Dear Editor,

The association between cardiac arrhythmias and obstructive sleep apnoea (OSA) is well established.1-5 Both conditions lead to significant morbidity and mortality if left untreated.6 Recurrent episodes of apnoea, hypoxaemia and hypercapnia in patients with OSA lead to chemoreceptor excitation, increased sympathetic drive and cardiac arrhythmias.7-9 Given the crucial role of oxygen desaturation in arrhythmogenesis, evidence describing lowest oxygen saturation (LSAT), duration of LSAT (hypoxic time) and cardiac arrhythmias in OSA patients is lacking from existing studies. Moreover, accurately establishing predictors of cardiac arrhythmia is crucial in order to accurately identify high-risk OSA patients who require closer monitoring during overnight polysomnography, outpatient follow-up and more aggressive treatment. This is because the risk of sudden cardiac death during sleep is increased in OSA patients with cardiac arrhythmias. Cardiac deaths may be due to ventricular arrhythmias from left heart remodelling, overwork and ischaemia; sinus arrest or atroioventricular block while asleep from higher vagal tone.10-13 Therefore, this study was undertaken to evaluate the relationship between hypoxic time and cardiac arrhythmias, and identify the predictors of cardiac arrhythmias in a cohort of patients with OSA.

Materials and Methods

Of the 1457 patients diagnosed with OSA during overnight in-laboratory polysomnogram at a single tertiary institution from January 2011 to December 2012, retrospective chart reviews were performed on 117 patients with coexisting cardiac arrhythmia. Patients with cardiac arrhythmia not previously evaluated were referred to a cardiologist for further investigation.

Demographical data (including gender, age, ethnicity, neck circumference and body mass index [BMI]) were recorded. All patients underwent overnight in-laboratory polysomnography (diagnostic gold standard), which included continuous monitoring of electroencephalogram, submental and anterior tibial electromyogram, chest wall and abdominal excursions with plethysmography, oxygen saturation with finger oximeter, and cardiac monitoring with modified lead II electrocardiogram (ECG) tracing. Patients with cardiac arrhythmias (atrial, ventricular, conduction delay arrhythmias) detected during polysomnogram were included in the study. Hypopnoea was defined as incomplete cessation of breathing lasting longer than 10 seconds whereby there was decreased ventilation of ≥50% leading to reduction in oxygen saturation of ≥4%. Apnoea was defined as complete cessation of breathing lasting longer than 10 seconds. The apnoea-hypopnoea index (AHI) was the number of apnoeic or hypopnoeic events per hour based on the American Academy of Sleep Medicine (AASM) Scoring Manual Version 2.2. OSA was defined as AHI of ≥5, and further stratified into mild (AHI 5-15), moderate (AHI 15-30) and severe (AHI >30). Hypoxic time was defined as the duration (min) when lowest oxygen saturations (LSAT) were <85% and <90%.

Predictors of cardiac arrhythmias in patients with OSA were identified using univariate analysis with chi-square test and Mann Whitney U test (R 3.0.2). P value <0.05 was considered statistically significant. Prediction performance of hypoxic time when LSAT were <85% and <90% were analysed using receiver operating characteristic (ROC) curve from a univariable logistic model. A cutoff point which achieved best sensitivity and specificity was obtained. Log transformation was used to reduce the skewness of hypoxic time.

Results

Of the 1457 patients diagnosed with OSA, 117 patients (8%) had cardiac arrhythmias. Out of the 117 patients with cardiac arrhythmias, 22 were pre-existing. Age (P <0.01), neck circumference (P = 0.036), BMI (P = 0.006), AHI (P = 0.004), LSAT (P = 0.006) and hypoxic time when LSAT <90% (P = 0.013) and <85% (P = 0.002) were significantly associated with incidence of cardiac arrhythmias. Table 1 shows the characteristics of the study population. Demographics of patients with cardiac arrhythmias were statistically similar to those without arrhythmias. Cardiac arrhythmias encountered in our study include atrial arrhythmias (n = 38, 32.5%), ventricular arrhythmias (n = 57, 48.7%), conduction delay arrhythmias (n = 8, 6.8%) and multiple arrhythmias (n = 14, 12.0%).
OSA patients with cardiac arrhythmias were further stratified according to OSA severity (Table 2). The association between hypoxic time and cardiac arrhythmia was dependent on the severity of OSA ($P = 0.028$). Analysis with ROC curve showed that when LSAT <85%, hypoxic time cutoff of 4.2 min had 64% sensitivity and 50% specificity of predicting cardiac arrhythmia (area under ROC curve, AUC = 0.59). When LSAT <90%, hypoxic time cutoff of 13.2 min had 63% sensitivity and 53% specificity (AUC = 0.59). Therefore, the sole utilisation of hypoxic time as predictor of cardiac arrhythmia showed poor performance.

When age and BMI were included in a multivariable model: for LSAT <85%, adjusted odds ratio (aOR) was 1.22 (AUC = 0.7, $P = 0.11$); for LSAT <90%, aOR was 1.25 (AUC = 0.69, $P = 0.097$).

Analysing AHI as a continuous variable in a univariate model showed that when LSAT <85%, aOR was 1.38 ($P = 0.005$); LSAT <90%, aOR was 1.45 ($P = 0.002$). Results were not significant when age, BMI, AHI and LSAT were included in a multivariate model.

**Discussion**

Our study found that patients with older age, larger neck circumference, higher BMI, more severe OSA, lower LSAT and longer hypoxic time were more likely to have cardiac arrhythmias. This is similar to the predictors identified in several studies.1-5,13-14 However, the prevalence of cardiac arrhythmias in our study (8%) is lower compared to others. In a study conducted by Hoffstein et al,2 58% of OSA patients had cardiac arrhythmias. The higher prevalence in their study could be due to a greater proportion of patients with severe OSA (AHI >30)—74.4% vs 54.7% in our study. It is known that patients with more severe OSA have higher risk of cardiac arrhythmias. Guilleminault et al analysed 400 OSA patients and found 48% had cardiac arrhythmias during overnight polysomnography. This could be attributed to lower LSAT range in their study population, given that mean age and OSA severity were similar in both studies.

Although hypoxic time when LSAT <85% and <90% were significantly associated with cardiac arrhythmia, using hypoxic time as sole predictor of arrhythmia produced poor results. However, the inclusion of age and BMI makes hypoxic time a better predictor of cardiac arrhythmia. Patients with older age and higher BMI were 1.22 times more likely to have cardiac arrhythmias when hypoxic time >4.2 min at LSAT <85% (AUC = 0.7) and 1.25 times when hypoxic time >13.2 min at LSAT <90% (AUC = 0.69). Therefore, these high-risk patients should be monitored more closely when hypoxic time of >13.2 min is detected with LSAT <90% as the risk of cardiac arrhythmias significantly increases. There is currently no other study demonstrating the association between specific hypoxic time cutoffs and the risk of cardiac arrhythmias for comparison. Our study is the only study that looked at this factor in arrhythmogenesis.

One of the limitations of our study was that comorbid diseases (hypertension, hyperlipidaemia, diabetes mellitus, cardiovascular disease and stroke) were not analysed as these parameters were not recorded at the time of polysomnography. Hence, the confounding effects of comorbid conditions on cardiac arrhythmias in OSA patients could not be analysed. In addition, only a single ECG lead (modified lead II) was available for analysis. Although this is unlikely to affect the detection of cardiac arrhythmias, the absence of a full 12-lead ECG meant that abnormal axis and ST-T wave abnormalities in other leads could possibly be undetected. Ambulatory 24-hour Holter
monitoring results were not available for all patients with cardiac arrhythmias. Hence, the association of cardiac arrhythmias between wakefulness and sleep were not established. Lastly, day-to-day variability in the frequency of cardiac arrhythmias could not be demonstrated as the cardiac arrhythmias were identified during a single overnight polysomnography session. This may not reflect the actual severity of arrhythmias in our study population.

Conclusion
Our study aims to evaluate the relation of cardiac arrhythmias to hypoxic time and LSAT in patients with OSA. Older age, larger neck circumference, higher BMI, more severe OSA, lower LSAT and longer hypoxic time significantly increases the risk of cardiac arrhythmias in OSA patients. Although hypoxic time when LSAT <85% and <90% were significantly associated with cardiac arrhythmia, using hypoxic time as sole predictor of arrhythmia produced poor results. However, when age and BMI were taken into consideration, hypoxic time is a good predictor of cardiac arrhythmia—relative risk of 1.22 (LSAT <85%) to 1.25 (LSAT <90%). This enables identification of high-risk patients for closer follow-up and more aggressive treatment of OSA and cardiac arrhythmias.

REFERENCES

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