Atrial Fibrillatory Rate Characterization Extracted from Implanted Cardiac Monitor Data

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Abstract

The aim of this study is to characterize atrial fibrillatory rate (AFR) extracted from a cohort of continuously monitored atrial fibrillation (AF) patients as function of episode duration and onset time. The f-wave signal used to compute the AFR was extracted from a single lead ECG strip of the first 2 minutes of the AF episodes recorded by an Implantable Cardiac Monitor (ICM) in a cohort of 99 patients. The f-wave signals were obtained from 1400 AF episodes using a spatiotemporal QRST cancellation process and the AFR was estimated as the fundamental frequency of a harmonic model fitted to the extracted f-waves. We investigated the relationship between AFR and episode duration and episode onset time, respectively. AFR (median (interquartile range)) was significantly lower (p-value<0.05, Mann-Whitney U test) in short episodes (< 20 min) (5.15 (0.66) Hz) than in longer episodes (5.30 (0.74) Hz). AFR was significantly higher for episodes with onset time at night (00:00-06:00) (5.34 (0.82) Hz) than for episodes with onset during the day (10:00-20:00) (5.21 (0.70) Hz). Significant differences were found between the relative AFR (ratio between the AFR and the average AFR of the patient) and episode duration (Short: 99.2 (9.3) %; Long: 100.0 (8.9) %) while no significant differences were found between relative AFR and episode onset time. Data extracted from ICMs can be used to characterize the AFR of patients suffering from AF showing that that nighttime AF onset and longer duration AF episodes are more common in patients with higher AFR.

1. Introduction

The progressive aging of the general population is associated with an inevitable rising in incidence of atrial fibrillation (AF) [1] with predictions of affecting 6-12 million people in the USA by 2050 and around 18 million in Europe by 2060 [2]. This increase in incidence is associated with increased mortality.

The shortening of the atrial fibrillatory cycle length (AFCL) or the increase of atrial fibrillatory rate (AFR) which are considered a surrogate marker for the atrial refractory period is considered an indication for atrial electrical remodelling in patients suffering from AF [3]. Trying to predict AF behaviour, Bollman et al. studied the correlation between AFR and AF duration showing a positive correlation between them (R=0.53, p=0.002) [4] where having a higher AFR at the start of the AF episode could predict longer episodes. However, this study was conducted in a small dataset with only 31 episodes from 11 paroxysmal AF patients.

With the use of implantable cardiac monitors (ICMs) equipped with a highly sensitive AF detection algorithm (96%) [5], a higher number of AF episodes can be detected as patients are continuously monitored and a more detailed characterization of the patient's AFR could be achieved.

This study aimed to evaluate the relationship between AFR and the duration and onset time of the episode in continuously monitored patients as a way of better understanding the patient's condition.

2. Materials and Methods

2.1. Patient Population

This retrospective study included 99 patients (67% male; 57±12 years; 26% non-paroxysmal AF) which were implanted with an ICM. The patients were selected from Medtronic databases collected in multicenter studies in accordance with the Declaration of Helsinki. All patients provided written informed consent to the study protocol that was reviewed and approved by the human research ethics committee of each participating institution.

The available clinical baseline characteristics of the 99 patients are shown in Table 1.

The patients were continuously monitored for 5.9 ± 3.8 months to ensure the detection of AF episodes in both paroxysmal and non-paroxysmal patients. The device used was the Reveal LINQ (Medtronic Inc, Minneapolis, MN) which was implanted within the fourth intercostal space (V2-V3 electrode orientation) near the apex of the heart. The device senses and detects the rhythm with sampling frequency of 256 Hz and then, due to memory restrictions, stores a single-lead ECG signal of the first 2 minutes of the AF episode detected.

Table 1. Demographics of patients included in the study. PAF, Paroxysmal Atrial Fibrillation; CAD, Coronary Artery Disease

	Patients (n = 99)
Age, years	57 ± 12
Male	66 (67%)
PAF	73 (74%)
Coronary risk profile	
Hypertension	40 (40%)
Diabetes	13 (13%)
CAD	5 (5%)
Stroke	5 (5%)

2.2. QRST cancellation and AFR

The f-wave signal, from which the AFR is computed, is extracted from the stored AF episodes using spatiotemporal QRST cancellation [6] included in Cardiolund ECG Parser software.

Once the f-wave signal was obtained, AFR was estimated by fitting a complex harmonic model to the f-wave signal in 5 second windows by locally fitting the model in 0.5s subsegments. The model's performance is evaluated with a signal quality index (SQI), confined between [0, 1] and with larger values associated to better model fit. The AFR is estimated by the fundamental frequency of the fitted model, provided that the SQI is sufficient. A detail description of the harmonic f-wave model including estimation of AFR and SQI is found in [7]. Figure 1 shows the f-wave extraction process for the AFR estimation.

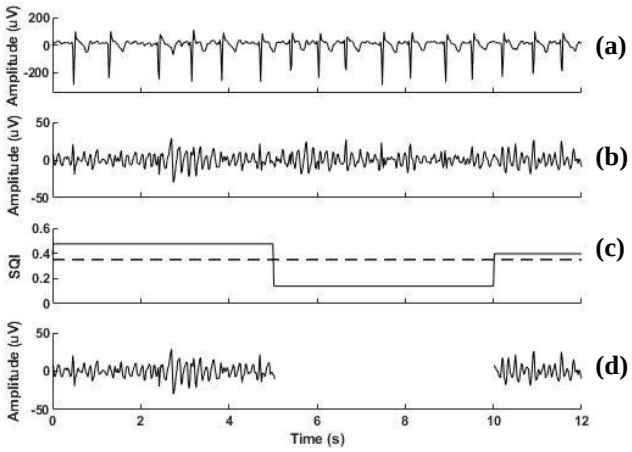

Figure 1. Illustration of f-wave extraction for AFR estimation. ***(a)*** *ECG signal extracted from ICM.* ***(b)*** *Estimated QRST-cancelled signal.* ***(c)*** *Signal quality index (solid line) with threshold for acceptable signal quality (dashed line).* ***(d)*** *Estimated f-wave signal*

For each patient, the mean AFR was computed from the AF segments within each episode that fulfilled the criterion SQI ≥ 0.35. The mean AFR of at least one acceptable 5 second segment was considered to be representative of the whole episode under the assumption that the AFR was stable within 2 minutes of AF. The stability of AFR within the episodes was studied by selecting the 24 episodes from 24 patients? where more than 80% of the episode had acceptable levels of SQI and iteratively computing the mean AFR for decreasing percentages of the signal and evaluating the relative absolute error between the mean AFR of the reduced signal segments and the mean AFR of the whole acceptable signal. Figure 2 shows the evolution of the relative error (%) for varying percentages of signal.

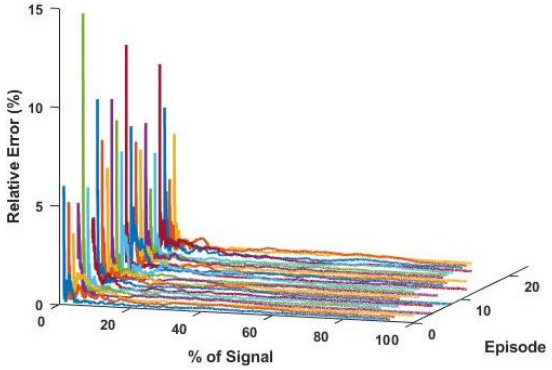

Figure 2. Relative error evolution with percentage of signal analyzed for those episodes containing more than 80% of acceptable segments.

The stability analysis showed a maximum relative error of 7.2 (4.4) % so AFR was assumed to be stable within the AF episodes. AF episodes without at least 5s (1 segment) of SQI ≥ 0.35 were excluded from the analysis. This mean AFR, hereinafter AFR, was used to characterize each episode.

In addition to the AFR, the relative AFR was also computed as:

$$relAFR\ (\%) = \frac{AFR}{AFR'} * 100 \qquad (1)$$

where AFR' is the average AFR for each particular patient.

The LINQ provides episode duration defined as short (episode duration < 20 minutes) or long (episode duration ≥ 20 minutes), and the onset time defined as night (00:00-06:00) or day (10:00-20:00) derived from the continuous monitoring of the patients. For the analysis of episode onset, any episodes outside the definition of night and day were not considered.

Continuous data are presented as mean ± SD if the null hypothesis H_0 of the Shapiro-Wilk test (H_0: data is normally distributed) was not rejected and were compared with the unpaired Student's t-test. Otherwise, continuous data are presented as median (IQR), being IQR the interquartile range, and compared using the Mann-Whitney U test.

3. Results

Out of 1815 episodes detected by the device, AFR was successfully extracted from 1400 AF episodes (18 ± 9 episodes/patient). The exclusion rate due to non-acceptable SQI levels was 15.4 (23.6) % and even if 23 (23.2%) of the patients had no episodes excluded, 2 (2.0%) had more than 80% of their detected episodes excluded.

699 episodes where considered to be short and 701 episodes where considered to be long. Out of the 99 patients, 9 (9.1%) had only short episodes, 6 (6.1%) had only long episodes and the remaining 84 (84.8%) had both short and long episodes. Exploring the onset times, 600 (42.9%) episodes occurred during the day (10:00-20:00), 377 (26.9%) occurred during the night (00:00-06:00) while 4223 (30.2%) of the episodes occurred outside the defined onset segments. Out of the 99 patients, 19 (19.2%) had only episodes during the day, 4 (4.0%) had only episodes during the night, 75 (75.8%) had episodes during both day and night and 1 (1.0%) only had episodes outside the defined segments.

The relationship between both AFR and relative AFR with episode length and episode onset was analysed. Figure 3 shows the distribution of AFR and relative AFR in time for short and long episodes.

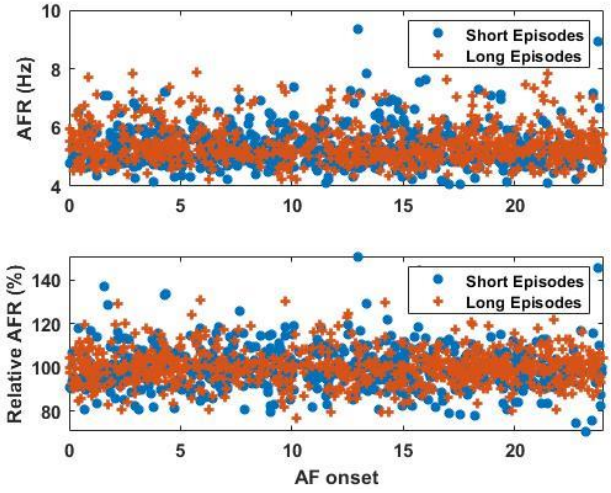

Figure 3. AFR and Relative AFR distribution in time (AF onset is time of day in hours).

AFR and relative AFR distribution with episode duration and episode onset are shown in Figure 4.

Considering AFR and episode onset (Figure 4(a)), it can be noted that AFR was significantly higher (p-value < 0.05, Mann-Whitney U test) in episodes with onset at night (00:00 - 06:00) than for episodes with onset during the day (10:00 - 20:00) where episodes with onset at night had an AFR of 5.34 (0.82) Hz and those with an onset during the day had an AFR of 5.21 (0.70) Hz.

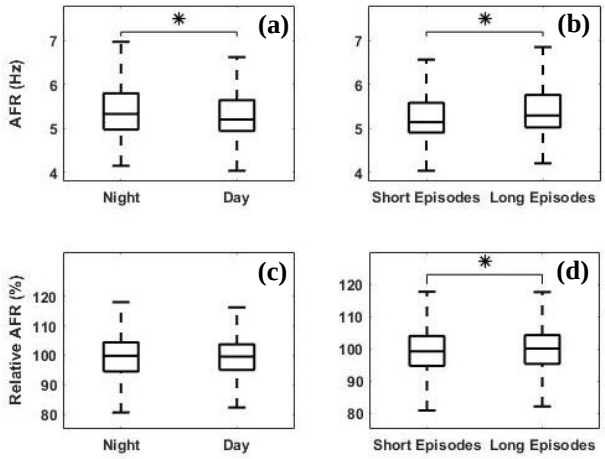

*Figure 4. Relationship between **(a)** AFR and episode onset, **(b)** AFR and episode duration, **(c)** relative AFR and episode onset, and **(d)** relative AFR and episode duration. Statistical significance (p-value < 0.05) is shown as *.*

AFR was also significantly higher in long episodes (≥ 20 mins) than in short episodes (< 20 mins) where the AFR in long episodes was 5.30 (0.74) Hz while in short episodes the AFR was 5.15 (0.66) Hz (Figure 4(b)).

While no significant differences were found between the relative AFR and episode onset time (Figure 4(c): Day: 99.5 (8.7) %; Night: 99.8 (9.9) %), significant differences were found between relative AFR and episode duration (Figure 4(d): Short: 99.2 (9.3) %; Long: 100.0 (8.9) %).

The population comprising all patients in the present study showed a weak correlation between episode duration and AFR (Spearman correlation R=0.16, p-value<0.001) however, when analyzing the individual patients, there were significant correlations (p-value<0.05) for 7 patients out of which 4 (57%) showed strong correlation (R>0.5) between episode duration and AFR. An example of one of these patients is shown in Figure 5.

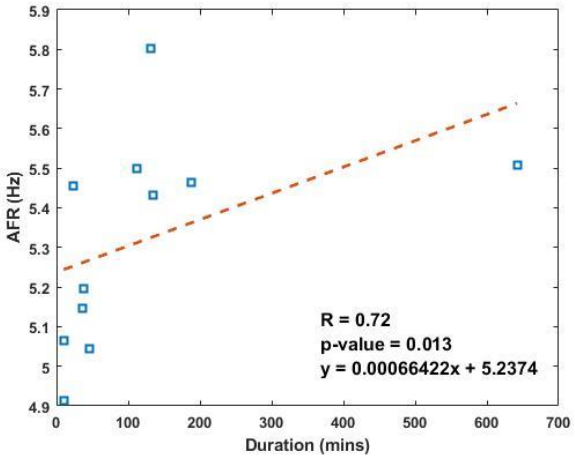

Figure 5. Example of strong significant correlation between AFR and Episode Duration.

4. Discussion

The main finding of this study is that the AFR observed in the first 2 minutes of the AF episodes is related to both the duration and the onset of the episode with higher AFR for episodes occurring during the night and for longer episodes. When evaluating the correlation between AFR and AF duration, we found weak correlation ($R=0.16$, $p\text{-value}<0.001$) when looking at the overall population while we found strong significant correlation ($R>0.5$, $p\text{-value}<0.05$) in 4 individual patients. The latter is in line with the findings by Bollman et al. where AFR and AF duration showed a positive correlation between them ($R=0.53$, $p=0.002$) [4]. However, this study was conducted in a small dataset with only 31 episodes from 11 paroxysmal AF patients. On the other hand, the use of Holter enabled a higher sampling rate and resolution.

The assumption of AFR stability within the first 2 minutes of the AF episodes was also evaluated. In the 24 episodes with enough data to run the analysis we found that for different percentages of signal, the error between the mean AFR of the signal and the mean AFR on the remaining segments was 7.2 (4.4) %. With this result in mind, AFR was considered stable and the mean AFR calculated on a single segment (5 seconds) was considered representative of the whole signal.

This retrospective study was made using a limited patient population with the data being extracted from the Reveal LINQ ICM which automatically detected AF episodes longer than 2 minutes therefore, episodes longer than 30s, which are defined as AF episodes by the guidelines, but shorter than 2 minutes were undetected by the ICM. Furthermore, the placement of the ICM near the apex of the heart is optimal for rhythm monitoring but is not ideal for atrial monitoring resulting in loss of stored AF episodes due to low SQI values.

However, the advantage of having continuous monitoring of the patient greatly outweighs the disadvantages of possible information loss due to memory restrictions or device signal quality.

5. Conclusion

The results of this study suggest that nighttime AF onset and longer duration AF episodes are more common in patients with higher AFR. This could potentially help clinicians in better characterize their patients as having AF episodes of longer durations is potentially linked to functional changes in the atrial tissue properties (‘remodeling’) and could result in more difficult and extensive catheter ablation procedures which increase the economic and personal burden of the procedure.

Disclosures

Mirko De Melis is a Medtronic employee and Javier Saiz-Vivo is affiliated to Medtronic.

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