Assessment of the Relational Strength Between Potential Triggers and the Occurrence of Ectopic Beats

Vilma Pluščiauskaitė[1] and Andrius Petrėnas[1,2]

[1] Biomedical Engineering Institute, Kaunas University of Technology, Kaunas, Lithuania
[2] Faculty of Electrical and Electronics Engineering, Kaunas University of Technology, Kaunas, Lithuania

Abstract

Atrial fibrillation (AF) is often preceded by increased ectopic activity; however, the role of triggering factors in the sequence of physiological processes is not yet understood. This study aims to explore the relation between potential triggers detected in wearable-based physiological signals and the occurrence of ectopic beats. Week-long ECG and acceleration signals were collected during free-living activities from 165 patients with paroxysmal AF. The signals were used for detecting potential triggers due to physical exertion, psychophysiological stress, lying on the left side, and sleep disturbances. Ectopic beats in acceptable-quality ECG segments were detected by analyzing beat-to-beat intervals. To assess the relation between detected triggers and ectopic beats, a measure of relational strength γ is used accounting for pre- and post-trigger ectopic burden. A control γ_c is computed using randomly placed triggers. For some patients, γ increases for all trigger types relative to γ_c. Overall, sleep disorders and physical exertion emerged as the most significant triggers, associated with the largest increase in γ, with $p = 0.028$ and $p = 0.046$, respectively. No significant difference was observed between γ and γ_c for psychophysiological stress and lying on the left side. Detection of triggers that initiate ectopic activity may become an important aspect of personalized AF management.

1. Introduction

A higher number of ectopic beats is associated with an increased likelihood of atrial fibrillation (AF) [1, 2], suggesting that ectopic activity may contribute to the initiation of AF episodes. Therefore, targeting or reducing ectopic activity could be a potential strategy for preventing AF episodes in patients with paroxysmal AF.

Modifiable physiological and behavioral factors, often referred to as triggers, are gaining research interest due to their potential role in initiating AF in certain patients [3]. Evidence suggests that the occurrence of AF episodes is associated with alcohol consumption [4], physical exertion [5], lying on the left side [6], psychophysiological stress [7], and sleep disorders [8]. In a recent study, we explored the relation between triggers detected in physiological signals and AF occurrence [9]. However, whether triggers are related to ectopic activity remains unclear.

This study explores the relation between potential triggers due to physical exertion, psychophysiological stress, sleep disturbances, and lying on the left side and the occurrence of ectopic beats.

2. Methods and Materials

2.1. Database

The study uses ECG and acceleration signals collected from 182 patients with paroxysmal AF. Patients were recruited at Vilnius University Hospital Santaros Klinikos, all provided written informed consent, and the study was approved by the Vilnius Regional Bioethics Committee (158200-18/7-1052-557). Signals were acquired using a chest-worn Bittium OmegaSnap™ one channel ECG patch (Bittium, Finland) at a sampling rate of 500 Hz for ECG and 25 Hz for acceleration signals. Cardiology residents annotated AF episodes, consulting an experienced cardiologist in uncertain cases.

Seventeen patients were excluded due to lack of acceptable quality ECGs or had AF during the entire observation interval. The demographic and clinical characteristics of remaining 165 patients are provided in Table 1.

2.2. Detection of Potential Triggers

Physical exertion is detected based on the metabolic equivalent of task (MET), a physiological measure of energy expenditure relative to resting metabolic rate. MET is estimated using the following regression equation [10]:

$$y_{\texttt{MET}} = 0.0043x_{\texttt{ACC}} + 0.047x_{\texttt{HRR}} + 1.4238, \quad (1)$$

Table 1. Demographic and clinical characteristics of patients with paroxysmal AF.

Women, *n*	60
Men, *n*	105
Age, yrs	59 ± 12
Height, cm	177 ± 10
Weight, kg	90 ± 18
Body mass index, kg/m^2	26.4 ± 2
Observation interval, days	6.7 ± 1.2
Medication (#patients)	
Beta adrenoblockers	120
Antihypertensive drugs	140
Comorbidities (#patients)	
Hypertension	136
Hyperthyroidism	30
Metabolic syndrome	67

where $x_{\texttt{ACC}}$ denotes the vector magnitude of the tri-axial acceleration with gravitational component removed, and $x_{\texttt{HRR}}$ represents heart rate (HR) reserve, reflecting the heart's capacity to increase HR during physical activity. A trigger is detected when the mean MET, computed for 1-minute non-AF intervals, exceeds 5 METs. To reduce false positives from elevated HR without movement, a 91.5 mg mean absolute deviation (MAD) threshold, indicating moderate activity [11], is applied.

Psychophysiological stress is detected based on the assumption that a sudden rise in HR, not caused by physical activity or arrhythmia, indicates a stress-related event. A trigger is detected if HR increases by more than 15 beats per minute within a 1-minute interval, with no prior trigger in the past four hours and no physical activity present. Physical activity is considered absent if the average MAD during both the preceding 5-minute and current 1-minute intervals remains below 22.5 mg, a threshold indicating sedentary behavior like sitting or standing still.

The trigger of the left lateral lying position is detected when the mediolateral acceleration remains below -600 mg for at least 1 hour, with no prior trigger in the preceding four hours. As position changes often occur during the night, only the first detected trigger is considered within each 4 hour window.

Sleep disorders, particularly obstructive sleep apnea, are often accompanied with cyclic variations in HR. In this study, nocturnal alterations in HR are explored using the standard deviation of normal-to-normal RR intervals (SDNN), serving as an indicator of the dominant component of sympathetic and vagal activity. Sleep intervals were detected in a 15-minute moving average intervals in which MAD remains below 10 mg. A threshold of 116 ms is employed to determine the large variations in HR [12]. When the SDNN exceeds the threshold in a 1-hour interval, the onset of the interval is taken as the occurrence time of the trigger.

2.3. Detection of Ectopic Beats

Ectopic beats are detected using beat-to-beat intervals derived from ECG signals of acceptable quality. Signal quality is assessed using a quality index based on the agreement between two R-peak detectors [13, 14]. A threshold of $\geq 90\%$ is used to determine acceptable quality. AF episodes are excluded from the peak detection.

Ectopic beats are detected by comparing each RR interval to a reference value, calculated as a weighted average of the three preceding normal RR intervals, with weights of 0.5, 0.3, and 0.2, giving the greatest importance to the most recent interval. An ectopic beat is detected when there is a shortening of at least 10% in the RR interval followed by a prolongation of at least 5% relative to the reference value [15].

2.4. Quantifying Relational Strength

We adopt an approach for assessing the relational strength between potential triggers and the occurrence of AF episodes, as described in [16]. This approach is based on the assumption that the post-trigger AF burden, defined as the ratio of time spent in AF to the total duration of the analysis window, is greater than the pre-trigger AF burden. However, in this study, the equation for quantifying relational strength is modified to reflect the number of ectopic beats rather than the AF burden. The modified equation, which accounts for the cumulative effect of potential triggers detected within the observation interval, is as follows:

$$\gamma = \sum_{n=1}^{N_t} \frac{\bar{E}_{1,n}/E_m}{1 + \bar{E}_{0,n}/E_m} H(\bar{E}_{1,n} - \bar{E}_{0,n}), \tag{2}$$

where N_t denotes the number of detected potential triggers during the observation interval; $\bar{E}_{0,n}$ and $\bar{E}_{1,n}$ represent the mean ectopic beat counts within 1-minute segments in the pre- and post-trigger analysis windows for the n-th trigger, respectively; and E_m is the maximum ectopic beat count observed in any 1-minute segment during the entire observation interval. The Heaviside step function $H(\cdot)$ is used to exclude cases where the pre-trigger ectopic count exceeds the post-trigger ectopic count. A time window of 4 hours is used for both the pre- and post-trigger analysis windows, unless shortened by the occurrence of an AF episode.

To evaluate the relational strength that may arise by chance and is unrelated to the detected potential triggers, $\gamma_{\texttt{c}}$ is computed using randomly placed control triggers. The number of control triggers is set equal to the number of detected potential triggers to ensure a balanced comparison. To improve robustness, this process is repeated 100 times with different random placements, and $\gamma_{\texttt{c}}$ is reported as the median.

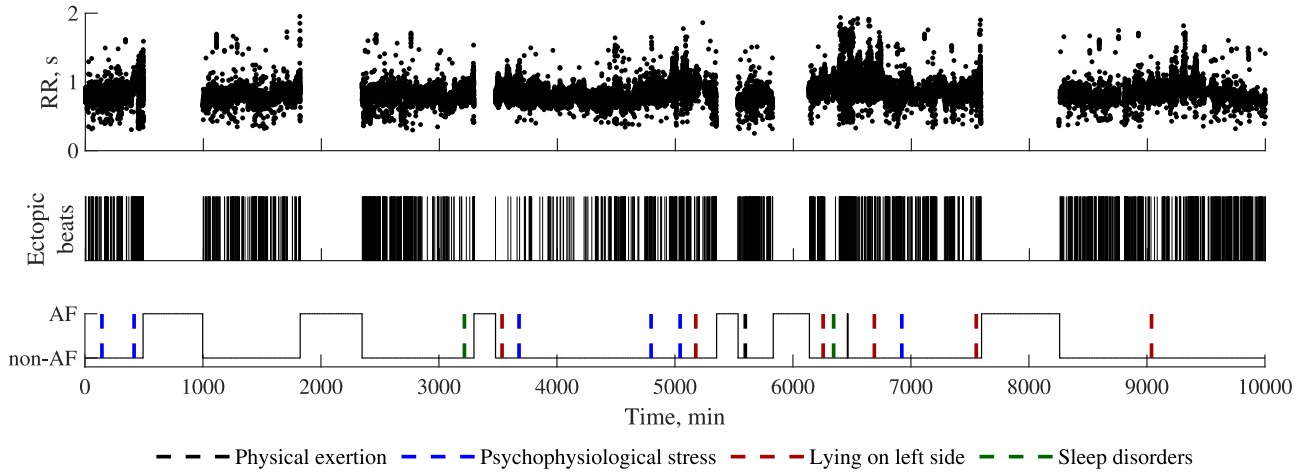

Figure 1. RR interval series (black circles), ectopic beats (black lines), annotated AF episodes, and four types of detected potential triggers in a patient with paroxysmal AF.

2.5. Statistical Analysis

Due to the non-normal distribution, the Wilcoxon signed-rank test is used to compare the relational strengths γ and γ_c for each patient. To evaluate sex-based differences in γ, the Mann-Whitney U test is applied.

3. Results

Figure 1 illustrates the temporal distribution of ectopic beats in relation to detected potential triggers. In this patient, the most frequently detected potential triggers were due to lying on the left side and psychophysiological stress. Additionally, two triggers related to sleep disorders and one to physical exertion were identified.

Figure 2 shows that sleep disorders and physical exertion emerged as the most significant triggers, associated with the increase in γ across the largest number of patients, with p-values of 0.028 and 0.046, respectively. No significant difference was observed between γ and γ_c for psychophysiological stress and lying on the left side, with p-values of 0.603 and 0.239, respectively. Additionally, the relational strength γ was significantly higher in males than females for physical exertion and psychophysiological stress, with p-values of 0.041 and 0.036, respectively.

4. Discussion

The main finding is that, for some patients, the relational strength γ increased for all trigger types compared to the control γ_c, suggesting that ectopic activity may be initiated by potentially modifiable factors. Therefore, patient-specific detection of potential triggers that initiate ectopic activity may become an important component of personalized AF management, enabling clinicians to target the underlying causes of increased ectopic activity in individual

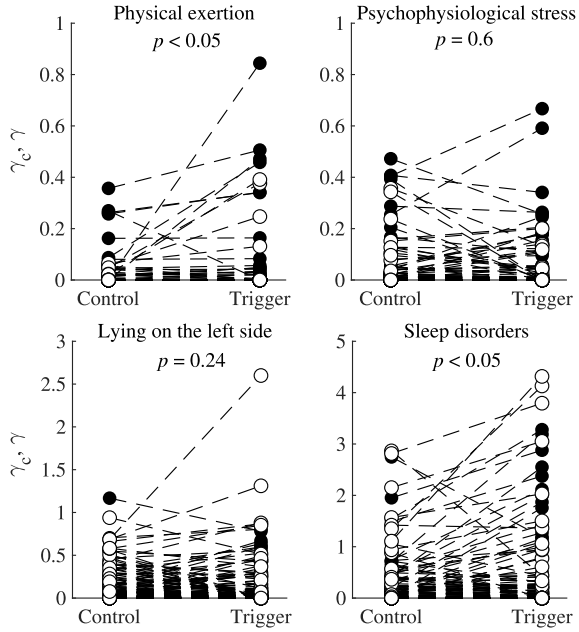

Figure 2. Relational strengths γ_c and γ, computed for each patient and different types of potential trigger. Female patients are represented by white circles.

patients.

The selection of triggers investigated in this study was based on the ability to detect them from physiological signals. For example, although other potential triggers such as alcohol, dehydration, or large meals may affect autonomic function or cardiovascular dynamics, their physiological manifestations do not produce distinctive features that can be reliably detected in physiological signals.

A limitation of this study is that ectopic beats were not differentiated by their origin. Since atrial ectopic beats are more difficult to detect due to their close resemblance to normal beats, the analysis relied solely on RR intervals. As

a result, ventricular ectopic beats were also included. Because AF is often associated with increased atrial ectopic activity [1, 2, 17, 18], the inclusion of ventricular ectopic beats in the beat count may have influenced the results.

5. Conclusion

An approach to identifying ectopic beat triggers in individual patients has been proposed which relies on pre- and post-trigger ectopic beat count. Sleep disorders and physical exertion emerged as the most significant triggers, associated with the largest increase in the relational strength across the largest number of patients. No significant difference was observed for psychophysiological stress and lying on the left side. The proposed approach to identifying triggers in individual patients should facilitate the implementation of longitudinal studies for the objective assessment of trigger effect on ectopic activity.

Acknowledgment

This work was supported by the Research Council of Lithuania (Agreement No. S-MIP-24-73).

References

[1] Wallmann D, et al. Frequent atrial premature beats predict paroxysmal atrial fibrillation in stroke patients: an opportunity for a new diagnostic strategy. Stroke 2007;38(8):2292–2294.

[2] Gladstone DJ, et al. Atrial premature beats predict atrial fibrillation in cryptogenic stroke: results from the EMBRACE trial. Stroke 2015;46(4):936–941.

[3] Groh CA, et al. Patient-reported triggers of paroxysmal atrial fibrillation. Heart Rhythm 2019;16(7):996–1002.

[4] Marcus GM, et al. Acute consumption of alcohol and discrete atrial fibrillation events. Annals of Internal Medicine 2021;174(11):1503–1509.

[5] Guasch E, Mont L. Diagnosis, pathophysiology, and management of exercise-induced arrhythmias. Nature Reviews Cardiology 2017;14(2):88–101.

[6] Gottlieb LA, et al. A left lateral body position increases pulmonary vein stress in healthy humans. Physiological Reports 2021;9(18):e15022.

[7] Leo DG, et al. At the heart of the matter: How mental stress and negative emotions affect atrial fibrillation. Frontiers in Cardiovascular Medicine 2023;10:1171647.

[8] Wong CX, et al. Preceding night sleep quality and atrial fibrillation episodes in the I-STOP-AFIB randomized trial. Clinical Electrophysiology 2024;10(1):56–64.

[9] Pluščiauskaitė V, et al. Assessment of the relational strength between triggers detected in physiological signals and the occurrence of atrial fibrillation episodes. Physiological Measurement 2024;45(9):095011.

[10] Nakanishi M, et al. Estimating metabolic equivalents for activities in daily life using acceleration and heart rate in wearable devices. BioMedical Engineering Online 2018; 17(1):1–18.

[11] Sjöros T, et al. Both sedentary time and physical activity are associated with cardiometabolic health in overweight adults in a 1 month accelerometer measurement. Scientific Reports 2020;10(1):20578.

[12] Roche F, Gaspoz JM, Court-Fortune I, Minini P, Pichot V, Duverney D, Costes F, Lacour JR, Barthélémy JC. Screening of obstructive sleep apnea syndrome by heart rate variability analysis. Circulation 1999;100(13):1411–1415.

[13] Behar J, et al. ECG signal quality during arrhythmia and its application to false alarm reduction. IEEE Transactions on Biomedical Engineering 2013;60(6):1660–1666.

[14] Vest AN, et al. An open source benchmarked toolbox for cardiovascular waveform and interval analysis. Physiological Measurement 2018;39(10):105004.

[15] Paliakaitė B, et al. Wrist photoplethysmography-based assessment of ectopic burden in hemodialysis patients. Biomedical Signal Processing and Control 2023; 84:104860.

[16] Pluščiauskaitė V, et al. An objective approach to identifying individual atrial fibrillation triggers: A simulation study. Biomedical Signal Processing and Control 2024; 87:105369.

[17] Himmelreich JC, et al. Frequent premature atrial contractions are associated with atrial fibrillation, brain ischaemia, and mortality: a systematic review and meta-analysis. EP Europace 2019;21(5):698–707.

[18] Dewland TA, et al. Atrial ectopy as a predictor of incident atrial fibrillation: a cohort study. Annals of internal medicine 2013;159(11):721–728.

Address for correspondence:

Vilma Pluščiauskaitė
Biomedical Engineering Institute
Kaunas University of Technology
K. Baršausko st. 59, LT-51423 Kaunas, Lithuania.
vilma.plusciauskaite@ktu.lt