Hypoxaemic load in sleep apnoea is associated with acute changes in T-wave amplitude

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Detailed analyses of nocturnal ECG data using computational methods enable the detection of subtle changes in cardiac activity indicative of an increased risk of cardiac morbidity and mortality in sleep apnoea https://bit.ly/3X127HW

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Abstract

Aims Obstructive sleep apnoea (OSA) imposes significant stress on the cardiovascular system and the heart. While long-term cardiac effects are understood, the immediate impact of hypoxaemia on the heart's electrophysiology lacks understanding. Our study aims to explore desaturation severity on cardiovascular repolarisation.

Methods We retrospectively analysed ECGs from full diagnostic polysomnographies from 492 patients with suspected OSA. The analyses were conducted before, during and after 9137 nocturnal apnoea- or hypopnoea-related desaturations. The mean and SD of T-wave amplitude change from the baseline level to the level during and after desaturations (ΔT_{amp_mean} and ΔT_{amp_SD}) were calculated. To investigate the modulatory effects of desaturation severity, the data were divided into subgroups based on the desaturation duration (T_{des}; $10\ s \leqslant T_{des} < 20\ s$, $20\ s \leqslant T_{des} < 30\ s$, $30\ s \leqslant T_{des} < 45\ s$ and $T_{des} \geqslant 45\ s$) and magnitude of blood oxygen saturation drop (change in peripheral oxygen saturation (ΔS_{pO_2}); $3\% \leqslant \Delta S_{pO_2} < 4.5\%$, $4.5\% \leqslant \Delta S_{pO_2} < 6\%$, $6\% \leqslant \Delta S_{pO_2} < 7.5\%$ and $\Delta S_{pO_2} \geqslant 7.5\%$) for men and women.

Results Desaturations caused significant ($p<0.01$) changes in ΔT_{amp_mean} during and after desaturations. In men, the median ΔT_{amp_mean} during and after deep ($\Delta S_{pO_2} \geqslant 7.5\%$) desaturations were 21 µV and 24 µV, respectively. In women, the median ΔT_{amp_mean} in deep desaturations was 15 µV during and 21 µV after desaturations. Similarly, the ΔT_{amp_SD} increased during and after deep desaturations. In regression analysis, the desaturation depth was an independent predictor for ventricular repolarisation instability.

Conclusion We found an association between the severity of nocturnal desaturations and cardiac repolarisation instability. These findings hold particular importance, as repolarisation instability has been linked with cardiovascular morbidity and could potentially serve as a trigger for arrhythmias and sudden cardiac death.

Introduction

Obstructive sleep apnoea (OSA) is a prevalent sleep disorder that affects approximately one billion adults worldwide and shares several common risk factors and comorbidities with cardiovascular disease [1]. Studies have shown that OSA patients have over five times higher risk for overall cardiovascular mortality and almost three times higher risk of nocturnal sudden cardiac death (SCD) [2, 3]. Also, the severity of apnoea and hypopnoea events and related desaturations has been shown in previous studies to be a useful marker for identifying patients with OSA who are at increased risk of cardiovascular morbidity and

mortality [4, 5]. Recurrent breathing cessations and subsequent desaturations in OSA are thought to partly contribute to the relationship between OSA and cardiovascular disease through their impact on autonomic regulation dysfunction, potentially serving as a substrate for electrophysiological change [6, 7].

The T-wave represents the repolarisation of the cardiac ventricles, and its amplitude and polarity changes are signs of cardiac repolarisation instability [8]. The T-wave variation (called T-wave alternans, a phenomenon where there is a beat-to-beat alternation in the morphology, amplitude or polarity of the T-wave on an ECG) signifies an inhomogeneity in the refractoriness of the myocardium, setting the stage for re-entry and facilitating the onset of malignant ventricular arrhythmias and can lead to SCD [9–11]. Moreover, even minor changes in T-wave alternans can be utilised for noninvasive risk stratification of cardiac arrhythmias and SCD [12–14]. In turn, a previous study has proposed that stability in T-wave alternans measurements among patients with heart failure could be indicative of a lower tendency to SCD [14]. Given this background, we hypothesised that desaturation severity affects T-wave amplitude variability, indicating an increased risk of cardiac arrhythmias in patients with suspected OSA.

Methods

Study population

We retrospectively analysed a subset from data comprising 916 consecutive full diagnostic polysomnography (PSG) recordings of suspected OSA patients. PSGs were conducted at the Princess Alexandra Hospital (Brisbane, Australia) during 2015–2017 using the Compumedics Grael acquisition system (Compumedics, Abbotsford, Australia). Approval for retrospective data collection and reuse was obtained from The Metro South Human Research Ethics Committee, Brisbane, Australia (LNR/2019/QMS/54313). All procedures performed in studies involving human participants were done in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The need for informed consent was waived by the Metro South Human Research Ethics Committee due to the retrospective nature of the study.

The PSG recordings were manually scored in concordance with the American Academy of Sleep Medicine 2012 guidelines [15]. The scoring was conducted by experienced sleep technicians in Princess Alexandra Hospital using Compumedics ProFusion PSG 4 software (Compumedics, Abbotsford, Australia). All desaturations with $\geqslant$3% blood oxygen saturation drop (change in peripheral oxygen saturation (ΔS_{pO_2})) were scored manually from the onset of the desaturation to the recovery of oxygenation. The scoring process has been described in previous work [16]. The detailed information of each desaturation (start time, end-point, duration and depth) was exported from ProFusion to MATLAB (version R2019b; MathWorks, Natick, MA, USA) for data processing. All scored desaturations during wake were excluded.

We excluded patients having a pacemaker (n=26), atrial fibrillation/flutter (n=41), insufficient ECG signal quality (n=135), less than 4 h of sleep (n=197) or diagnosis of previous heart failure (n=23) or respiratory failure (n=25). ECG signals were manually reviewed and subjects with apparent T-wave abnormalities (inverted T-wave, biphasic T-wave and prominent U-wave; n=121) were also excluded. It should be noted that some patients may have met multiple exclusion criteria, resulting in the exclusion of 425 patients from the study (supplementary figure S1). The final dataset comprised 492 patients (table 1).

ECG analysis

Nocturnal ECGs (modified lead II) were recorded during the diagnostic PSG study, with a sampling frequency of 256 Hz. ECG signals were filtered with a fourth-order Butterworth bandpass filter with a bandpass frequency of 0.5–40 Hz. Based on the start and end times of each desaturation within each PSG recording, time-matched ECG samples were extracted. ECG signals were examined in three parts: 1) a 10-s baseline sample starting from 10 s before the onset of the related respiratory event; 2) an ECG sample during desaturation; and 3) a 15-s post-desaturation sample. If the post-desaturation and baseline sample of two consecutive desaturations overlapped, all samples related to the latter desaturation were excluded from further analyses. In addition, desaturations shorter than 10 s were excluded. Also, desaturations related to a respiratory event accompanied by arousal were not considered in this study.

ECG delineations were carried out automatically using a wavelet-based delineation method [17]. Each segment was automatically checked for the presence of ectopic beats [18]. Segments in which 20% of the beats were excluded due to the noise or containing an ectopic beat were left out of the analysis. To exclude possible low-quality ECG samples, only segments with a mean heart rate of at least 30 beats per min were included in the analysis. If any segment related to the baseline, during desaturation or post-desaturation of a desaturation event was excluded, the whole sequence was also excluded. In total, 8159 desaturations were excluded from the analysis. After quality checking, 9137 desaturations were included in the analyses

TABLE 1 Demographics and characteristics of the studied population

Clinical characteristics	Men	Women
Patients	256	236
Age, years	51.2 (40.1–62.1)	51.0 (41.0–61.3)
BMI, kg·m^{-2}	32.1 (27.8–38.4)	35.6 (30.1–42.7)*
AHI, events·h^{-1}	21.8 (9.5–36.5)	10.5 (4.0–18.5)*
AI, events·h^{-1}	28.7 (19.3–42.9)	20.6 (14.1–30.1)*
ODI, events·h^{-1}	16.8 (5.2–37.2)	7.5 (2.2–20.8)*
TST, min	328.0 (283.4–370.0)	338.5 (300.8–382.0)
T90, min	2.4 (0.1–25.5)	1.6 (0.1–17.7)
Comorbidities		
Atrial dysrhythmia	12 (4.7)	9 (3.8)
COPD	14 (5.5)	18 (7.6)
Dyslipidaemia	45 (17.5)	38 (16.1)
Hypertension	94 (36.7)	87 (36.9)
Stroke history	7 (2.7)	13 (5.5)
T2DM	45 (17.5)	36 (15.3)
Medications#		
Antipsychotics	8 (5.6)	7 (5.2)
Beta-blockers	21 (14.9)	24 (17.6)
Other antiarrhythmics	0 (0)	0 (0)

Data are presented as n, median (interquartile range) or n (%). BMI: body mass index; AHI: apnoea–hypopnoea index; AI: arousal index; ODI: oxygen desaturation index; TST: total sleep time; T90: sleep time with oxygen saturation <90%; T2DM: diabetes mellitus type II. #: due to the lack of a complete list of medications for all patients, medication data are available for a subpopulation (men n=141, women n=136). *: p<0.05 (statistically significant difference between men and women).

(supplementary figure S1). T-wave amplitude was calculated in a beat-to-beat manner for baseline, during and post-desaturation samples of a desaturation event (figure 1). T-wave amplitude was calculated as the difference between the T-wave peak and the previous isoelectric line (median of 20 ms) before the onset of the P-wave.

To investigate repolarisation instability, the T-wave amplitude change from the baseline level to the level during and after desaturations was calculated. The T-wave amplitude was calculated for every beat within a segment. Changes in the mean and SD of T-wave amplitude (ΔT_{amp_mean} and ΔT_{amp_SD}) were calculated from the baseline segments to during and after desaturation segments. ΔT_{amp_mean} and ΔT_{amp_SD} were calculated once from the baseline segment to during the desaturation segment and once from the baseline segment to after the desaturation segment. To investigate the modulatory effects of desaturation severity, the data were divided into four subgroups based on the desaturation duration (T_{des}; 10 s$\leqslant T_{des}$<20 s, 20 s$\leqslant T_{des}$<30 s, 30 s$\leqslant T_{des}$<45 s and $T_{des}\geqslant$45 s) and magnitude of blood oxygen saturation drop (3%$\leqslant\Delta S_{pO_2}$<4.5%, 4.5%$\leqslant\Delta S_{pO_2}$<6%, 6%$\leqslant\Delta S_{pO_2}$<7.5% and $\Delta S_{pO_2}\geqslant$7.5%) for men and women (table 2), which reflects the methodology used in our previous study [7].

Statistical analysis

We conducted a normality test on the dataset, which revealed that not all data groups exhibited a normal distribution. Consequently, we opted to proceed with nonparametric statistical tests to accommodate the non-normality observed. We used a Wilcoxon's signed-rank test to evaluate the statistical significance of the change from baseline to during and post-desaturation values. We considered different desaturation groups not to be statistically independent because desaturations from the same patient were present in multiple groups. As Wilcoxon's signed-rank test utilises pairwise comparison, we used the test iteratively to evaluate the statistical significance of the difference between desaturation groups: we computed 5000 randomly chosen permutations of value pairs between two groups at a time and calculated the median of all p-values to represent the statistical significance of the change between two groups in a similar manner as described in the previous studies [19, 20]. Measures of effect size for between-group comparisons were calculated using Pearson's correlation. In addition, two multivariate regression models were used to analyse and identify the effects of possible confounding factors and comorbidities: a regression model for the magnitude of absolute ΔT_{amp_mean} and ΔT_{amp_SD} from baseline to during desaturation and another model for absolute ΔT_{amp_mean} and ΔT_{amp_SD} from baseline to post-desaturation. Separate regression

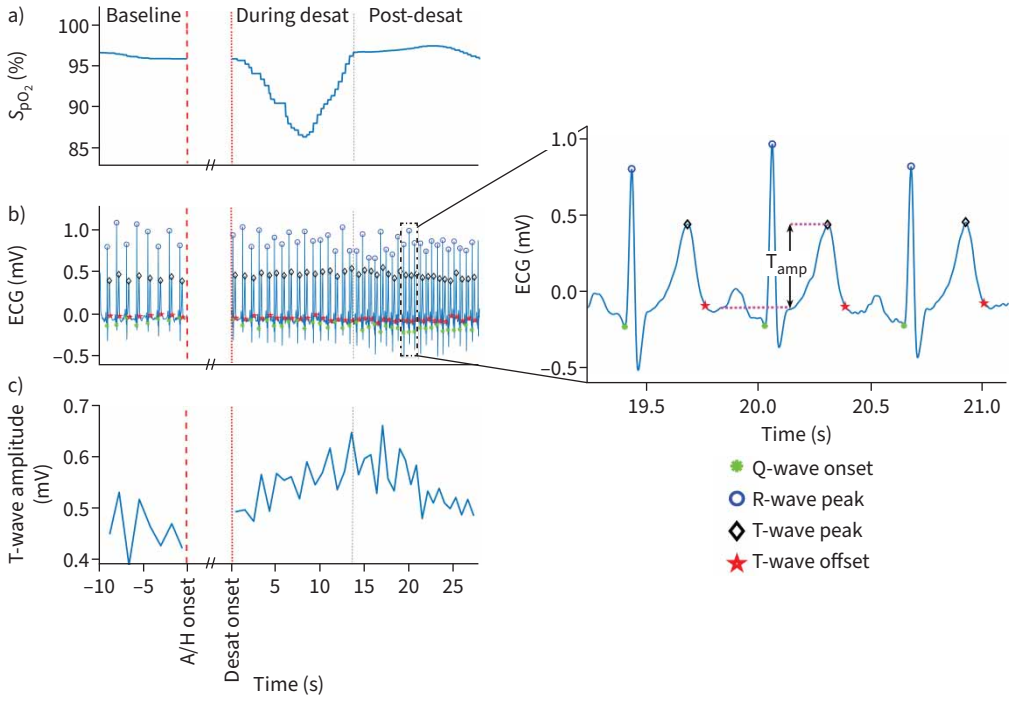

FIGURE 1 Demonstration of how T-wave amplitudes (T_{amp}) were calculated. a) Detection of desaturation (desat) events. b) Delineated time-matched baseline, during and post-desaturation ECG samples. c) Calculation of T-wave amplitude time series. S_{pO_2}: peripheral oxygen saturation; A/H: apnoea/hypopnoea.

models were utilised to analyse the effects of possible confounding medications on baseline T-wave amplitude values and absolute changes in the mean and SD of T-wave amplitude from baseline segments to during desaturation segments in a subpopulation of the dataset due to the lack of a complete list of medications for all patients in the studied population. Patients contributed varying numbers of datasets to the regression models, with each patient contributing at least one set of data to the models. Statistical data analysis was performed with MATLAB R2022b. A p-value <0.05 was considered to represent a statistically significant change.

TABLE 2 The numbers of analysed desaturations in different subgroups based on duration and depth

	Men (n=256)		Women (n=236)	
	Desaturations, n	Patients contributing, %	Desaturations, n	Patients contributing, %
Duration				
10 s⩽T_{des}<20 s	1194	61	1281	59
20 s⩽T_{des}<30 s	1689	70	1302	69
30 s⩽T_{des}<45 s	1439	67	1057	65
T_{des}⩾45 s	656	52	519	50
Total	4978	100	4159	100
Depth				
3%⩽ΔS_{pO_2}<4.5%	3344	84	2754	79
4.5%⩽ΔS_{pO_2}<6%	536	50	470	52
6%⩽ΔS_{pO_2}<7.5%	513	39	508	45
ΔS_{pO_2}⩾7.5%	585	34	427	31
Total	4978	100	4159	100

T_{des}: desaturation duration; ΔS_{pO_2}: change in peripheral oxygen saturation.

Results

The mean T-wave amplitude before desaturations was 356 µV (95% interquartile range (IQR) 138–641 µV) in men and 278 µV (95% IQR 120–545 µV) in women. In general, desaturations caused significant ($p<0.01$) changes in the mean and SD of T-wave amplitude during and after desaturations (figures 2 and 3). The ΔT_{amp_mean} in deep desaturations ($\Delta S_{pO_2} \geqslant 7.5\%$) was significantly ($p<0.05$) higher compared with less severe desaturations (figure 2a). In women, the median ΔT_{amp_mean} in deep desaturations ($\Delta S_{pO_2} \geqslant 7.5\%$) was 15 µV (95% IQR 7–30 µV) during desaturation and 21 µV (95% IQR 9–35 µV) after desaturation. In men, the median ΔT_{amp_mean} during and after deep desaturation was 21 µV (95% IQR 9–43 µV) and 24 µV (95% IQR 11–48 µV), respectively. It is noteworthy, that in almost all depth and duration groups, the post-desaturation changes were even higher than during the desaturation. Measures of the effect size for between-group comparisons are presented in supplementary tables S1–4.

The regression analysis for the changes in T-wave amplitude from baseline to during desaturation showed a similar phenomenon (table 3). Deepening of the desaturations increased the magnitude of both ΔT_{amp_mean} and ΔT_{amp_SD} ($\beta=1.138$, $p<0.001$ and $\beta=0.346$, $p<0.001$, respectively) showing increased levels of ventricular repolarisation instability in deep desaturations. On the other hand, longer desaturations decreased the magnitude of ΔT_{amp_SD} ($\beta=-0.030$, $p<0.05$) with no significant effect on ΔT_{amp_mean}. Apart from desaturation parameters, also higher baseline levels of T-wave amplitude ($\beta=0.013$, $p<0.001$) and longer RR intervals ($\beta=0.025$, $p<0.001$) during desaturation were significant predictors of the increased

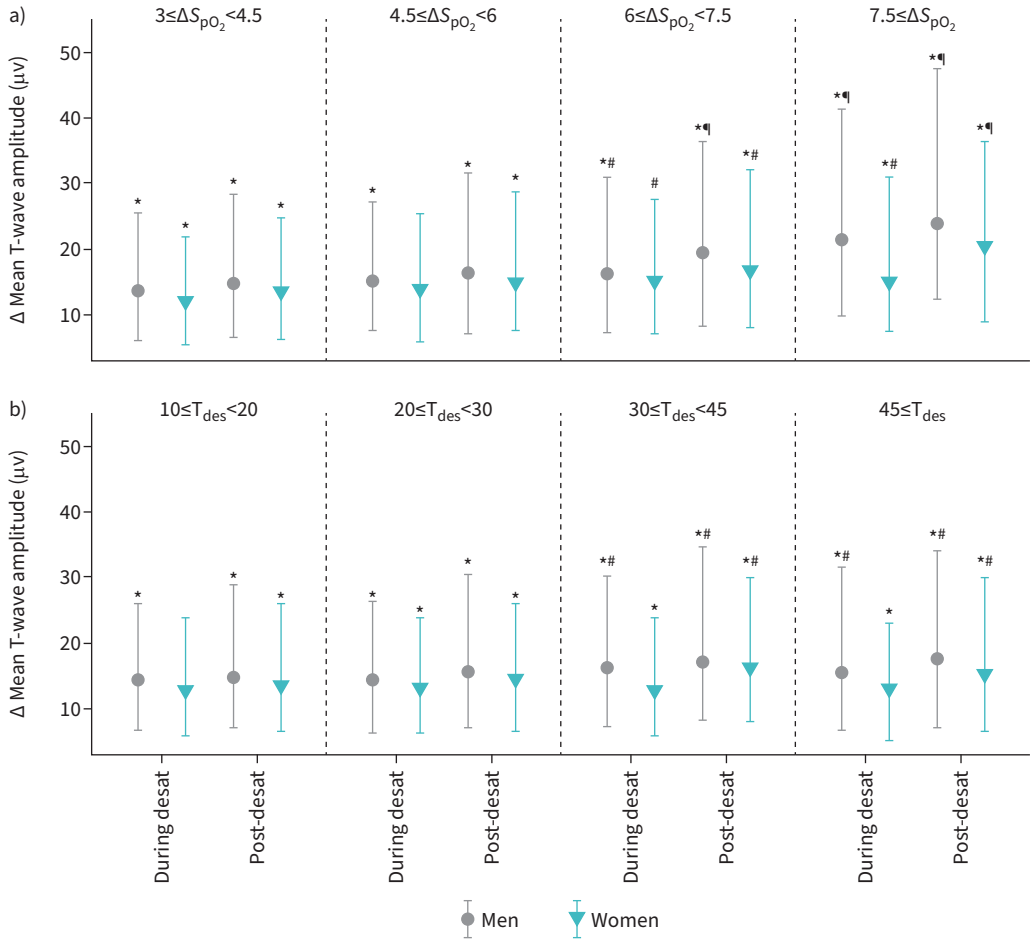

FIGURE 2 Changes compared with the baseline measure in mean T-wave amplitude in desaturations for men and women (n=492) in a) subgroups based on desaturation depth (change in peripheral oxygen saturation (ΔS_{pO_2}) percentage) and b) subgroups based on desaturation duration (T_{des}; in s). *: $p<0.05$; statistical significance was calculated with the Wilcoxon signed-rank test and the change compared with the baseline T-wave amplitude. #: $p<0.05$; statistically significant change compared with the 10–20 s or 3–4.5% group. ¶: $p<0.05$; statistically significant change compared with all duration and depth groups.

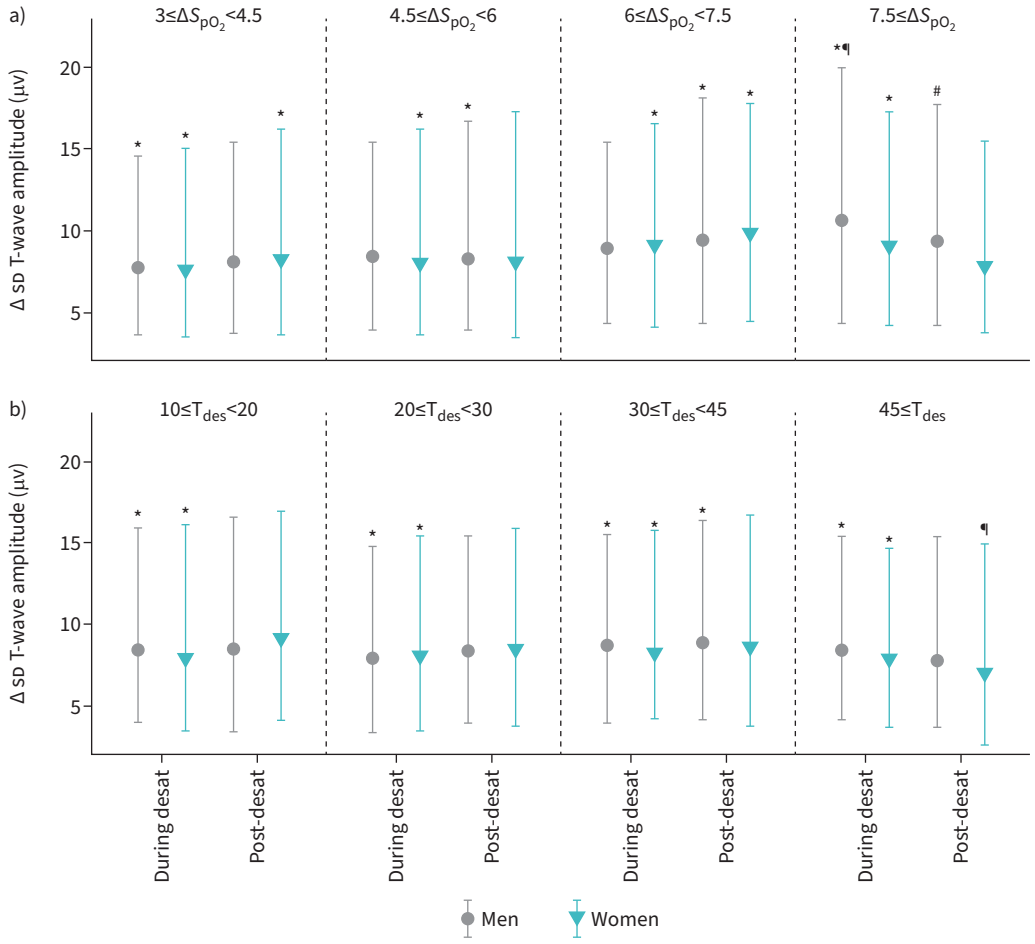

FIGURE 3 Changes compared with the baseline measure in the SD of T-wave amplitude in desaturations for men and women (n=492) in a) subgroups based on desaturation depth (change in peripheral oxygen saturation (ΔS_{pO_2}) percentage) and b) subgroups based on desaturation duration (T_{des}; in s). *: p<0.05; statistical significance was calculated with the Wilcoxon signed-rank test and the change compared with the baseline T-wave amplitude. #: p<0.05; statistically significant change compared with the 10–20 s or 3–4.5% group. ¶: p<0.05; statistically significant change compared with all duration and depth groups.

magnitude in ΔT_{amp_mean} (table 3). An increase in age was shown to be accompanied by a decrease in the magnitude of both ΔT_{amp_mean} and ΔT_{amp_SD} ($\beta=-0.056$, $p<0.01$ and $\beta=-0.084$, $p<0.001$, respectively). Furthermore, the existence of COPD increased the magnitude of ΔT_{amp_SD} (table 3). The effects of variables and their significance in T-wave amplitude from baseline to post-desaturation (supplementary table S5) were similar to the changes from baseline to during desaturations. The regression model for considering the effects of medication revealed that a history of using beta-blockers decreased the magnitude of ΔT_{amp_mean}, whereas antipsychotic drugs significantly increased it. Neither of these medications affected the magnitude of ΔT_{amp_SD} (table 4). The effects of medications were also present in the baseline T-wave amplitude values (supplementary table S6), yet the associations were in the opposite directions compared with T-wave amplitude changes from baseline to during desaturations.

Discussion

The present study shows that there are significant changes from baseline in T-wave amplitude during and after desaturations. Deeper desaturations ($\Delta S_{pO_2} \geq 6\%$) resulted in higher changes in T-wave amplitude. Regression analysis showed that deeper desaturations independently increased the magnitude of T-wave amplitude changes, indicating increased ventricular repolarisation instability. We also discovered that age, comorbidities and medications modulated the response of T-wave amplitude to desaturations. These findings highlight two critical aspects. First, the apnoea–hypopnoea index may not be sufficient to evaluate the severity of OSA in terms of cardiac event risk, especially in the case of repolarisation instabilities. In

TABLE 3 Multivariate regression model for absolute ΔT_{amp_mean} and ΔT_{amp_SD} during desaturations

	ΔT_{amp_mean}		ΔT_{amp_SD}	
	β-Coefficient	p-value	β-Coefficient	p-value
Age, years	**−0.060**	**0.017**	**−0.106**	**<0.001**
BMI, kg·m^{-2}	−0.059	0.117	**−0.097**	**<0.001**
Sex, men	0.403	0.487	−0.032	0.938
AHI, events·h^{-1}	**−0.057**	**0.001**	**−0.036**	**0.005**
AI, events·h^{-1}	**0.086**	**<0.001**	**0.061**	**<0.001**
Desaturation depth, %	**1.313**	**<0.001**	**0.408**	**<0.001**
Desaturation duration, s	−0.022	0.218	**−0.039**	**0.003**
S_{pO_2} nadir, %	0.140	0.080	0.048	0.403
Baseline T_{amp}, mV	**0.011**	**<0.001**	−0.001	0.619
QT interval, ms	**−0.061**	**<0.001**	**0.036**	**<0.001**
RR interval, ms	**0.025**	**<0.001**	−0.003	0.150
Atrial dysrhythmia	−1.230	0.423	−1.474	0.186
COPD	0.820	0.423	**3.098**	**<0.001**
Dyslipidaemia	**−2.119**	**0.003**	−0.431	0.416
Hypertension	−0.482	0.387	−0.018	0.963
T2DM	**−3.588**	**<0.001**	0.202	0.656
Stroke history	**−2.111**	**0.050**	1.459	0.068

Data are presented as raw values for β-coefficients. Statistically significant ($p<0.05$) values are in bold. Except for desaturation duration, desaturation depth, RR interval, QT interval and baseline T-wave amplitude (T_{amp}), parameters were treated patient-wise; these parameters were computed for each desaturation separately. ΔT_{amp_mean}: change in the mean of T-wave amplitude from baseline to during desaturation; ΔT_{amp_SD}: change in the SD of T-wave amplitude from baseline to during desaturation; BMI: body mass index; AHI: apnoea–hypopnoea index; AI: arousal index; S_{pO_2}: peripheral oxygen saturation; T2DM: diabetes mellitus type II.

line with previous studies [4, 5], our observations also demonstrate that OSA can have more severe health impacts despite a lower frequency of events, as more severe desaturations have bigger impacts on ventricular repolarisation regardless of the number of occurrences. Second, the nocturnal ECG provides valuable information that is easily extractable from PSG and conversely, similar ECG findings in, for example, 24 h Holter recordings should lead to an investigation of possible confounding sleep disorders for cardiac patients.

TABLE 4 Multivariate regression model for absolute ΔT_{amp_mean} and ΔT_{amp_SD} during desaturations for the confounding effect of medications in a subpopulation of the data (n=277)

	ΔT_{amp_mean}		ΔT_{amp_SD}	
	β-Coefficient	p-value	β-Coefficient	p-value
Age, years	−0.061	0.064	**−0.056**	**0.003**
Sex, men	−0.807	0.301	−0.276	0.547
BMI, kg·m^{-2}	**−0.132**	**0.007**	**−0.076**	**0.007**
AHI, events·h^{-1}	−0.003	0.828	0.009	0.274
Desaturation duration, s	0.001	0.970	−0.007	0.626
Desaturation depth, %	**1.139**	**<0.001**	**0.323**	**<0.001**
Baseline T_{amp}, mV	**0.009**	**<0.001**	0.001	0.621
RR interval, ms	**0.049**	**<0.001**	−0.001	0.423
QT interval, ms	**−0.108**	**<0.001**	**0.022**	**0.017**
Beta-blockers	**−6.296**	**<0.001**	−0.430	0.440
Antipsychotics	**8.840**	**<0.001**	1.638	0.120

Data are presented as raw values for β-coefficients. Statistically significant ($p<0.05$) values are in bold. ΔT_{amp_mean}: change in the mean of T-wave amplitude from baseline to during desaturation; ΔT_{amp_SD}: change in the SD of T-wave amplitude from baseline to during desaturation; BMI: body mass index; AHI: apnoea–hypopnoea index; T_{amp}: T-wave amplitude.

It is well known that OSA causes sympathetic autonomic nervous system (ANS) activation by increasing pulmonary artery pressure and chemoreceptor activation (acidosis, hypoxia and hypercapnia) [6]. Chemoreceptor activation caused by apnoeas increases the respiratory drive causing hyperventilation after arousal [21]. Voluntary hyperventilation has shown the capability to induce repolarisation abnormalities [22]. In addition, the nocturnally dominant acidosis caused by the hypoxic load can turn into wake-time alkalosis *via* elevated bicarbonate levels. Moreover, TAVARES *et al.* [6] showed that when arterial oxygen saturation (S_{aO_2}) declines there is a progressive increase also in sympathetic activation and another study showed that ANS activation regulates further the T-wave amplitude [23]. Together with our results, these findings show that desaturations are associated with greater repolarisation instability during and after desaturations. The hypoventilation–hyperventilation cycle resulting from OSA together with instability in acid–base levels may lead to ANS impairment causing the observed instability in repolarisation dynamics. Moreover, the sympathetic stimulation influences different aspects of myocardial function, leading to increased heart rate, faster conduction and accelerated repolarisation of myocardial cells [24]. These alterations may further manifest as changes in T-wave morphology on the ECG, reflecting underlying disturbances in myocardial repolarisation. In the current research, we showed that the desaturation depth effect on T-wave amplitude changes during desaturation and the change seems to be most profound after desaturation (figures 2 and 3). This finding is in line with a previous study showing that the activity of the sympathetic nervous system fluctuates throughout the apnoea event, reaching its peak during the post-apnoeic hyperventilation stage [25]. The post-apnoeic phase is characterised by a dynamic period of sympathetic activation and physiological adaptation aimed at maintaining cardiac function and oxygen delivery during episodes of sleep-disordered breathing. Understanding more about the mechanisms underlying this phase is crucial for unravelling the cardiovascular consequences of sleep apnoea and developing targeted therapeutic interventions. The present results show that in this cohort, desaturation depth was independently associated with higher repolarisation instability. Therefore, it is essential to address OSA and the associated hypoxaemic events in a detailed manner to mitigate the risk of cardiovascular disease and other complications. Moreover, these results support the view that ECG provides valuable information as a part of the sleep recording and could be beneficial to consider in diagnostic decision making. In addition, the typical OSA-related ECG waveform and RR series fluctuations are observable in Holter recordings, for example, and thus can give direct information on the presence of OSA contributing to cardiac load.

Cardiac repolarisation is affected by sex hormones [26, 27]. Women have naturally longer QT times than men and long QT syndrome is more prevalent in women [28]. However, men tend to have greater T-wave amplitude than women [29]. In the current study, men also had higher T-wave amplitude values and greater T-wave amplitude changes during and after desaturations (figures 2 and 3). However, sex was not independently associated with changes in T-wave amplitude (tables 3 and 4). In addition, age affects repolarisation as T-wave amplitude decreases with age [29]. Our study also showed that age had an independent effect on T-wave amplitude changes associated with desaturations and T-wave amplitude instability was more pronounced in younger study subjects.

The prevailing view is that certain drugs increase the risk of having life-threatening arrhythmias. Repolarisation abnormalities are suspected to lie in the background of these arrhythmias and SCD due to unrecognised adverse drug effects [30]. Therefore, we also evaluated the effect of potentially arrhythmogenic drugs, but we had only limited medication history available (56% of the study population; table 1). Regression analysis revealed significant confounding effects of both antipsychotics and beta-blockers. Patients with antipsychotics had greater T-wave amplitude changes compared with those without antipsychotic medication. Beta-blockers had the opposite effect as patients with beta-blockers had smaller T-wave amplitude changes compared with patients without them. In addition to medication, the plasma potassium level increase during hyperventilation may affect repolarisation [31]. The effects of medications were also present in baseline T-wave amplitude values (supplementary table S6) yet the associations were in the opposite directions compared with T-wave amplitude changes from baseline to during desaturation. Furthermore, several OSA-related comorbidities are associated with repolarisation abnormalities. We analysed the possible confounding effects of comorbidities through multiple regression analysis (table 3). Together with longer and deeper desaturations, having COPD might lead to greater changes in T-wave amplitudes. This is interesting as T-wave amplitude changes in COPD have not been extensively studied. Our finding might be due to chronic ventilation–perfusion mismatching, diffusion-type limitation and reduced S_{aO_2} levels [32]. Also, COPD-related anatomical changes such as hyper expansion of the lungs may cause lowering of the diaphragm and due to its fixed attachments to the great vessels, the heart rotates, which may affect the ECG [33]. Also, the presence of increased air between the heart and recording electrodes may affect ECG amplitudes to some extent. Hypertension did not influence the T-wave amplitude instability, and the history of atrial arrhythmia did not have an impact on T-wave amplitude. Unfortunately, we did not have information on the patients' coronary disease status.

We had some limitations in this study. First, we used only one lead (modified lead II) for analysis. However, this is the recommended ECG setting during PSG recordings [15]. Artefacts and noises can compromise ECG delineations and T-wave amplitude calculations. Therefore, all signals were monitored for the overall quality and presence of apparent T-wave abnormality. The segment exclusion criteria were designed to minimise the possibility of considering noisy beats in the analysis. As the delineation process of the beats was fully automated, some occasional incorrect beat delineation may occur in the analysed segments due to the artefacts. Moreover, we excluded desaturations that were accompanied by arousals. Previous studies demonstrated that arousals have acute effects on ventricular repolarisation [34]. To avoid misinterpretations of possible acute effects of desaturation events on T-wave morphology, we made a deliberate decision to not include desaturations accompanied by arousals in the current study. Second, we analysed both comorbidity and medication data as dichotomous variables. It is acknowledged that, for example, hypertension comes with high variation in terms of its severity, and different drugs have a dose-dependent relationship with cardiac electrophysiology. However, we consider that this does not jeopardise the conclusions made from the analyses. Furthermore, while the T-wave variations noted in our study may appear minimal (up to 24 µV from baseline) and imperceptible to the naked eye, there is evidence suggesting that even minor changes in T-wave instability can have clinical relevancy [12–14]. Typically, a T-wave alternans test conducted during bicycle stress testing is deemed positive when the alternans are $\geqslant$1.9 µV. Yet, it is important to note that our method of quantifying repolarisation changes is distinct from that used in T-wave alternans tests.

Conclusion

In conclusion, analysing nocturnal ECG data using computational methods enables the detection of subtle changes in cardiac activity. We found that severe desaturations are associated with greater T-wave amplitude changes during and after desaturations than mild desaturations. This could indicate an increased risk of cardiac morbidity and mortality, yet more research is needed on long-term influence.

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