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Atrial fibrillation density: A novel measure of atrial fibrillation temporal aggregation for the characterization of atrial fibrillation recurrence pattern

Efstratios I. Charitos[1], Paul D. Ziegler[2], Ulrich Stierle[1], Hans-Hinrich Sievers[1], Hauke Paarmann[3], Thorsten Hanke[1]

[1]Department of Cardiac and Thoracic Vascular Surgery, University of Luebeck, Luebeck, Germany; [2]Medtronic Inc. Minneapolis, MN, USA; [3]Department of Anesthesia, University of Luebeck, Luebeck, Germany

Abstract

Aim: The atrial fibrillation (AF) burden presents a step towards a quantitative approach to AF, however, the temporal distribution of AF episodes over time cannot be expressed with the AF burden alone. We present the concept of AF density, a novel measure to evaluate and describe the temporal pattern of AF recurrence.
Methods: AF episodes and rhythm histories captured by continuous monitoring devices in a large collective of 647 patients with AF were evaluated and reconstructed.
Results: For the calculation of the AF density, the minimum time required to develop each proportion of the patient's total burden is calculated. AF density is defined as the ratio of the cumulative deviation of the patient's actual burden development from the hypothetical uniform burden development to that of the hypothetical maximum possible burden aggregation for that level of burden from the hypothetical uniform burden development. The AF density as the ratio of the above mentioned areas is a dimensionless quantity and assumes values between 0 and 1, with values close to 0 denoting low burden aggregation, whereas values close to 1 denoting maximal burden temporal aggregation.
Conclusions: We present a methodology that evaluates the temporal distribution pattern of AF recurrence which may aid, together with the AF burden, to a better classification and description of AF recurrence patterns. The latter may be of interest in the evaluation of the risk of thromboembolism that AF patients face. Larger studies are required to investigate if AF density can influence patient specific outcomes.

Key Words: atrial fibrillation, arrhythmia, monitoring

What's New?

- The atrial fibrillation (AF) burden is defined as the proportion of time a patient is in AF and represents a step towards a quantitative approach to AF.
- The temporal distribution of AF episodes cannot be expressed with the AF burden alone.
- We present the concept of AF density, a novel measure to evaluate the temporal distribution of AF, which can assist in the classification and description of AF recurrence patterns.
- The AF density is a dimensionless quantity and assumes values between 0 and 1. Values close to 0 indicate low burden aggregation (AF episodes evenly spread

throughout the monitored period), whereas values close to 1 denote maximal burden temporal aggregation ("block of AF", the complete burden as one continuous episode).

Introduction

The introduction of implantable devices able to detect atrial fibrillation (AF) episodes and monitor their incidence and frequency has initiated a change of mentality regarding AF from a qualitative ("yes/no") to a quantitative ("amount" of AF) approach. The AF burden, defined as the proportion of the total monitored time a patient is in AF, has been utilized as a quantitative descriptor of AF for the evaluation success of therapeutic treatments as well as for risk stratification in patients with AF [1–7]. However, the AF burden cannot evaluate the dynamic incidence of AF recurrence and ignores the temporal dispersion or temporal aggregation of the AF episodes and AF burden. For example, patients A and B (Figure 1 and Figure 2A and B) spend the same time in AF (17% of the monitored time in AF, AF burden = 0.17, 364 days of continuous heart rhythm monitoring). In patient A, the AF recurrence appears to have a greater temporal aggregation, with the majority of AF burden recurrence taking place between days 30 and 80. In contrast, the recurrence of AF in patient B appears to consist of episodes of shorter duration, spread almost evenly throughout the observation period. This additional information on the AF temporal aggregation cannot be expressed with the AF burden alone and may be of interest for describing the AF recurrence pattern in patients with AF.

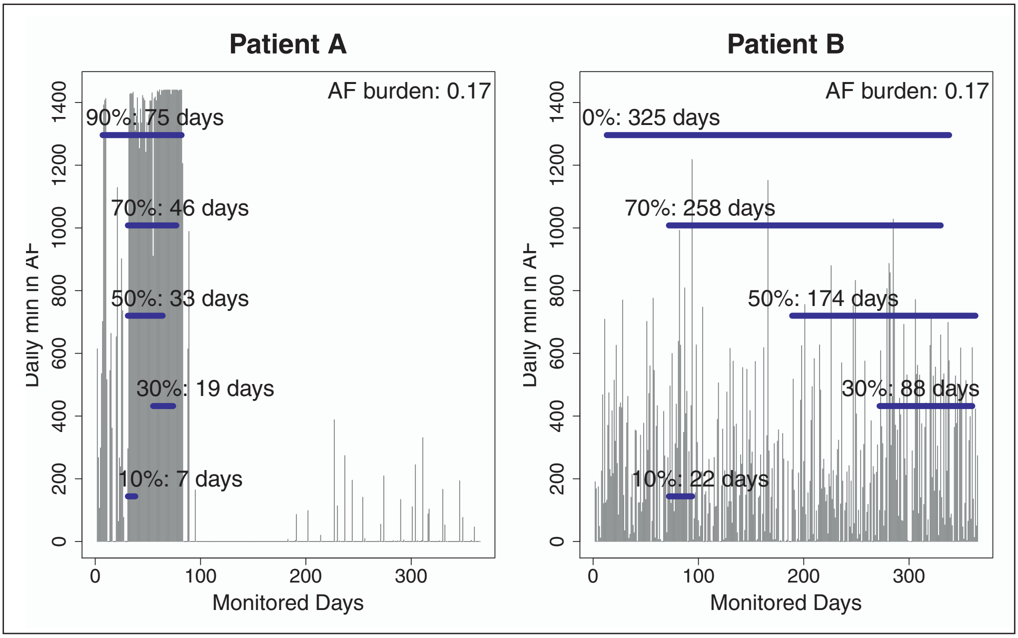

Figure 1: Two patients with the same amount of atrial fibrillation burden but different temporal dispersion. In patient A, the minimum time required for the development of 10% of his burden is 7 days and this occurs between the 31st till the 38th day of monitoring. Similarly, the minimum time required for the development of 50% of his total burden is 33 days and takes place between the 31st till the 64th day of monitoring. On the contrary, in patient B the minimum time required for the development of 10% and 50% of his total burden is 22 days (72nd to 94th day of monitoring) and 174 days (189th to 363rd day of monitoring)

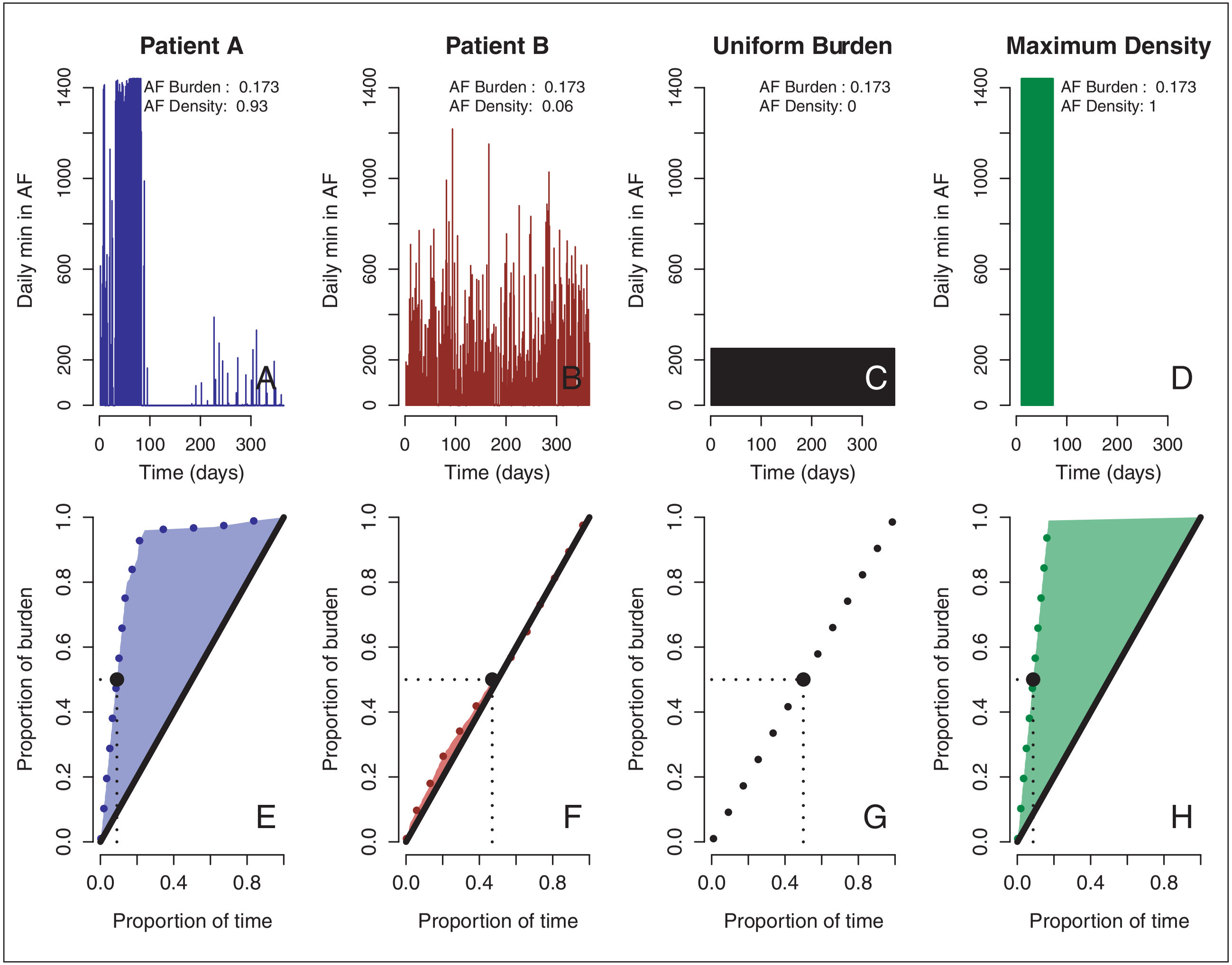

Figure 2: Four different types of temporal aggregation of the same AF burden (0.173). After reconstruction of the rhythm history (panels above), the minimum required for the development of each proportion of the patient's total observed AF burden throughout the monitored period is evaluated (panels below, dotted lines). As AF density is defined the ratio of the cumulative deviation of the patient's actual burden development (blue or red area) from the uniform burden development (black diagonal line, panels below and Uniform Burden), to that of the maximum possible burden aggregation for that level of burden (the complete burden as one continuous episode, green area). The black diagonal (panels below) represents a hypothetical uniform burden aggregation (Uniform Burden)

We present the concept of AF density, as a novel measure to evaluate and describe the temporal dispersion or aggregation of AF.

Methods

AF recurrence episodes captured by continuous monitoring devices in a large collective of 647 patients (Reveal XT 9529; AT500 pacemaker; Medtronic, Inc., Minneapolis, MN, USA) were evaluated and the complete rhythm history of every patient was reconstructed (Figure 1 and Figure 2A and 2B). The characteristics of the study population have been described in detail elsewhere [8,9,10]. All patients have provided informed consent for the data collection and use and the study has been approved by the local ethics committee (ClinicalTrials.gov ID: NCT00806689). AF burden was defined as the proportion of the time the patient is in AF to the total monitored time.

Results

For each patient, the course of the AF burden development over time throughout the monitored period was analyzed and the *minimum contiguous monitored time* required for the development of each proportion of the patient's total observed AF burden throughout the monitored period was calculated (Figure 1) and was evaluated for the overall observation period (blue or red dotted line, Figure 2E and 2F, respectively). For example, Figure 1 and Figure 2 presents two patients (A and B) who spend exactly the same amount of time in AF (AF burden 0.173, both patients monitored for 364 days). However, the temporal AF distribution of these 2 patients is vastly different. Patient A develops 10%, 30%, 50%, 70%, 90% of his total observed burden in 2%, 5%, 9%, 13%, 21% of the total monitored time, respectively (7, 19, 33, 46, 75 days, respectively; Figure 1), and most of the AF recurrence and burden development occurs between days 30 and 80. This information on the temporal burden development of patient A is displayed in Figure 2E. In contrast, patient B develops 10%, 30%, 50%, 70%, 90% of his total observed burden in 6%, 24%, 48%, 71% and 89% of the total monitored time, respectively (22, 88, 174, 258, 325 days, respectively; Figure 1) since the total burden is spread over more days and as such each day contributes less to the total burden development. This information on the temporal burden development of patient B is displayed in Figure 2F. The black diagonal line (Figure 2E and 2F) represents the hypothetical development of the patient's AF burden if this burden had been uniformly distributed over the monitored time (same AF duration every day throughout the observation period, uniform burden, Figure 2C and 2G). The green dotted line (Figure 2H) represents the burden development of a hypothetical patient in which the AF burden (equal in amount to that of patient A and B) occurs as one single continuous episode (maximum density, Figure 2D).

For the calculation of the AF density as a measure of temporal AF burden aggregation, the patient's complete rhythm history is scanned and the *minimum contiguous time* required to develop each proportion p of the patients total burden b is calculated (red and blue dotted line, Figure 2E and 2F). As *AF density*, we define the ratio of the cumulative deviation of the patients actual burden development (blue or red area, Figure 2E and 2F, respectively) from the hypothetical uniform burden development (black diagonal line, Figure 2E and 2F), to that of the hypothetical maximum possible burden aggregation for that level of burden from the hypothetical uniform burden development (the complete burden as one continuous episode, green area, Figure 2H). The black diagonal (Figures 2E, 2F, 2G, 2H) represents a hypothetical uniform burden aggregation (Figure 2C).

For the numerical evaluation of the AF density we define: For a patient with a total AF burden b (expressed as the proportion of the observation time the patient is in AF), who is monitored for time *T*, we denote the *minimum* contiguous monitored time throughout the monitored period *T* required for the development of a proportion *p* of the patient's total observed burden (*b*) as *T(p;b)*. This time, expressed as proportion of the total observed time *T*, is

$$F(p;b) = \frac{T(p;b)}{T}$$

Figures such as 2E, 2F, and Figure 3 are plots of *p* against *F(p;b)* for $0 \le p \le 1$.

The cumulative deviation of the patient's actual burden development from the hypothetical uniform burden development (black diagonal line, Figure 3) can be evaluated as

$$\int_0^1 |F(p;b) - p|\, dp$$

and is equal to the red shaded area (Figure 3). For the hypothetical patient with maximum temporal aggregation of burden *b* (the complete burden as one continuous AF episode) the cumulative deviation of this patient's burden development (green line, Figure 3) from the hypothetical uniform burden development (black diagonal line, Figure 3) is evaluated as

$$\frac{(1-b)}{2}$$

and is equal to the green shaded area (Figure 3). AF density, as the ratio of the red to green shaded areas (Figure 3) in then defined as:

$$AF\ density = 2 * \frac{\int_0^1 |F(p;b) - p|\, dp}{1-b}$$

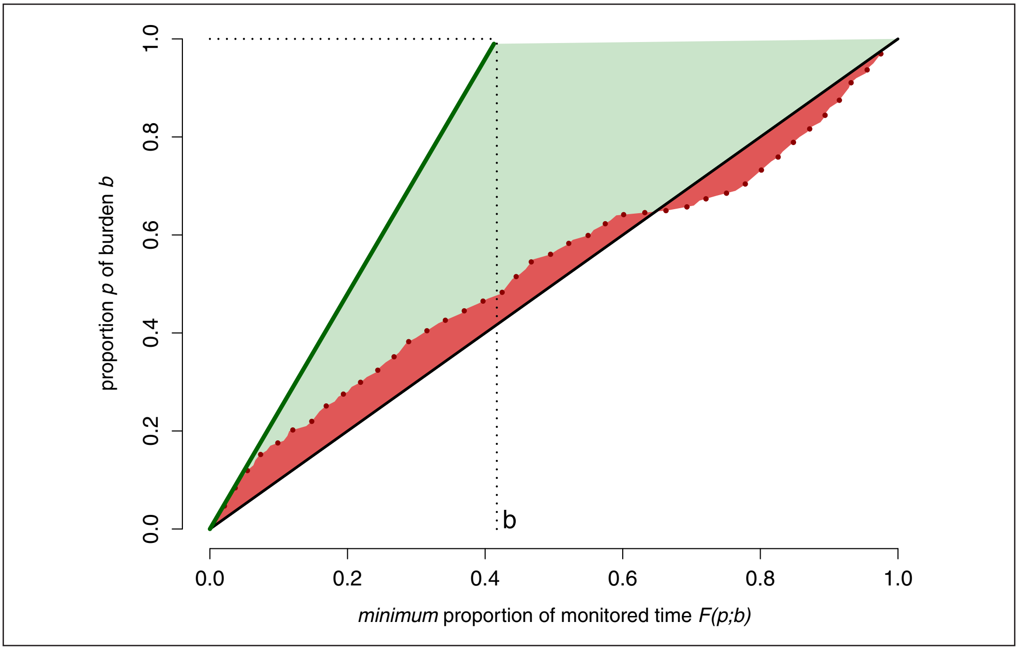

Figure 3: Calculation of the AF density: The patient's actual burden development from the hypothetical uniform burden development is evaluated as $\int_0^1 |F(p;b) - p|\, dp$ *and is equal to the red shaded area. If the same burden occurred with maximum temporal aggregation (the complete burden as one continuous AF episode) the cumulative deviation from the hypothetical uniform burden development (black diagonal line) is evaluated as* $\frac{(1-b)}{2}$ *and is equal to the green shaded area. AF density, as the ratio of the red to green shaded areas in then defined as:* $AF\ density = 2 * \frac{\int_0^1 |F(p;b) - p|\, dp}{1-b}$

The AF density as the ratio of the above mentioned areas is a dimensionless quantity and assumes values between 0 and 1, with values close to 0 denoting low burden aggregation (AF burden evenly spread throughout the monitored period, Figure 2B & 2F as well as Figure 2C & 2G), whereas values close to 1 denoting maximal burden temporal aggregation ("a block of AF", the complete AF burden as a single continuous episode, Figure 2A & 2E as well as Figure 2D & 2H).

Discussion

We present a novel parameter and methodology that can evaluate the temporal AF burden aggregation and characterize the AF recurrence during the monitored period. This parameter may be of some interest, providing temporal descriptive characteristics of the AF recurrence pattern. We have shown previously that the temporal pattern of AF recurrence plays a major role in determining the effectiveness of intermittent rhythm monitoring (Holter recordings) in identifying AF recurrence after therapeutic interventions [10]. In patients with high temporal AF aggregation (high AF density, "blocks" of AF), AF recurrence is much more difficult to capture with intermittent rhythm monitoring than in patients with low temporal AF aggregation (low AF density) (10). Since in the majority of studies as well as in the clinical practise, intermittent monitoring is employed to evaluate therapeutic success, the reduced sensitivity of intermittent monitoring for the detection of high density AF recurrence may render the reliable and accurate detection of AF recurrence after therapeutic interventions problematic [10].

Since the identification of AF as a risk factor for thromboembolic complications, many attempts have been made to identify the quantity of AF required to place a patient at a higher risk for thromboembolic complications. Although significant research has been performed in this area, there is still no clear answer to this question [11]. The AF time thresholds to identify patients with high risk for thromboembolism have been found to be 5 minutes [5] , 6 minutes [4], 3.8 hours [6], 5.5 hours [1], 17.7 hours [4], or 24 hours [7]. It is unknown where the temporal aggregation of AF recurrence plays a role in the thromboembolic risk that patients with AF face. Patients A and B (Figure 2) happen to spend exactly the same time in AF (17% of the observed time). However the temporal AF aggregation in these two patients is very different. The vast majority of AF burden in Patient A occurs between day 30 and 80, whereas in patient B the AF burden is distributed more evenly over time. Patient A develops 50% of his total burden in only 9% of the monitored time (high density AF), whereas patient B requires 50% of the total observation time to develop 50% of the observable AF burden (low density AF). It is unclear if patients with low AF density (Patient B, Figure 2) have the same risk for thromboembolic risk as patients with high density AF (Patient A, Figure 2), despite spending the same time in atrial fibrillation. We feel that the level of temporal aggregation of atrial fibrillation recurrence may deserve further investigation when evaluating the thromboembolic risk that patients with AF face.

Conclusions

We present a novel methodology that evaluates the temporal distribution pattern of AF recurrence. This can assist the further classification and description of AF recurrence patterns. We hope that with a more accurate description of the amount as well as of the temporal characteristics of AF recurrence, a more comprehensive understanding of the AF recurrence characteristics might be achieved. Both concepts of AF burden and AF density might serve as a first step towards a better description and evaluation of the quantitative and temporal characteristics of the AF recurrence.

Limitations

For the development of the AF density algorithm we retrospectively analyzed data from a large, albeit inhomogeneous population of continuously monitored AF patients, which has been described in detail previously [8–10] . Although for the methodology and the algorithm described in the present work, the specific characteristics of the study population are irrelevant, the fact that our study population is inhomogeneous renders it suboptimal and our follow up underpowered to evaluate clinical outcomes, such as the effect of AF density on the incidence of thromboembolic complications. We feel that this should be investigated in prospective, controlled, randomized studies.

Disclosures

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Correspondence address:
Efstratios I. Charitos, M.D.
Department of Cardiac and Thoracic
Vascular Surgery, University of Luebeck
Ratzeburger Allee 160
23568 Luebeck
Germany
E-Mail: efstratios.charitos@gmail.com