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Characterising RR Intervals in Atrial Fibrillation Detected through Screening

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Abstract

Atrial fibrillation (AF) is known to be characterised by increased RR interval variability. However, the characteristics of RR intervals in AF detected through screening have not been extensively studied. The aim of this study was to characterise RR intervals in AF detected in screening of older, community dwelling adults. RR interval characteristics were extracted from 2,709 ECGs from the SAFER AF Screening Programme, consisting of 671 ECGs exhibiting AF, and 2,038 non-AF ECGs. The characteristics included measures of the mean RR interval, the variability in RR intervals, and the proportion of successive RR intervals differing by at least 50ms (pNN50). All characteristics differed significantly between AF and non-AF ECGs. pNN50 provided the highest performance for discriminating between AF and non-AF, with an AUROC of 96%. In AF the majority of successive RR intervals differed by more than 50ms, although there was large variation in the level of RR interval variability between AF ECGs. This study contributes to furthering our understanding of RR interval characteristics in AF. In the future this could form the basis of an algorithm to automatically identify ECGs exhibiting AF with potential applications in AF screening.

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia globally, and confers a fivefold increase in stroke risk. However, it is often not diagnosed, and therefore the opportunity to prevent stroke through treatment with anticoagulation is missed. Screening presents a promising approach to identify AF, with work ongoing to determine whether it is effective for reducing the incidence of stroke [1].

Inter-beat intervals, known as RR intervals when derived from an electrocardiogram (ECG), are fundamental to the diagnosis of AF. Guidelines state that an ECG exhibiting "no discernible repeating P waves and irregular RR intervals … is diagnostic of AF" [2]. When conducting AF screening using ECG-based technologies, RR intervals are often used to automatically determine whether an ECG shows an irregular rhythm and therefore warrants clinical interpretation [3]. In addition, alternative technologies that have been proposed for AF screening, such as photoplethysmography, involve assessing inter-beat intervals to detect irregular rhythms followed by ECG-based assessment to confirm an AF diagnosis [2].

The aim of this study was to characterise RR intervals in AF detected through screening of older, community dwelling adults. Characteristics of RR intervals were extracted from single-lead ECGs collected in an AF screening study, and compared between AF and non-AF ECGs to identify those characteristics which best discriminate between AF and non-AF.

2. Methods

2.1. The SAFER Feasibility Study dataset

The data used in this study were collected in the SAFER Feasibility Study (Screening for Atrial Fibrillation with ECG to Reduce stroke, ISRCTN 16939438), which assessed the feasibility of systemic AF screening in primary care [4], [5]. The participants, all aged 65 and over, were asked to record four 30-second, single-lead ECGs each day for 1-4 weeks using the Zenicor EKG-2 device (Zenicor Medical Systems AB, Sweden). A total of

162,515 ECGs were recorded by 2,141 participants. All participants gave informed consent, and the study was approved by the London Central NHS Research Ethics Committee (18/LO/2066).

Labels of AF were assigned to the dataset as follows. First, the Cardiolund ECG Parser algorithm (Cardiolund AB, Sweden) was used to classify all ECGs as either pathological (abnormal rhythm) or non-pathological (normal sinus rhythm or minor rhythm deviations), and either high or poor quality [3]. Second, a nurse reviewed the ECGs to correct any algorithm misclassifications and identify participants requiring further review (those who had at least one ECG exhibiting possible AF). Third, two cardiologists independently reviewed the ECGs from these identified participants and determined which participants exhibited AF. These cardiologists provided diagnoses for individual ECGs, and labels of poor signal quality, on an *ad hoc* basis. Fourth, a third cardiologist resolved any disagreements on participant-level diagnoses.

2.2. Selecting ECGs for analysis

Table 1. Characteristics of ECGs and participants included in the analysis.

Characteristic	AF	non-AF
Number of ECGs	671	2,038
- per participant, med (quartiles)	8 (2-22)	1 (1-1)
Number of participants	43	2,038
- age (yrs), med (quartiles)	76 (71-83)	72 (69-77)
- female, n (%)	10 (23)	1,060 (53)

A subset of ECGs was selected for analysis as follows.

First, AF ECGs were defined as those diagnosed as AF by at least one cardiologist (with no disagreement amongst cardiologists), and recorded by a participant who was diagnosed with AF. A total of 745 ECGs from 48 participants met these criteria. Of these, 671 ECGs were included in the analysis (see Table 1). The remainder were excluded because: they were labelled as poor quality by the algorithm or cardiologists (40), no data file was available (2), or they could not be analysed (32).

Second, non-AF ECGs were defined as those which: (i) had no algorithm-identified abnormalities and were recorded by participants who were not diagnosed with AF; or (ii) the nurse excluded from review; or (iii) both initial cardiologists agreed didn't exhibit AF; or (iv) the third cardiologist diagnosed as non-AF. A total of 154,324 ECGs from 2,106 participants met these criteria. Only the last high-quality, non-AF ECG from each participant was eligible for inclusion (chosen to avoid including ECGs recorded whilst participants were still learning to use the device). This resulted in 2,096 ECGs as no high quality non-AF ECGs were available for 10 participants. Of these, 2,038 ECGs were included in the analysis (see Table 1). The remainder were excluded because: no data file was available (18), or they could not be analysed (40).

2.3. RR Interval extraction and analysis

RR intervals were extracted as follows. ECGs were filtered to eliminate very low frequencies below 0.5 Hz. QRS complexes were detected using the 'jqrs' algorithm [6], [7]. RR intervals were automatically calculated as the time delays between consecutive QRS complexes.

The following RR interval characteristics were calculated for each ECG: mean RR interval (RRmean, ms); standard deviation of RR intervals (RRstd, ms); variability of RR intervals (RRvar = 100*RRstd/RRmean, %); root mean square of successive RR interval differences (RMSSD, ms); standard-deviation derived from the recurrence plot (Poincare plot SD1, ms); percentage of successive RR intervals that differ by more than 50ms (pNN50, %); and percentage of RR intervals within ±60ms of the median RR interval (RRpm60). Calculations were performed using the PhysioNet Cardiovascular Signal Toolbox [8] after modification to use a single QRS detector to facilitate analysis of ECGs with irregular rhythms.

2.4. Statistical Analysis

RR interval characteristics were reported as median (lower-upper quartiles). Characteristics in AF and non-AF were compared using a two-tailed Mann-Whitney U test at the 5% significance level. The utility of characteristics for distinguishing between AF and non-AF was assessed using the area under the receiver-operator curve (AUROC).

3. Results

The results are presented in Table 2 and Figure 1. All characteristics differed significantly between AF and non-AF ECGs, all with $p<0.01$. All characteristics were higher in AF, except RRmean and RRpm60 which were lower in AF. In AF, the level of variability (or irregularity) in RR intervals varied greatly between ECGs, as shown by wide inter-quartile ranges for RRstd, RRvar, and SD1.

The characteristics showed differing abilities to discriminate between AF and non-AF (see Table 2). pNN50 and RRpm60 provided excellent discriminatory ability (AUROCs of 96% and 95%). Indeed, the results for pNN50 indicate that 77% (68-84%) of successive RR intervals differed by more than 50ms in AF, compared to only 4% (0-18%) in non-AF. Characteristics indicative of variability in RR intervals (SD1, RMSSD, RRvar, and RRstd) provided good discriminatory ability, (AUROCs of 88 to 90%). RRmean provided the lowest discriminatory ability (AUROC of 64%).

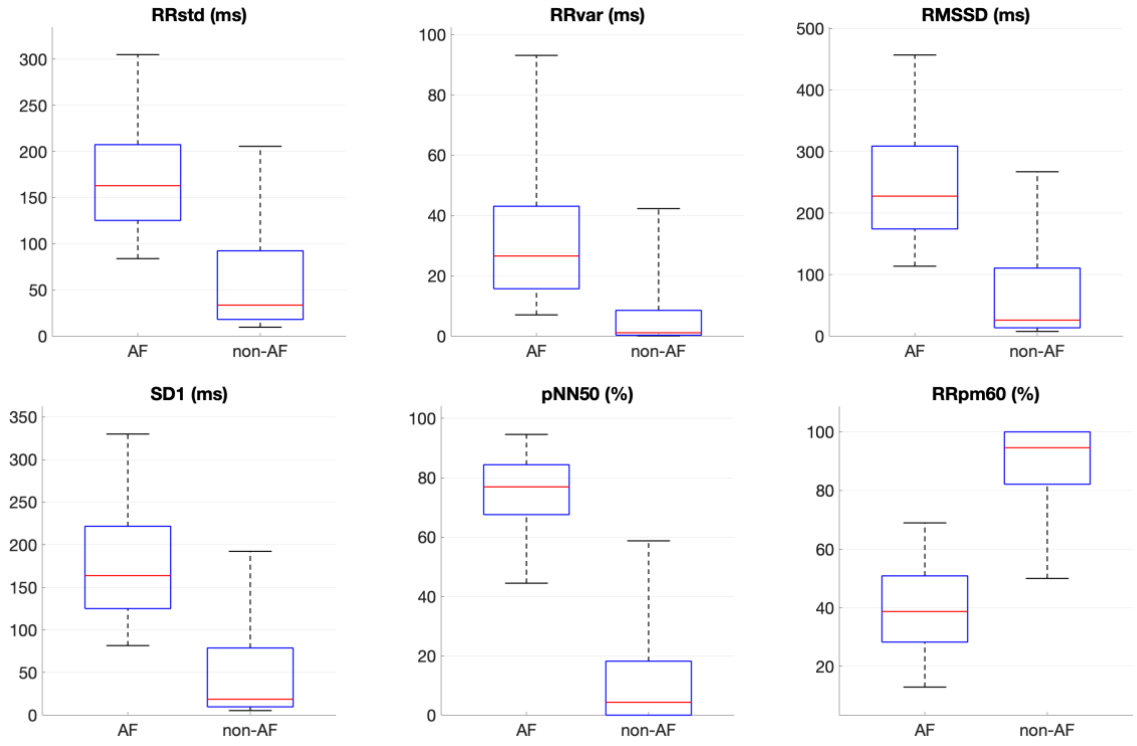

Figure 1. Boxplots comparing RR interval characteristics between AF and non-AF ECGs. Whiskers indicate 5th and 95th percentiles.

Table 2. RR interval characteristics in AF and non-AF, presented as median (lower – upper quartiles), and area under receiver operator curve (AUROC, %).

Characteristic	Value		AUROC
	AF	non-AF	
RRmean (ms)	733 (654-852)	819 (737-913)	63.8
RRstd (ms)	163 (125-208)	34 (18-92)	88.1
RRvar (%)	27 (16-43)	1 (0-9)	88.1
RMSSD (ms)	228 (174-309)	26 (14-111)	90.0
SD1 (ms)	164 (125-222)	19 (10-79)	90.0
pNN50 (%)	77 (68-84)	4 (0-18)	96.3
RRpm60 (%)	39 (28-51)	95 (82-100)	95.2

4. Discussion

4.1. Summary of Findings

This study characterised RR intervals in AF detected through population-based screening. In a comparison of RR interval characteristics between AF and non-AF data, the mean RR interval had moderate discriminatory ability, characteristics of RR interval variability had good discriminatory ability, and the best discriminatory ability was provided by the percentage of successive RR intervals that differ by more than 50ms. This indicates that AF is characterised by highly variable RR intervals, with the majority of successive RR intervals differing by more than 50ms. In contrast, in non-AF ECGs only a small minority of successive RR intervals differed by more than 50ms, indicating that other sources of variability such as respiratory sinus arrhythmia cause much lower levels of variability than AF.

4.2. Comparison with literature

This study complements previous research by studying RR intervals from self-captured, single-lead ECGs collected in an AF screening setting. In contrast, previous research has focused on ECGs acquired by trained operators using chest electrodes [9], and using long-term ECG monitoring devices [10]. Furthermore, this study provides insight into the RR interval characteristics of the general population, including both paroxysmal and permanent AF. Research has shown that RR interval variability differs between paroxysmal and permanent AF [9], highlighting the importance of studying RR intervals across different types of AF.

4.3. Strengths and limitations

A key strength of this study is that it used data from an AF screening study, collected from the target population for AF screening (older adults), in the target setting (home monitoring), using ECGs representative of those likely to be acquired in AF screening (lead I ECGs measured at the hands using dry electrodes). However, it only included ECGs where the diagnosis (AF or non-AF) was confidently known. In the future, it would be helpful to: (i) investigate ECGs with less certain diagnoses; (ii) include a wider range of RR interval metrics; and (iii) optimise the signal processing pipeline to ensure QRS complexes are identified as accurately as possible.

4.4. Implications

A better understanding of RR interval characteristics in AF could form the basis for improved AF detection algorithms specifically for use in AF screening. Indeed, the algorithm used in STROKESTOP and SAFER AF screening studies incorporates RR interval characteristics (RRstd and RRpm60) to identify irregular rhythms which may indicate possible AF [3], [11]. Algorithms incorporating additional characteristics may help reduce the costs of AF screening when compared to current algorithms which have been reported to have a high sensitivity for AF but a low specificity, resulting in a high number of ECGs being sent for manual cardiologist review [3]. This was shown in the 'PhysioNet/Computing in Cardiology Challenge 2017', in which a winning AF detection algorithm incorporated several RR interval characteristics [12].

5. Conclusion

RR intervals in screen-detected AF are characterised by increased variability where the majority of successive RR intervals differ by more than 50ms. The level of RR interval variability in AF varies greatly. RR interval characteristics may be useful for automatically identifying ECGs that may contain AF for manual review. Indeed, pNN50, the percentage of successive RR intervals that differ by more than 50ms, showed a high ability for discriminating between AF and non-AF ECGs in this study. Future research should investigate the performance and cost-effectiveness of automated algorithms to identify AF in self-captured ECGs, with potential applications in population-based and opportunistic AF screening.

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