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A B S T R A C T

Introduction: Palpitations occurring in specific body positions are often reported by patients, but the effect of body position on arrhythmia has received little research attention. We hypothesize that resting body position can exert pro-arrhythmogenic effects in various ways. For example, lateral body position is known to increase change atrial and pulmonary vein dimensions.
Methods: This observational study capitalizes on overnight polysomnography (PSG) recordings from a tertiary sleep clinic. PSGs were retrieved based on any mention of cardiac arrhythmia in the clinical report, irrespective of primary sleep diagnosis or (cardiac) comorbidities. Every instance of atrial ectopy was annotated and subgroups with a homogenous rate of atrial ectopy were created based on the Dunn index. A generalized linear mixed-effects model using age, sex, gender, sleep stage and body position was used to analyse the total amount of atrial ectopy in each combination of sleep stage and body position. Backward elimination was then performed to select the best subset of variables for the model. Presence of a respiratory event was then added to the model for the subgroup with a high atrial ectopy rate.
Results: PSGs of 22 patients (14% female, mean age 61y) were clustered and analysed. Body position, sleep stage, age or sex did not have a significant effect on atrial ectopy in the subgroup with a low rate of atrial ectopy (N = 18). However, body position did significantly affect the rate of atrial ectopy in the subgroup with a high rate of atrial ectopy (N = 4; 18%). Respiratory events significantly altered the atrial ectopy rate in only three body positions across two patients.
Discussion: In each individual with a high rate of atrial ectopy, the rate of atrial ectopy was significantly higher in either left or right decubital or supine position. Increase in atrial wall stretch in lateral decubital position and obstructive respiratory events in positional sleep apnea are two possible pathophysiological mechanisms, while avoidance of a body position due to symptomatic atrial ectopy in that position is an important limitation.
Conclusion: In a selected cohort of patients with a high rate of atrial ectopy during overnight polysomnography, the occurrence of atrial ectopy is related to resting body position.

1. Introduction

Palpitations occurring in a specific body position are often reported in the outpatient clinic [1]. However, there is only little knowledge on the effect of different body positions on the occurrence of arrhythmia to support this clinical observation. Left and right decubital position (LLDP and RLDP) increase pulmonary vein strain [2], which can lead to premature atrial contractions (PAC) [3]. Supine position is infamous for evoking more apneas in obstructive sleep apnea (OSA) [4], which in turn correlates with an increase in

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Abbreviation list

AHI	apnea-hypopnea index
GLMM	Generalized linear mixed-effects model
LLDP	left lateral decubital position
OSA	obstructive sleep apnea
PAC	premature atrial contraction
PSG	polysomnography
RLDP	right lateral decubital position
SOMNIA	Sleep and Obstructive Sleep Apnea Measuring with Non-Invasive Applications

PAC's [5]. Here we assess the hypothesis that resting body position can exert atrial proarrhythmogenic effects by capitalizing on overnight sleep studies to study atrial ectopy − an umbrella term for PAC, onset of atrial tachycardia and atrial bigeminy.

2. Methods

2.1. Study cohort

This study was conducted using polysomnography (PSG) recordings from the Sleep and Obstructive Sleep Apnea Measuring with Non-Invasive Applications (SOMNIA) database [6]. PSGs for this study were selected when the associated clinical report written by a sleep technician contained any of the terms “atrial fibrillation, premature atrial contraction (PAC), atrial tachycardia or arrhythmia”. For this study we only considered atrial ectopy, as available evidence supports a role for body position in atrial ectopy [2–5] and not ventricular ectopy.

2.2. Polysomnographic data

Body position was detected using a position band. Sleep stage and respiratory events were annotated to the guidelines of the American Academy of Sleep Medicine [7]. Respiratory events were labelled obstructive apnea, hypopnea (using the 4% oxygen desaturation threshold or arousal criteria [7]), central apnea and mixed apnea. ECG lead II was annotated post-hoc by a cardiologist (MB) for the occurrence of PAC, atrial tachycardia, atrial fibrillation and atrial bigeminy using custom software (Matlab, version R2019a; Natick MA).

2.3. Statistical analysis

Hierarchical clustering was applied to the atrial ectopy rate to create homogeneous subgroups of patients, determined by the Dunn index. An analysis of the total amount of atrial ectopy at each combination of sleep stage and body position was conducted with a negative binomial distribution using its canonical link function, conditionally on a latent variable for each patient. This demonstrated whether differences between patients were systematic. Thus, a generalized linear mixed-effects model (GLMM) determined if one body position or sleep stage was most likely to increase the risk of experiencing atrial ectopy. The model was adjusted for age and sex. The latent variable acted as a random intercept for each patient having a normal distribution with mean zero and a variance that depends on subgroup. Likelihood ratio tests were used to perform variable selection to select the best subset of independent variables. Backward elimination removed insignificant independent variables (p-value >0.05). Patients with a high rate of atrial ectopy were analysed further to demonstrate in which body position atrial ectopy is more prevalent. Finally the presence of (any) respiratory event was added to the GLMM for the subgroup with a high rate of atrial ectopy.

3. Results

A total of 22 PSG were identified mentioning presence of arrhythmia in the report. Patients (14% female, median age 61y [IQR 53-69y]) had a mean sleep time of 6.50 h (SD 1.3 h). The median time spent in LLDP, supine, RLDP, prone and upright position was 155, 116, 49, 3 and 0 min respectively. The median atrial ectopy rate was 17.5/h and consisted mostly of PAC's (16.5/h). Nine patients showed moderate or severe sleep apnea (AHI $\geq$15). Variable selection with a GLMM demonstrated that none of the included variables affected atrial ectopy rate in the overall group. Using the Dunn index, two groups were identified (index 5.555). Subgroup 1 (4/22) with high rate of atrial ectopy (mean 152.8/h, SD 35.8) and subgroup 2 (18/22) with a low rate of ectopy (mean 3.9/h, SD 5.1). Sex, apnea-hypopnea index (AHI), age, body position and sleep stage did not significantly differ between the subgroups. Subgroup 2 was not analysed further as the very low atrial ectopy rate hindered a robust statistical analysis.

Fig. 1 shows time spent per body position (blue bars), amount of atrial ectopy (red bars) per body position as a percentage of total time per patient in subgroup 1. The green bars represent the cumulative duration of all respiratory events, as a percentage of the total time spent in that body position. The yellow bars represent the percentage of atrial ectopy (in that position) occurring during a respiratory event. The four patients had 1,050, 805, 1099 and 1050 instances of atrial ectopy and 14, 424, 115 and 87 respiratory events, respectively. Variable selection with a GLMM demonstrated that body position ($P = 0.032$) significantly affected the amount of atrial ectopy, while age ($P = 0.936$), sex ($P = 0.967$), and sleep stage ($P = 0.754$) did not. The likelihood ratio test per patient was 105.19, 214.09, 856.95 and 44.82, respectively (all $P < 0.001$, Bonferroni), demonstrating a significant difference between the amount of atrial ectopy per body position in every patient. RLDP, LLDP and supine position had significantly more atrial ectopy than prone and upright position (Table 1), with specific body positions per patient being most proarrhythmogenic.

In patients 1 and 2, atrial ectopy rate was higher in both RLDP and LLDP, compared to supine and upright (patient 1) or prone (patient 2) position (p-values in Table 1). Patient 1 had an AHI of 2.7 and the presence of a respiratory event did not significantly alter the rate of atrial ectopy. In patient 2 (AHI 61.3), the atrial ectopy rate in LLDP and prone position was higher during a respiratory event compared to normal breathing in the same body position, with respective relative rates of 1.43 (95% CI 1.15–1.75, p = 0.002) and 1.75 (95% CI 1.20–2.56, p = 0.006).

In patient 3, atrial ectopy rate was highest in LLDP, followed by the supine position, compared to RLDP (p-values in Table 1). 97% (112/115) of respiratory events occurred in supine position, resulting in a supine-AHI of 21.4/h (non-supine AHI 1.2). Furthermore, 98% of atrial ectopy occurred in supine position, however the rate of atrial ectopy was significantly lower during the presence of a respiratory event (relative rate 0.44, 95% CI 0.34–0.58, p < 0.0001).

In patient 4 atrial ectopy rate was highest in RLDP compared to both LLDP and supine position (p-value in Table 1). Presence of respiratory events had no significant effect on the atrial ectopy rate (AHI 12.1).

4. Discussion

Using overnight PSG, we demonstrated that the occurrence of atrial ectopy can be dependent on body position in patients with a

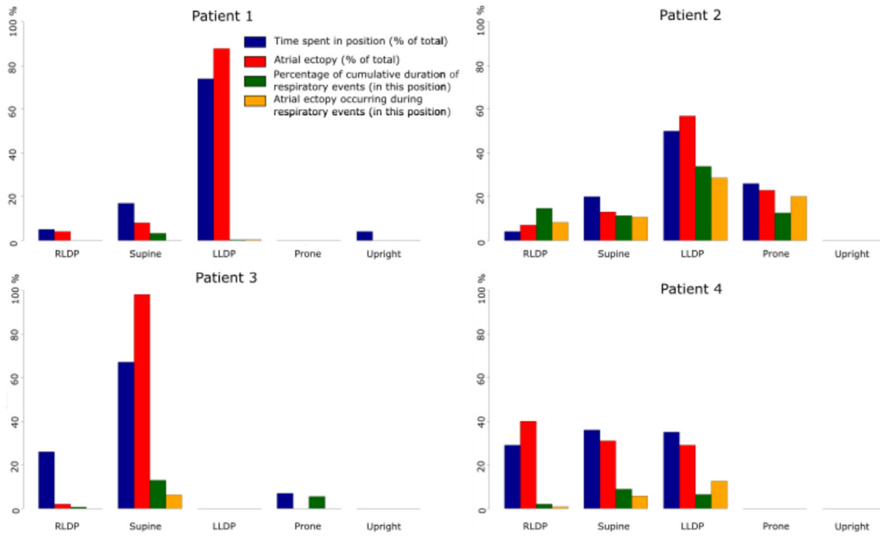

Fig. 1. Percentage of time spent (blue bars) and atrial ectopy (red bars) in each body position. The green bars represent the total duration of respiratory events as a percentage of the total time spent in that body position. The yellow bars represent the represent the percentage of atrial ectopy (in that position) that occurred during a respiratory event. RLDP right lateral body position, LLDP left lateral body position. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

high rate of atrial ectopy. The aim of our study was to demonstrate body position as a possible factor related to atrial ectopy. The generalizability of the findings need to be assessed in future studies.

Two pathophysiological mechanisms potentially explain the arrhythmogenicity of body position. First, in patients with OSA, breathing events occur more often in the supine position [4]. Apneas can exert various arrhythmogenic effects through intrathoracic pressure shifts, changes in blood gasses and sympathovagal imbalance [8]. Respiratory events could be an important mediator in patient 2, however this is not consistent over all patients; we were unable to demonstrate this mechanism in patient 3, although not all instances of atrial ectopy were outside respiratory events. However the antiarrhythmic effect of respiratory events might extend beyond the period of the annotated apnea [9].

Second, changes in atrial wall strain constitute a proarrhythmogenic substrate by an overall decrease in conduction velocity, increased incidence of slow conduction sites and local conduction blocks [10]. An MRI study demonstrated higher flow and vessel area in the veins of the lowermost lung in lateral decubital position [11]. In another, especially LLDP increased strain in the pulmonary veins [2]. This mechanism could explain the results in patient 1, 2 and 4; in these patients LLDP or RLDP had a significantly higher rate of atrial ectopy (Table 1).

4.1. Limitations

Symptomatic positional atrial ectopy could cause patients to change or avoid body positions. The arrhythmogenic effects of that body position would then not be observed in this study. Patient 2 and 3 both had a high event rate in RLDP and LLDP, respectively, and both spent very little time in these respective positions (Fig. 1). Based on the retrospective nature of the study and unbeknownst to these patients' symptoms, this hypothesis could not be tested here, but could be subject of future studies.

Most patients in the SOMNIA database are suspected for OSA; 9/22 patients in this study had at least moderate OSA (AHI ≥15/h), and only 1/4 patients with a high rate or atrial ectopy. Nonetheless, the results of this study using PSG-data from a tertiary referral centre may not necessarily be applicable to the population at large. SOMNIA does not contain information on cardiac comorbidities and beta-mimetic usage, two risk factors for atrial ectopy.

Despite the relatively low number of subjects, the long recording times provided by assessing PSG data provide relevant evidence that body position during sleep can have effect on atrial ectopy rate in patients with high rates of atrial ectopy. Further research is warranted to explore the broader prevalence and pathophysiological background of this observation.

5. Conclusion

In patients with a high atrial ectopy rate, the occurrence of atrial ectopy during overnight polysomnography can be related to body position.

Data availability

The data used in this study is available upon request for non-commercial use.

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All authors contributed to the research and manuscript.

CRediT authorship contribution statement

JLPM (Maarten) van den Broek: Conceptualization, Software, Investigation, Data curation, Writing – original draft, Visualization,

Table 1
The relative rate of atrial ectopy (95% CI) between two body positions in subgroup 1. Bold indicates significant *P*-values. RLDP right lateral body position, LLDP left lateral body position, inf infinite.

All patients	Relative rate (95% CI)	*P*-value
RLDP Vs. Supine	0.95 [0.55, 1.65]	0.848
RLDP Vs. LLDP	0.63 [0.55, 1.65]	0.117
RLDP Vs. Prone	**2.36 [1.17, 4.81]**	**0.016**
RLDP Vs. Upright	**11.25 [1.79, 71.52]**	**0.010**
Supine Vs. LLDP	0.67 [0.39, 1.14]	0.140
Supine Vs. Prone	**2.51 [1.27, 4.90]**	**0.007**
Supine Vs. Upright	**11.94 [1.90, 74.44]**	**0.008**
LLDP Vs. Prone	**3.74 [1.88, 7.54]**	**0.002**
LLDP Vs. Upright	**17.81 [2.83, 112.17]**	**0.002**
Prone Vs. Upright	4.76 [0.72, 31.19]	0.104
Patient 1		
RLDP Vs. Supine	2.75 [1.70, 4.47]	**0.003**
RLDP Vs. LLDP	1.09 [0.73, 1.64]	0.573
RLDP Vs. Prone	28395 [0, Inf]	0.977
RLDP Vs. Upright	7.75 [2.02, 29.63]	**0.011**
Supine Vs. LLDP	0.39 [0.29, 0.53]	**<0.001**
Supine Vs. Prone	10309.28 [0, Inf]	0.979
Supine Vs. Upright	2.81 [0.75,10.61]	0.101
LLDP Vs. Prone	25853.47 [0, Inf]	0.977
LLDP Vs. Upright	7.05 [1.92, 25.87]	**0.011**
Prone Vs. Upright	0 [0, Inf]	0.982
Patient 2		
RLDP Vs. Supine	2.69 [1.88, 3.85]	**<0.001**
RLDP Vs. LLDP	0.86 [0.63, 1.16]	0.300
RLDP Vs. Prone	3.31 [2.37, 4.63]	**<0.001**
RLDP Vs. Upright	22114.75 [0, Inf]	0.977
Supine Vs. LLDP	0.32 [0.24, 0.41]	**<0.001**
Supine Vs. Prone	1.23 [0.93, 1.62]	0.123
Supine Vs. Upright	8229.66 [0, Inf]	0.979
LLDP Vs. Prone	3.85 [3.07,4.85]	**<0.001**
LLDP Vs. Upright	25768.29 [0, Inf]	0.977
Prone Vs. Upright	6676.84 [0, Inf]	0.980
Patient 3		
RLDP Vs. Supine	0.02 [0.01,0.04]	**<0.001**
RLDP Vs. LLDP	0.01 [0.003, 0.02]	**<0.001**
RLDP Vs. Prone	347458.30 [0, Inf]	0.974
Supine Vs. LLDP	0.42 [0.21, 0.85]	**0.021**
Supine Vs. Prone	149751.09 [0, Inf]	0.967
LLDP Vs. Prone	355020.15 [0, Inf]	0.965
Patient 4		
RLDP Vs. Supine	1.62 [1.35, 1.93]	**<0.001**
RLDP Vs. LLDP	1.42 [1.19, 1.70]	**0.002**
Supine Vs. LLDP	0.88 [0.73, 1.06]	0.156

Project administration. **Samaneh Heydari:** Methodology, Validation, Formal analysis, Writing – original draft, Visualization. **Zhuozhao Zhan:** Methodology, Writing – review & editing. **Marcel van 't Veer:** Software. **Federica Sammali:** Software, Data curation. **Sebastiaan Overeem:** Conceptualization, Writing – review & editing, Supervision. **Edwin R. van den Heuvel:** Methodology, Writing – review & editing, Supervision. **Lukas R. Dekker:** Conceptualization, Writing – review & editing, Supervision, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

None declared

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2023.03.004.

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