Force-Interval Relationships of the Heart Measured With Photoplethysmography During Atrial Fibrillation

Linda M Eerikäinen[1,2], Alberto G Bonomi[2], Lukas Dekker[1,3],
Fons Schipper[2], Rik Vullings[1], Ronald M Aarts[1,2]

[1]Department of Electrical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands
[2]Philips Research, Eindhoven, The Netherlands
[3]Department of Cardiology, Catharina Hospital Eindhoven, Eindhoven, The Netherlands

Abstract

Force-interval relationships (FIRs) of the heart represent the relationships between inter-beat intervals (IBIs) and strength of the ventricular contractions. These relationships are typically measured invasively and are altered from normal in heart failure (HF). An unobtrusive and continuous measurement of FIRs could be beneficial when HF and atrial fibrillation (AF) coexist in order to understand if AF causes progression of HF. We hypothesize that FIRs could be assessed during AF with IBIs and hemodynamic changes captured unobtrusively by photoplethysmography (PPG) at the wrist. FIRs were assessed by using Spearman's rank correlation between the pulse onset change in the PPG waveform and either the preceding or pre-preceding IBIs (r_{pre} and $r_{pre-pre}$) in 5-minute segments. 32 patients (14 continuous AF, 18 no AF) were measured during the night with PPG and electrocardiography as a reference. The mean and standard deviation of r_{pre} were -0.25 $\pm$ 0.08 and 0.05 $\pm$ 0.12 ($p < 0.0001$), and of $r_{pre-pre}$ 0.60 $\pm$ 0.09 and 0.16 $\pm$ 0.14 ($p < 0.0001$), during AF and sinus rhythm, respectively. Areas under the Receiver Operating Characteristics curve were 0.987 and 0.998, respectively. Thus, during AF the IBIs correlate with the beat-to-beat changes of blood volume measured with PPG, likely to indicate that FIRs can be measured unobtrusively with the PPG signal.

1. Introduction

Force-interval relationships (FIRs) of the heart, i.e. post-extrasystolic potentiation (PESP) and mechanical restitution (MR), represent the relation between the length of a preceding or a pre-preceding inter-beat interval (IBI) and the strength of contraction that follows [1]. In PESP, the beat following an extrasystole is potentiated, i.e. the contraction is stronger, which is a phenomenon known already for 120 years [2]. The MR, in turn, represents the recovery of the contractile strength after an extrasystolic beat [1].

In heart failure (HF) the contractile capacity of the heart is reduced and a number of studies have shown that FIRs of a failing heart are different to those of non-failing hearts [3–5]. The cause of the difference is not entirely understood, but is presumably due to altered Ca^{2+} handling of the myocardial cells [6]. Studies of FIRs have been commonly conducted with invasive measures in laboratory settings, although recently Sinnecker et al. [7] stated that FIR assessed by an unobtrusive blood pressure measurement predicts mortality in survivors of myocardial infarction with atrial fibrillation (AF).

AF is the most commonly experienced sustained cardiac arrhythmia. It is characterized by an abnormal electrical activity of the atria which causes the heart to beat irregularly. Studies have shown that, related to this irregularity, the contractility of the heart varies beat-to-beat as a consequence of FIRs [8–10]. AF often coexists with HF and the clinical outcome of patients with this coexistence is particularly poor compared to those having only one of the two conditions [11]. For some HF patients with reduced ejection fraction, AF causes symptomatic deterioration whereas for others AF does not affect the patient's condition, the difficulty being the identification of the two groups of patients [12].

Photoplethysmography (PPG) is an unobtrusive measurement modality that has recently gained much interest due to its ease of use and applicability for long-term monitoring, e.g. in wrist-based wearable devices. PPG measures blood volume changes in the vascular bed of the tissue and enables heart rate detection from the pulses in the signal. In case of AF, promising results have been presented for detection of AF episodes with continuously measured wrist-worn PPG by assessing rhythm irregularities [13]. However, there is limited knowledge whether

 ISSN: 2325-887X DOI: 10.22489/CinC.2018.111

continuous PPG monitoring during AF could have additional value beyond rhythm irregularity assessment, considering that PPG also captures hemodynamic effects.

We hypothesize that the beat-to-beat contractility variations during AF may be reflected as pulse-to-pulse variations in the PPG waveform. The assumption is that during irregular rhythm FIRs can be observed and there is a stronger correlation between IBIs and variations in pulse morphology. In this paper we present a study about the relationships between IBIs and PPG signal morphology variations during AF that could possibly serve as an unobtrusive method to assess FIRs.

2. Methods

2.1. Data

The dataset consisted of 24-hour measurements of electrocardiography (ECG), PPG and accelerometer from 40 subjects. PPG and accelerometer were measured with a wrist-worn data logging device equipped with the Philips Cardio and Motion Monitoring Module (CM3 Generation-3, Wearable Sensing Technologies, Philips, Eindhoven) and an ECG reference with a 12-lead Holter monitor (H12+, Mortara, Milwaukee, WI, USA). The measurement protocol and devices are described in more detail in [13].

The ECG data were visually analyzed by a clinical expert using an automated rhythm detection software (Veritas, Mortara, Milwaukee, WI, USA). The ECG beat times were extracted by the software and every beat was classified either as normal, supraventricular or ventricular premature contraction, AF, paced, artifact, or unknown. The rhythm was then confirmed or corrected by the expert. In addition to rhythm information, the collected data included patient diaries of the daily activities, and baseline characteristics, medical characteristics, and information about medication which were retrieved from the medical records.

For the analysis, patients with atrial flutter or very noisy ECG reference were excluded. This resulted in 32 patients of which 14 had continuous AF (age (years, m $\pm$ sd): 68 $\pm$ 11, males: 71%, BMI (kg/m^2, m $\pm$ sd): 29.8 $\pm$ 6.9) and 18 showed normal sinus rhythm with premature contractions (age, (years, m $\pm$ sd): 67 $\pm$ 14, males: 50%, BMI (kg/m^2, m $\pm$ sd): 28.1 $\pm$ 5.6).

2.2. Features

The PPG data was downsampled from 128 Hz to 64 Hz and preprocessed by filtering with a bandpass filter to the range from 0.3 to 5 Hz. The pulses were detected by identifying fiducial points in the PPG waveform such as the onset of the pulse. The major fluctuations in the PPG signal were removed by subtracting a cubic spline fitted to the point of the maximum gradient of the rising pulse slope [14]. The IBIs were calculated as the time differences between two consecutive pulse onset times. Based on the IBI sequence from PPG and the IBI sequence from the ECG reference beat-times, the reference beat labels were aligned with the PPG pulses.

The analysis was limited to the period at night between the times that patient had reported going to bed and getting up in the morning with the purpose of having less movement artifacts in the signal. The time stamps were selected manually around the reported sleep and awake times by looking at the accelerometer data.

Figure 1 shows an example of recorded PPG waveform during AF with six PPG pulses and the variables that from here on will be referred as pre-preceding inter-beat interval ($\mathrm{IBI}_{pre-pre}$), preceding inter-beat interval (IBI_{pre}), and difference in the PPG signal between two consecutive pulse onsets (i) and (i$-$1) (onset_{diff}). IBI_{pre} is the time difference between the pulses (i) and (i$-$1) and $\mathrm{IBI}_{pre-pre}$ between the pulses (i$-$1) and (i$-$2). The onset_{diff} could indirectly reflect the change in end-diastolic volume. This is, in turn, related to the change in stroke volume and end-systolic volume, which are known to be influenced by FIRs [10].

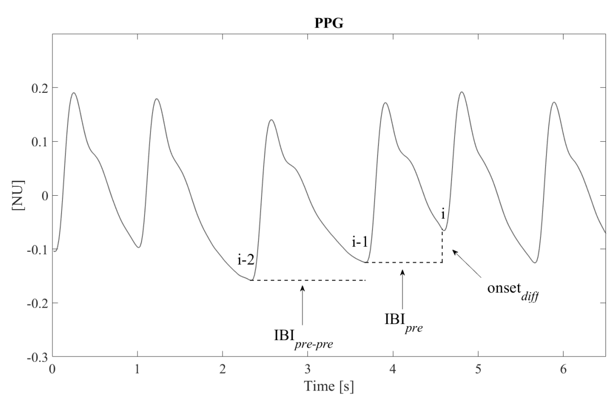

Figure 1. Example of PPG pulses, onset_{diff}, IBI_{pre}, and $\mathrm{IBI}_{pre-pre}$ during AF.

The relationship between IBIs and onset_{diff} were analyzed with Spearman's rank correlation. Spearman's rank correlation was selected because of the non-linearity of the relationship. IBIs $<$ 200 ms and $>$ 2000 ms were discarded from the analysis before assessing the correlation. The correlation coefficients between $\mathrm{IBI}_{pre-pre}$ and onset_{diff} ($r_{pre-pre}$), and IBI_{pre} and onset_{diff} (r_{pre}) were computed in 5-minute segments shifting by 60s and including segments containing at least 180 IBIs. In every segment top and bottom 2% of onset_{diff} values and corresponding IBIs were discarded to exclude outliers. Moreover, segments including premature contractions were excluded from the analysis since these also induce FIRs and the focus of the analysis was in FIRs during AF.

2.3. Statistical analysis

The difference between the distributions of correlation coefficients r_{pre} and $r_{pre-pre}$ during AF compared to sinus rhythm was assessed with Mann-Whitney U-test. In addition, Receiver Operating Charateristics (ROC) were analyzed in order to understand to which extent the two correlations are different in the AF and sinus rhythm groups.

3. Results

The relationships between the inter-beat intervals ($\mathrm{IBI}_{pre-pre}$ and IBI_{pre}) and onset_{diff} when computed in a 5-minute segment during AF are shown in figure 2. It illustrates a similar positive trend of onset_{diff} in relation to pre-preceding IBI and a negative trend in relation to preceding IBI which is similar to the relationships of the IBIs and end-systolic volume as in [10] during AF.

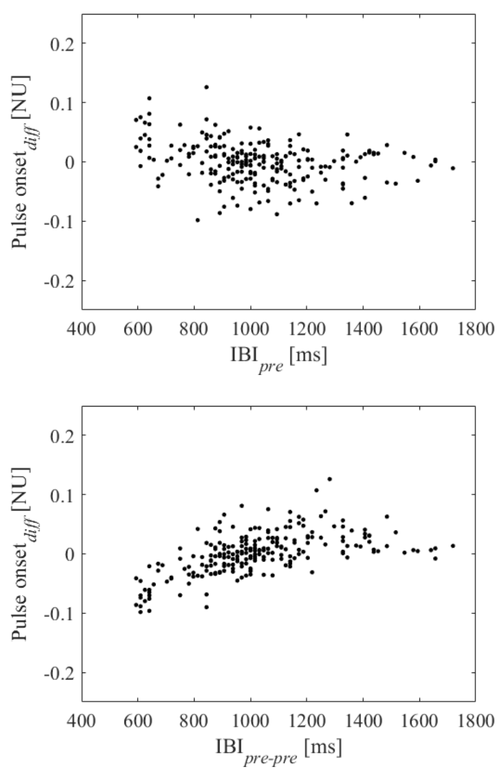

Figure 2. The relation between preceding IBI (IBI_{pre}) and pulse onset difference (onset_{diff}) (top) and between pre-preceding IBI ($\mathrm{IBI}_{pre-pre}$) and pulse onset difference (below) in a 5-minute segment when every point represents a beat.

Histograms of correlation coefficients r_{pre} and $r_{pre-pre}$ computed for IBI_{pre} and onset_{diff}, and $\mathrm{IBI}_{pre-pre}$ and $\mathrm{onset}_{\mathrm{diff}}$, respectively, are presented in figure 3. The mean and standard deviation of r_{pre} were -0.25 $\pm$ 0.08 and 0.05 $\pm$ 0.12, for AF and sinus rhythm, respectively, and of $r_{pre-pre}$ 0.60 $\pm$ 0.09 and 0.16 $\pm$ 0.14. In both cases the Mann-Whitney U-test confirmed that the difference in the distributions of r_{pre} and $r_{pre-pre}$ between the AF and sinus rhythm group was statistically significant ($p <$ 0.0001). Of all computed r_{pre} 94.84% were significantly different from zero ($p <$ 0.05) during AF with respect to 23.66% when AF was not present. For $r_{pre-pre}$ the percentages of nonzero correlation were 99.98% and 58.37% for AF and sinus rhythm, respectively.

Figure 4 shows the ROC curves for the correlation coefficients r_{pre} and $r_{pre-pre}$, with the areas under the curve 0.987 and 0.990, respectively.

4. Discussion

In this paper we presented two features that could represent FIRs in the PPG signal during AF. The beat-to-beat variability of IBIs during AF shows a relation with blood volume changes which cannot be observed when there is little variability, i.e. during sinus rhythm. The mean correlation coefficients between IBIs and pulse onset changes during AF obtained in this study are similar to the ones presented by Brookes et al. [10] with IBIs and end-systolic volume. The unobtrusive continuous assessment of FIRs, and whether they change with time, can be particularly interesting when AF and HF coexist, since AF can increase symptoms and cause further progression of HF [11]. Moreover, AF can induce HF. Continuous monitoring could possibly help in noticing early on deterioration in the patient's condition, enabling interventions or changes to treatment and preventing further deterioration.

As a limitation, an invasive reference measure of contractility was missing in this study. In addition, new studies are required for investigating whether the unobtrusive measures from PPG presented here show a difference between HF patients and patients with non-failing hearts.

5. Conclusion

The relationship between IBIs and pulse-to-pulse morphology variations in the PPG signal during AF could reflect the FIRs of the heart. This will provide an interesting unobtrusive parameter to study further in the group of patients with AF and HF, first by confirming the findings with experiments in a controlled setting using an invasive measurement as a reference, and later on with the aim of improving disease management in this patient group.

Acknowledgements

This research was performed within the framework of the strategic joint research program on Data Science between TU/e, Catharina Hospital Eindhoven, and Philips

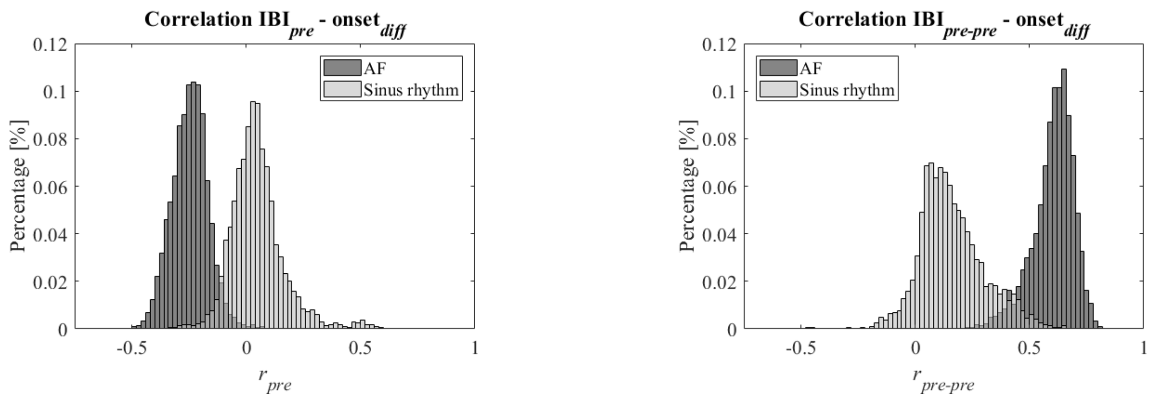

Figure 3. Histograms of r_{pre} (left) and $r_{pre-pre}$ (right) during AF and sinus rhythm.

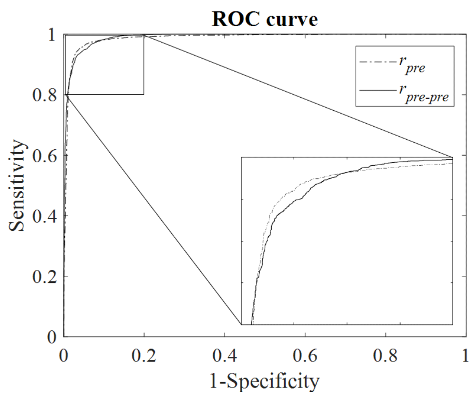

Figure 4. ROC curves for r_{pre}, and $r_{pre-pre}$.

Electronics Nederland B.V. and partly funded by ITEA3 project, 15032, eWatch. The authors would like to thank everybody who contributed to the data collection.

References

[1] Cooper MW. Postextrasystolic potentiation. Do we really know what it means and how to use it? Circulation 1993; 88:2962–2971.

[2] Lagendorff O. Untersuchungen am überlebenden Säugetierherzen III. Vorübergehende Unregelmässigkeiten der Herzschlages und ihre Ausgleichung. Pflugers Archiv 1898;70:473–486.

[3] Merillon JP, et al. Post-extrasystolic left ventricular peak pressure with and without left ventricular failure. Cardiovascular Research 1979;13:338–344.

[4] Hoffman BF, Bartelstone HJ, Scherlag BJ, Cranefield PF. Effects of Postextrasystolic Potentiation on Normal and Failing Hearts. Bulletin of the New York Academy of Medicine 1965;41(5):498–534.

[5] Seed WA, et al. Relationships between beat-to-beat interval and the strength of contraction in the healthy and diseased human heart. Circulation 1984;70(5):799–805.

[6] Sprenkeler DJ, Vos MA. Post-extrasystolic potentiation: link between Ca2+ homeostasis and heart failure? Arrhythmia Electrophysiology Review 2016;5(1):20–26.

[7] Sinnecker D, et al. Force-interval relationship predicts mortality in survivors of myocardial infarction with atrial fibrillation. International Journal of Cardiology 2015;182:315–320.

[8] Hardman SM, Noble MI, Seed WA. Postextrasystolic potentiation and its contribution to the beat-to-beat variation of the pulse during atrial fibrillation. Circulation 1992; 86(4):1223–1232.

[9] Hardman SMC, Noble MIM, Biggs T, Seed WA. Evidence for an influence of mechanical restitution on beat-to-beat variations in haemodynamics during chronic atrial fibrillation in patients. Cardiovascular Research 1998;38(1):82–90.

[10] Brookes CI, White PA, Staples M, Oldershaw PJ, Redington AN, Collins PD, Noble MI. Myocardial contractility is not constant during spontaneous atrial fibrillation in patients. Circulation 1998;98(17):1762–1768.

[11] Ling LH, Kistler PM, Kalman JM, Schilling RJ, Hunter RJ. Comorbidity of atrial fibrillation and heart failure. Nature Reviews Cardiology 2015;13(3):131–147.

[12] Verma A, Kalman JM, Callans DJ. Treatment of patients with atrial fibrillation and heart failure with reduced ejection fraction. Circulation 2017;135(16):1547–1563.

[13] Bonomi AG, Schipper F, Eerikäinen LM, Margarito J, Aarts RM, Babaeizadeh S, Morree HMD, Dekker L. Atrial fibrillation detection using photo-plethysmography and acceleration data at the wrist. Computing in Cardiology 2016; 277–280.

[14] Yang L, Zhang S, Li X, Yang Y. Removal of pulse waveform baseline drift using cubic spline interpolation. 2010 4th International Conference on Bioinformatics and Biomedical Engineering iCBBE 2010 2010;1–3.

Address for correspondence:

Linda M. Eerikäinen
P.O. Box 513, 5600 MB Eindhoven, The Netherlands
L.M.Eerikainen@tue.nl