Quantitative Evaluation of Temporal Episode Patterns in Paroxysmal Atrial Fibrillation

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Abstract

Flow velocity in left atrial appendage decreases when paroxysmal atrial fibrillation (PAF) progresses to longer episodes, suggesting that the temporal PAF episode pattern may be related to risk of thrombus formation. This study investigates the feasibility of discriminating episode patterns based on two descriptors: the aggregation characterizes the temporal distribution of PAF episodes, whereas the Gini coefficient characterizes differences in episode duration. The descriptors were studied on three PhysioNet databases with annotated PAF episodes, resulting in a total of 102 recordings. Three types of patterns were defined: congregation of several episodes in a single and multiple clusters, and episodes dispersed over the entire monitoring period. The results show that the aggregation descriptor achieves large values for patterns with a single and multiple clusters (0.76 ± 0.07 and 0.60 ± 0.08, respectively). In contrast, much lower values are obtained for dispersed episode patterns (0.10 ± 0.05). The Gini coefficient is better suited for discriminating among the patterns with high PAF burden and, therefore, represents a descriptor which is complementary to aggregation. Both descriptors may have relevance when studying the relationship between episode pattern and the risk of thrombus formation.

1. Introduction

Reduction of flow velocity in left atrial appendage is associated with an increased risk of thrombus formation in patients with paroxysmal atrial fibrillation (PAF) [1]. Since the velocity decreases as PAF progresses to longer episodes, analysis of the temporal episode pattern may provide risk information [2]. Understanding of PAF patterns may have implications on patient-specific therapy management. Prediction of health outcome (e.g., stroke) and episode self-termination are aspects which may benefit from such understanding.

The statistical distribution of the time interval between consecutive PAF episodes was found to be non-exponential, suggesting that the interval is not modeled by a homogeneous Poisson process [3]. The results also indicated that episodes are often clustered. An important disadvantage of this approach is that it is less effective for short monitoring periods due to an insufficient number of PAF episodes. This restriction does not apply to the descriptor "AF density", which depends on the temporal dispersion of PAF episodes over the monitoring period [4, 5]. However, it is still unclear whether different patterns, such as single and multiple clusters, and episodes dispersed over the monitoring period, can be captured using this approach.

The aim of this study is to investigate the feasibility of discriminating temporal PAF episode patterns found in the publicly available *PhysioNet* databases with annotated episodes. The patterns are characterized with respect to aggregation over time and differences in duration.

2. Quantification of PAF pattern

2.1. Episode aggregation

The descriptor aggregation $\mathcal{A}$ quantifies the deviation between and observed PAF pattern and a hypothesized uniformly distributed pattern. Its definition is inspired by AF density [4–6]. The aggregation $\mathcal{A}$ has the RR interval sequence as its starting point and provides detailed information of temporal distribution of PAF episodes.

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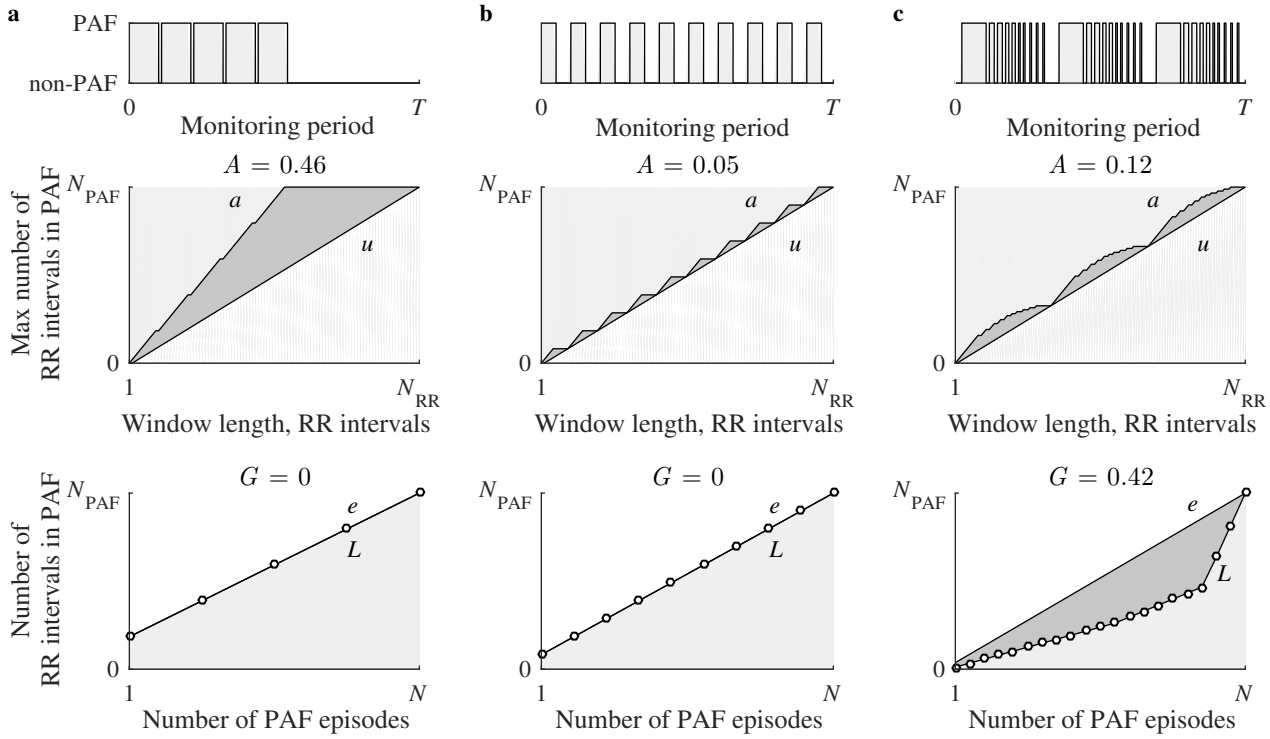

Figure 1. (**a**) Different PAF patterns: a single cluster with equal episode duration (left column), dispersed episodes (middle column), and multiple clusters with varying episode duration (right column). Graphical illustration of (**b**) aggregation $\mathcal{A}$ and (**c**) Gini coefficient $\mathcal{G}$. $\mathcal{A}$ is obtained by dividing the dark gray area by the total area above the uniform cumulative distribution u. Similarly, $\mathcal{G}$ is obtained by dividing the dark gray area by the total area under the line of equality. Note that the PAF burden, defined as the proportion of the total monitoring time the patient is in PAF, is the same for all three patterns ($\mathcal{B} = 0.5$).

The sequence i_n, $n = 1, ..., N_{\text{RR}}$, indicates whether the n:th RR interval is contained in an PAF episode,

$$i_n = \begin{cases} 1, & \text{RR}_n \in \text{PAF}, \\ 0, & \text{otherwise}, \end{cases}$$

where N_{RR} is the total number of analyzed RR intervals and $N_{\text{PAF}} = \sum_{n=1}^{N_{\text{RR}}} i_n$ is the total number of RR intervals in PAF.

To characterize the temporal distribution of PAF episodes, the actual a and the reference uniform u cumulative distributions have to be identified. The actual a distribution is obtained by moving a sliding window throughout the entire binary sequence i_n (step size is equal to one RR interval), and finding the maximal number of RR intervals assigned to PAF. The window length is selected from 1 to the maximal number of RR intervals. When the window length is the same as the length of i_n, the window embraces the entire PAF pattern. The uniform u cumulative distribution represents evenly spread PAF episodes throughout the entire monitoring period, and serves as a reference for finding the difference between the a and u cumulative distributions.

The aggregation $\mathcal{A}$ is defined by,

$$\mathcal{A} = \frac{2}{N_{RR} N_{PAF}} \sum_{n=1}^{N_{RR}} |a_n - u_n|. \tag{1}$$

Graphically, $\mathcal{A}$ is defined as the ratio between the area that lies between the a and u cumulative distributions (dark gray area in Fig. 1(b)) and the total area above u (dark and light gray areas in Fig. 1(b)).

The aggregation $\mathcal{A}$ takes values between 0 and 1. Values close to 1 indicate high temporal aggregation, inherent for patterns with a single short continuous PAF episode. Values close to 0 indicate low aggregation, this applies to PAF patterns with episodes evenly spread over the entire monitoring period.

2.2. Episode duration inequality

Another way to characterize differences in PAF episode duration is by the Gini coefficient, which is a common descriptor of income inequality [7]. The Gini coefficient $\mathcal{G}$

has the number of PAF episodes N as its starting point and provides detailed information on differences in episode duration. The descriptor $\mathcal{G}$ is defined as the ratio between the area that lies between the line of equality e_i and cumulative sum of episode durations sorted in ascending order L_i (dark gray area in Fig. 1(c)), and the total area under the line of equality e_i (dark and light gray areas in Fig. 1(c)),

$$\mathcal{G} = \frac{2}{NN_{PAF}} \sum_{i=1}^{N} |e_i - L_i|. \quad (2)$$

The Gini coefficient $\mathcal{G}$ takes values from 0 to 1, where 0 is obtained for the uniform distribution (all PAF episodes are of the same duration), whereas values close to 1 are obtained for widely different episode durations.

3. PAF pattern database

The descriptors were investigated on three *PhysioNet* databases with annotated PAF episodes: MIT–BIH Arrhythmia Database (MITDB), MIT–BIH Atrial Fibrillation Database (AFDB), Long-Term Atrial Fibrillation Database (LTAFDB). In total, 102 recordings with 7742 episodes were analyzed, see Table 1. Recordings without episodes (40 from the MITDB and 1 from the LTAFDB) or entirely in AF (2 from the AFDB and 12 from the LTAFDB) were excluded from the study.

Table 1. Description of PAF databases.

Database	Duration	No. of recordings	No. of episodes
MITDB	30 min	8	106
AFDB	10 h	23	297
LTAFDB	24–25 h	71	7339

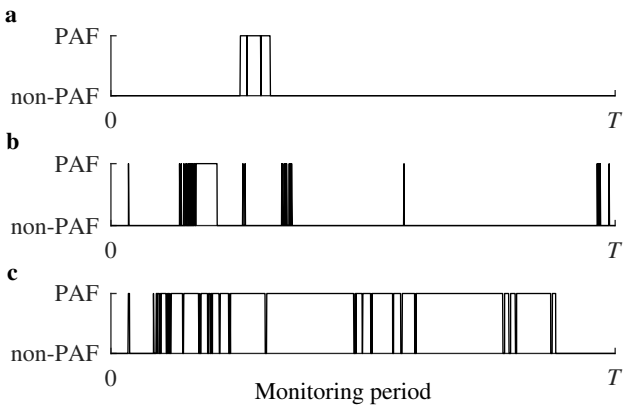

Figure 2. Illustration of different episode patterns: (**a**) a single episode or cluster, (**b**) multiple clusters, and (**c**) episodes dispersed over the monitoring period.

Three types of PAF pattern were manually defined according to temporal characteristics: congregation of several episodes in a single and multiple clusters, and episodes dispersed over the monitoring period (Fig. 2).

4. Results

The descriptors $\mathcal{A}$ and $\mathcal{G}$ are presented in Table 2 for different types of pattern. Patterns with a single cluster take large $\mathcal{A}$ values, while patterns with episodes dispersed over the monitoring period take much smaller values. On the other hand, $\mathcal{G}$ is similar for all types of pattern.

Table 2. $\mathcal{A}$ and $\mathcal{G}$ for different PAF patterns. The results are shown as mean $\pm$ confidence interval.

Pattern type	No.	$\mathcal{A}$	$\mathcal{G}$
Single cluster	31	0.76 ± 0.07	0.50 ± 0.11
Multiple clusters	33	0.60 ± 0.08	0.62 ± 0.08
Dispersed episodes	38	0.10 ± 0.05	0.61 ± 0.09
Entire database	102	0.46 ± 0.07	0.58 ± 0.05

Figure 3(a) shows that $\mathcal{A}$ is negatively correlated with PAF burden $\mathcal{B}$, and the correlation increases for an increasing $\mathcal{B}$. On the other hand, $\mathcal{G}$ is independent of $\mathcal{B}$ (Fig. 3(b)). Even for $\mathcal{B}$ values close to 1, $\mathcal{G}$ takes different values since episode duration inequality is highly variable among the distinct recordings.

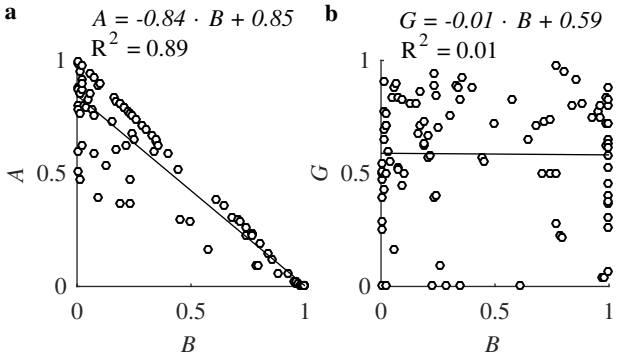

Figure 3. Relationship between the PAF burden $\mathcal{B}$ and (**a**) $\mathcal{A}$ and (**b**) $\mathcal{G}$.

Figure 4 shows that $\mathcal{A}$ depends on the temporal distribution of PAF episodes, while $\mathcal{G}$ depends on episode duration. That is, $\mathcal{A}$ differs considerably between patterns with highly aggregated episodes and those with dispersed episodes. Meanwhile, $\mathcal{G}$ is similar due to the presence of episodes with widely varying duration (see the upper two patterns in Fig. 4). On the other hand, the patterns with a high burden $\mathcal{B}$ are better reflected by $\mathcal{G}$ values (see the last two patterns on the bottom of Fig. 4). Therefore, it is

obvious that the descriptors provide different information about a PAF pattern.

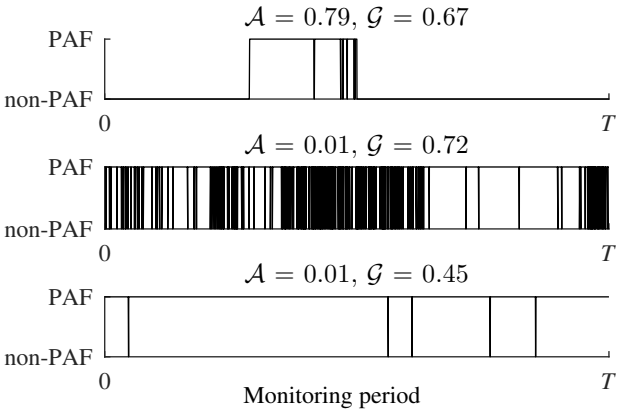

Figure 4. $\mathcal{A}$ and $\mathcal{G}$ for different PAF patterns.

5. Discussion

This study investigates two descriptors for quantitative evaluation of temporal episode patterns. Several studies have shown a link between PAF burden and increased risk of stroke, however, the threshold of the PAF burden is unclear and varies considerably among studies [8, 9]. Therefore, there is good reason to presume that the pattern itself may have a role on thrombus formation.

Our findings show that the aggregation descriptor is capable of differentiating patterns even when only day-long recordings are available. This is in contrast to model-based fitting to the theoretical distributions, which requires a large number of PAF episodes, therefore, day-long recordings are usually insufficient. Given that PAF is defined by termination within 7 days, a week long window is a better option for analysis.

Due to the lack of knowledge about PAF pattern, each observed pattern was assigned to one of three types of pattern heuristically defined based on manual inspection. Some patterns could not be easily assigned to a specific pattern type, thus the results should be interpreted with caution.

In contrast to the commonly used PAF burden, the investigated descriptors are not as easily interpreted. Therefore, future studies are needed to define what ranges characterize different patient group.

6. Conclusions

The results show that the aggregation descriptor is better suited for discriminating different temporal PAF occurrence patterns. On the other hand, the Gini coefficient is useful for discriminating patterns with high PAF burden, and can thus be used as a complementary to the aggregation. Both descriptors may have relevance when studying the relationship between episode pattern and the risk of thrombus formation, however, it remains to be shown in the future.

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