA, these AECG-based AF predictors did not appear useful in identifying those at greatest risk. Furthermore, the presence of symptomatology, both specific and in general, was also similar between the two groups.

The negative results may be explained, in part, by the aforementioned pathophysiological mechanisms by which OSA may predispose towards AF. The parameters reported from a 24-h AECG recording may be too crude to reflect the changes in the atrial microenvironment promoting electrical remodeling and ultimately, the development of a pro-arrhythmic substrate [11]. Predictors for the development of AF in

this population may be found instead in more refined measures of ECG morphology [12]. P wave duration and morphology criteria of interatrial block is present in approximately one third of cases of moderate to severe OSA [13]. This ECG diagnosis has been demonstrated to have a strong association with AF [14,15] and atrial high rate episodes on cardiac implantable electronic devices [16].

AECG monitoring heart rate variability analysis has been shown to detect OSA [17]. Furthermore, various polysomnography (PSG) pulse rate variability parameters have been associated with a higher incidence of AF. These include a lower low frequency power, a lower low-to-high frequency power ratio, and a higher short-to-long term variability ratio [18]. However, these indices are not readily available on standard PSG reports. Additional analysis is required with specialist software [18]. Given their limited availability in current clinical practice, we did not include PSG-based AF predictors in this study.

The Reveal XT-SA study [6] is a pilot study on cardiac monitoring in patients with severe OSA and no history of AF, and thus, is limited by a small size. As a result, weak AECG-based AF predictors may have been detected in a larger population.

Conclusion

AECG-based AF predictors were not effective in this cohort of severe OSA patients.

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Declaration of Competing Interest

Authors declare no conflicts of interest for this article.

Table 1
Parameters from 24-h ambulatory ECG recordings for patients with severe obstructive sleep apnea who did and did not develop atrial fibrillation.

	Atrial fibrillation (*n* = 5)	No atrial fibrillation (*n* = 20)	*p* value
Heart rate			
Minimum	50.4 ± 8.4	50.4 ± 6.5	0.99
Mean	74.2 ± 8.3	74.7 ± 9.8	0.87
Maximum	119.7 ± 19.4	119.8 ± 19.6	0.99
Ventricular beats			
Isolated premature ventricular contractions	415 ± 964	648 ± 2286	0.63
Couplets (%)	40	25	0.60
Bigeminal (%)	0	15	1.00
Runs (%)	20	0	0.20
Beats >1% (%)	20	10	0.50
Supraventricular beats			
Isolated premature supraventricular contractions	64 ± 74	89 ± 313	0.65
Couplets (%)	60	55	1.00
Runs >4 beats (%)	40	40	1.00
Runs <4 beats (%)	0	20	0.55
Beats >1% (%)	0	5	1.00
Maximum R-R interval >2 s (%)	0	5	1.00

Table 2
Symptoms reported by patients with severe obstructive sleep apnea who did and did not develop atrial fibrillation.

	Atrial fibrillation (n = 5)	No atrial fibrillation (n = 20)
Fatigue (%)	20	10
Dizziness (%)	20	10
Dyspnea (%)	10	5
Presyncope (%)	10	0
Palpitations (%)	0	15
Weakness (%)	0	10
Syncope (%)	0	0
Chest Pain (%)	0	0

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