The P-wave Time-domain Significant Features to Evaluate Substrate Modification After Catheter Ablation of Paroxysmal Atrial Fibrillation

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Abstract

The outcome of catheter ablation (CA) of atrial fibrillation (AF) is vastly analyzed by the entire P-wave duration (PWD). However, the first and second P-wave parts, corresponding to right (RA) and left atrial (LA) wavefront propagation, may be unequally modified. Five-minute lead II recordings before and after the first-ever CA of 40 paroxysmal AF patients were analyzed and P-wave features were calculated: $PWD_{on\text{–}off}$ of the entire P-wave and each P-wave part (RA: $PWD_{on\text{–}peak}$, LA: $PWD_{peak\text{–}off}$) and the time from P-wave onset or offset to the R-peak ($PWD_{on\text{–}R}$ and $PWD_{off\text{–}R}$, respectively). Heart-rate (HR) adjustment (HRA) mitigated the HR fluctuations. Pre/post-CA comparison was performed with Mann-Whitney U-test and median values were calculated. Pearson's correlation was calculated between PWD and the remaining features. The effect of CA with ($\Delta : -17.96\%$) or without HRA ($\Delta : -9.84\%$) was significant at the entire $PWD_{on\text{–}off}$ and at the $PWD_{peak\text{–}off}$ (HRA: $\Delta : -27.77\%$, no HRA: $\Delta : -22.03\%$). $PWD_{on\text{–}off}$ showed a stronger correlation with RA than LA ($\rho_{max} = 0.805$ vs $\rho_{max} = 0.541$). P-wave features corresponding to RA are more strongly related to the entire P-wave. Nevertheless, only the P-wave part associated with LA is significantly affected by CA. That being so, studies are encouraged to incorporate part-time P-wave analysis.

1. Introduction

Atrial fibrillation is the most widespread cardiac arrhythmia, strongly connected with stroke and other comorbidities [1]. AF impact is not restricted to health complications but can also cause economical and psychological burden [1]. The early AF treatment is considered of paramount importance in order to augment the efficiency of the chosen strategy and to ensure a higher quality of life for the individual [1]. Catheter ablation (CA) is the principal AF treatment, performed by isolating the areas showing arrhythmogenic activity in order to restrain AF and hinder the AF propagation [1]. Due to specific anatomical and cellular mechanisms, pulmonary veins (PVs) are the primary source of arrhythmogenic activity, hence being the CA of PVs considered the star AF treatment [2–4].

CA of PVs shows outstanding results mainly in paroxysmal AF patients, where foci are limited to PVs [5]. Notwithstanding, as prolonged time in AF may provoke significant anatomical alterations, favoring the AF initiation and sustaining the AF propagation, persistent AF patients often present variable drivers spanning across the atria [1, 3]. These alterations may happen to anatomical, electrical or functional level and are described under the term atrial remodeling [1, 6]. Although left atrium (LA) seems to be more affected by the AF mechanisms, drivers can also be present in the right atrium (RA) [6, 7].

Atrial remodeling is not an irreversible phenomenon [6]. Degenerative mechanisms can be inverted, depending on the early action and the severity of the remodeling. P-waves are vastly used to assess the status of both remodeling and reverse remodeling [8]. Time-domain P-wave features, such as P-wave duration (PWD) and P-R interval have been extensively recruited for this purpose [9–12]. Nevertheless, analysis of these parameters is performed assuming a uniform impact of the AF mechanisms to RA and LA as well as equal reverse remodeling for both atrial sides. This study aims to investigate the theory of different extent of reverse remodeling right after CA of PVs, targeting a more precise analysis of the AF mechanisms and a more efficient follow-up of the patient.

2. Materials and Methods

Twelve-lead electrocardiogram (ECG) recordings of 40 paroxysmal AF patients undergoing their first-ever CA of

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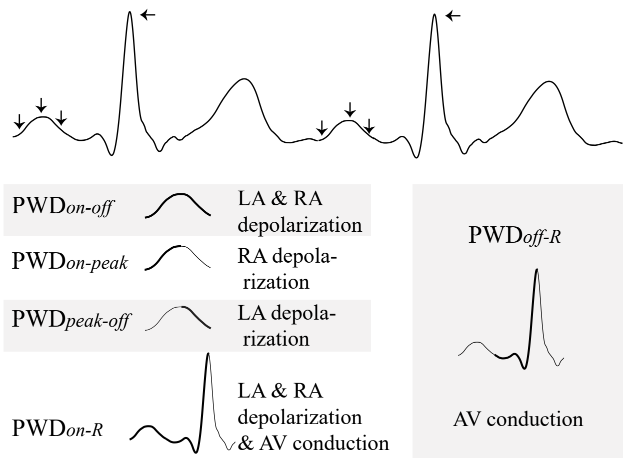

Figure 1. The five features that were calculated and the phase of the cardiac cycle they illustrate. The arrows indicate the defined fiducial points. AV: atrioventricular.

PVs were acquired. Patients were in sinus rhythm (SR) during the procedure and continuous recordings were extracted for five minutes before and after CA with 1 kHz sampling frequency. Due to the fact that P-waves are more prominent in lead II, this channel was chosen for further analysis [13].

Preprocessing started with powerline interference removal via a wavelet-based denoising method, followed by removal of muscle noise and baseline wander through a bidirectional low-pass and a high-pass filter with cut-off frequencies at 70 and 0.8 Hz, respectively [14, 15]. Since some recordings contained ectopic beats $\leq 4\%$ of total beats, these were detected and corrected via linear interpolation [16, 17].

For each recording, P-waves and R peaks were detected and delineated and the following time-related characteristics were calculated: $\text{PWD}_{\text{on–off}}$, $\text{PWD}_{\text{on–peak}}$, $\text{PWD}_{\text{peak–off}}$, $\text{PWD}_{\text{on–R}}$ and $\text{PWD}_{\text{off-R}}$. Figure 1 shows how each of the features is calculated and the phase of the cardiac cycle it corresponds to.

Heart-rate (HR) fluctuations may affect all of the aforementioned features, with more vigorous HR leading to shortening and slower HR to increment of their values. In order to remove this bias, features were adjusted to a neutral-to-HR analysis, by being multiplied by the following factor:

$$A_x = \frac{1000}{IBI_i}, \quad (1)$$

where x corresponds to each of the calculated features and IBI_i to the interbeat interval of the i^{th} activation.

Median values before and after CA were defined and compared with a Mann-Whitney U-test (MWU). Pre\post variation (percentage of variation-POV) was defined in form of percentage. In order to define the exact relationship between PWD and the remaining features, Pearson correlation coefficient (PCC) was recruited. PCC was calculated for the values before and after CA as well as for the POV.

3. Results

Figure 2 shows the bar chart of the values before and after CA as well as the POV. Before adjustment, $\text{PWD}_{\text{on–off}}$, corresponding to the traditional entire PWD, shows a statistical shortening of -9.84%. Looking closer, this shortening seems to be provoked by $\text{PWD}_{\text{peak–off}}$, corresponding to LA depolarization time, which was statistically shortened by -22.03%. Regarding RA depolarization time ($\text{PWD}_{\text{on–peak}}$), the decrease was limited to -8.96% without any statistical significance. As for the P-R interval features, neither of them varied significantly. Interestingly enough, $\text{PWD}_{\text{off–R}}$, reflecting the pure AV conduction time, got increased by $+10.24\%$.

Results after HR-adjustment were quite similar to the ones before the mitigation, with both $\text{PWD}_{\text{on–off}}$ and $\text{PWD}_{\text{peak–off}}$ preserving the statistical significance and potentiating the POV results, which were -17.96% and -27.77%, respectively. $\text{PWD}_{\text{on–peak}}$ continued to show insignificant variation, which was slightly weakened to -6.81%. The same trend as before adjustment was also maintained for the P-R interval-related features.

Table 1 shows the correlations between $\text{PWD}_{\text{on–off}}$ and the rest of the features. As all features, besides $\text{PWD}_{\text{off-R}}$, include the entire or some part of the PWD, the correlations were mostly positive and moderate to high. More specifically, PCC indicated a strong correlation between $\text{PWD}_{\text{on–peak}}$ (RA) and the entire PWD at all analysis scenarios (before and after CA, POV), which was additionally intensified after the HR-adjustment. Compared to $\text{PWD}_{\text{on–peak}}$, $\text{PWD}_{\text{peak–off}}$ (LA) showed a notably weaker relationship with the entire PWD. P-R interval features showed statistically significant correlations with the entire PWD before and after CA, but lost statistical power for the POV case, where $\text{PWD}_{\text{on–R}}$ only showed statistical signfiicance after HR-adjustment. Nevertheless, $\text{PWD}_{\text{on–R}}$ was the most correlated feature with PWD in almost all cases before and after CA as well as in POV after HR-adjustment. On the contrary, $\text{PWD}_{\text{off–R}}$ showed negative correlations in almost every case without HR-adjustment.

4. Discussion

Despite the undoubted contribution of PWD and P-R interval analysis to the evaluation of the remodeling and inverse remodeling after CA of PVs, the lack of a universal threshold classifying an atrium as remodelled complicates the analysis. Some studies consider PWD longer than 120

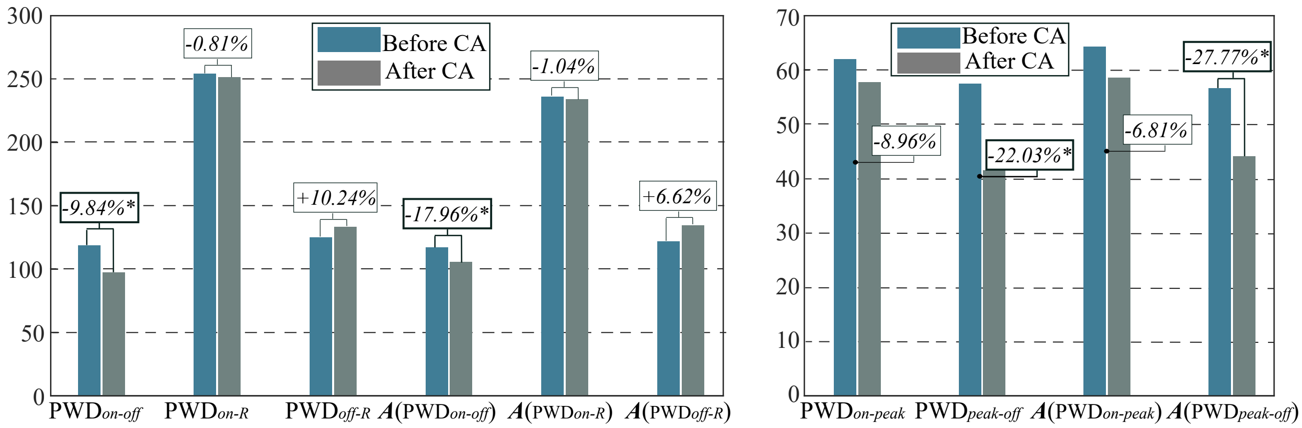

Figure 2. Bar chart of the values before (blue) and after (gray) CA. POV is shown in square boxes for each feature.

Table 1. Correlation (ρ) and p values between $\text{PWD}_{\text{on–off}}$ and the remaining features. Asterisk(*) shows statistically significant values.

	Before CA		After CA		POV	
Feature	ρ	p value	ρ	p value	ρ	p value
$\text{PWD}_{\text{on–peak}}$	0.7473	$< 0.0001*$	0.7458	$< 0.0001*$	0.5405	$0.0114*$
$\text{PWD}_{\text{peak–off}}$	0.4773	$< 0.0001*$	0.4194	$< 0.0001*$	0.6142	$0.0031*$
$\text{PWD}_{\text{on–R}}$	0.7222	$< 0.0001*$	0.7528	$< 0.0001*$	0.2403	0.2942
$\text{PWD}_{\text{off–R}}$	-0.5027	$< 0.0001*$	-0.2578	$< 0.0001*$	-0.4010	0.0716
$\mathbf{A}(\text{PWD}_{\text{on–peak}})$	0.8051	$< 0.0001*$	0.8028	$< 0.0001*$	0.7681	$0.0001*$
$\mathbf{A}(\text{PWD}_{\text{peak–off}})$	0.5412	$< 0.0001*$	0.5309	$< 0.0001*$	0.7098	$0.0003*$
$\mathbf{A}(\text{PWD}_{\text{on–R}})$	0.8328	$< 0.0001*$	0.8553	$< 0.0001*$	0.7854	$0.0001*$
$\mathbf{A}(\text{PWD}_{\text{off–R}})$	0.0993	$< 0.0001*$	0.2687	$< 0.0001*$	0.3249	0.1508

ms to stem from remodeled tissue, while other studies use a threshold of 140 ms for the same purpose [9, 18]. A possible parameter highly affecting the classification problem might be the trend to analyze the PWD indivisibly, considering that RA and LA depolarization are equally affected by CA, despite the fact that LA is considered more relevant to atrial remodeling and inverse remodeling [6]. Although not affecting directly the PWD thresholding, calculating P-R with the P-wave component included implies a direct impact of the atrial depolarization to what was supposed to be the evaluation of the AV conduction. The current study has attempted a more exclusive approach of the analysis, by focusing on indivisible ECG components.

As expected, the entire PWD was statistically shortened in coherence with relevant studies [9, 18]. Analysis in first and second P-wave parts revealed that P-wave shortening originated from the srhinking of the second P-wave part, corresponding to LA depolarization time, regardless of the HR-adjustment. In fact, shortening of LA depolarization time seemed to be higher than the value estimated when PWD was analyzed homogeneously. Correlation analysis revealed that the first P-wave part, illustrating the RA depolarization time, was highly associated with the entire PWD, probably due to higher duration of RA depolarization time. This observation may explain the fact that the entire PWD presents a lower-level shortening with respect to the second P-wave part, implying the underestimation of inverse remodeling at each one of the atria in the case of the entire PWD analysis.

As with PWD, this study demonstrated that P-R analysis can also be optimized by focusing on the part between the end of the P-wave and the R peak, corresponding to AV conduction. As shown from the correlation analysis, when the P-wave is included in the P-R estimation, the extracted information resembles to a high degree the information extracted from the P-wave analysis, losing the trace of the AV conduction time variation. While P-R interval, including the P-wave, seemed to be shortened after CA, an increase was observed from the P-R interval calculation without the P-wave component. According to previous studies, while P-R prolongation, including the P-wave, may be associated with inverse remodeling, due to the high effect of P-wave in this case, a short P-R interval, when P-wave is excluded, may be connected with atrial remodeling, as an outcome of the P-wave prolongation [19]. If this holds, P-R prolongation after CA, without the P-wave component, may also be indicative of a positive CA outcome, as it may occur due to PWD restoration. This observation would have been masked in case of uniform P-R analysis.

5. Conclusions

P-wave and P-R analysis can be optimized by targetting integral ECG parts, providing more accurate and consistent information. PWD shortening stems from the LA depolarization time shortening, which seems to happen to a higher degree but masked due to a higher effect of RA depolarization on the PWD analysis. Therefore, it is of paramount importance to focus on each P-wave part separately.

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