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Additional Information

Alternative Time-Domain P-wave Analysis for Precise Information on Substrate Alteration After Pulmonary Vein Isolation for Atrial Fibrillation

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Abstract—While P-wave duration (PWD) is primarily employed to observe the atrial substrate alterations after pulmonary vein isolation (PVI) on atrial fibrillation (AF) patients, the acquired information corresponds to the entire atria. Left (LA) and right atrium (RA), though, may be differently affected by PVI, implying the need for different after-PVI handling. In order to clarify this assumption, five-minute lead II recordings from 29 paroxysmal AF patients undergoing first-ever PVI were recruited before and after PVI. PWD was analyzed integrally and in parts, with the first part (PWD_1) from the onset to the peak corresponding to RA and the second part (PWD_2) to LA depolarization. Time from P-wave onset or offset to the R peak were also calculated ($P_{on} - R$ and $P_{off} - R$, respectively). Normalization (N) to mitigate heart-rate effect was applied. Results before and after PVI were compared with Mann-Whitney U-test (MWU). Median values and variations due to PVI were calculated for all features and compared between PWD and the remaining features via Pearson correlation. After PVI, PWD (−9.84%, $p = 0.0085$, N : −17.96%, $p = 0.0442$) and PWD_2 (−22.03%, $p = 0.0250$, N : −27.77%, $p = 0.0268$) were significantly decreased. PWD_1 did not shorten significantly (up to −8.96%, $p > 0.05$ at either cases). $PWD - PWD_1$ ($\rho > 74.5\%$, $p < 0.0001$) showed higher correlation than $PWD - PWD_2$ ($\rho > 41.9\%$, $p < 0.0001$) in before and after PVI analysis but not for PVI-related variation ($\rho_{PWD-PWD_1} = 54.0\%$, $p = 0.0114$ and $\rho_{PWD-PWD_2} = 61.4\%$, $p = 0.0031$). While RA depolarization time is more in line with PWD analysis, the effect of PVI in PWD is more coherent with LA's findings. Additionally, PWD shortening is only observed in the LA. Therefore, LA is crucial for the assessment of the atrial substrate alteration after PVI and its analysis should be considered by future studies.

Keywords—Atrial fibrillation; pulmonary vein isolation; P-wave; left atrium; partial analysis.

I. INTRODUCTION

Pulmonary vein (PV) isolation (PVI) is considered the main treatment of atrial fibrillation (AF), which is in turn thought to be the most common cardiac arrhythmia [1], [2]. While

PVs are found in the left atrium (LA), fibrosis can be present in both atria [3]–[5]. Therefore, AF mapping is performed by searching for fibrotic areas in both right atrium (RA) and LA.

A successful PVI procedure eliminates fibrotic areas and conduction blocks and is connected with lack of AF recurrences. P-wave analysis is the most popular technique investigating the atrial condition before and after PVI by analyzing fundamental P-wave characteristics, with P-wave duration being the most prevalent [6]–[8]. Long P-wave duration has been connected with AF recurrences, as it is thought to describe heterogeneous tissue favoring the AF perpetuation [9], [10]. Hence, P-wave shortening predicts a favorable PVI outcome.

Despite the high importance of P-wave duration analysis for the evaluation of the atrial substrate after PVI, conventional techniques employ the P-wave as an entity. Notwithstanding, a separate P-wave analysis into parts could provide with more specific information regarding each atrium separately. The first P-wave part, starting from the P-wave onset and extending up to the peak of the P-wave, is the outcome of the RA depolarization. Consequently, the second half of the P-wave, from the P-wave peak to the P-wave offset corresponds to the depolarization of the LA [11], [12]. The analysis of these two P-wave parts as completely independent and separate entities would be meaningful in order to investigate the extent of the PVI effect on each atrium side. The aim of the present study is to perform this separate P-wave analysis so that the side that is more relative to the substrate alterations is detected and its analysis is prioritized in future studies.

II. MATERIALS AND METHODS

Lead II recordings of 29 paroxysmal AF patients undergoing radiofrequency (RF) PVI for the first time were employed. Recordings were acquired for five minutes before and after PVI at a sampling rate of 1 kHz. Denoising was the first

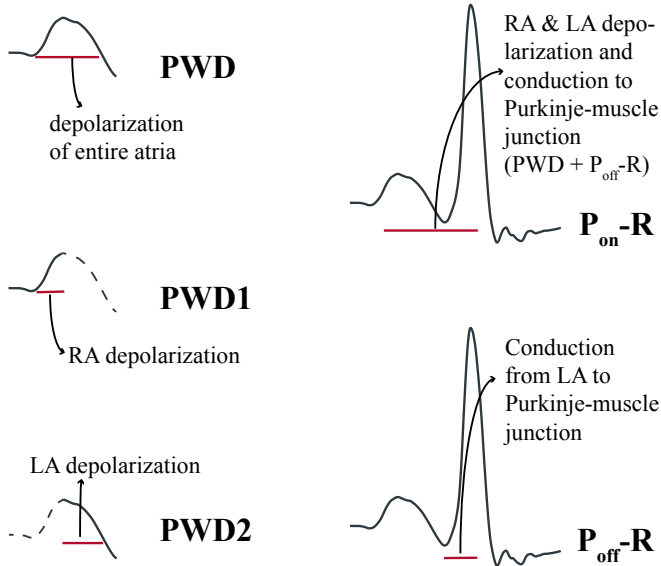


Fig. 1. The calculated features. Red lines show the interval that is taken into account for their calculation. Arrows show the heartbeat action they correspond to.

preprocessing step. A wavelet-based method was adopted in order to remove powerline interference, followed by muscle noise and baseline wander removal via bidirectional low-pass and high-pass filters, respectively [13], [14]. Finally, ectopic beats cancellation was performed by linear interpolation [15].

P- and R-wave detection as well as P-wave delineation followed the preprocessing [16], [17]. Then, main features were calculated:

Duration: P-wave duration (PWD) is considered the distance from the onset to the offset of each P-wave. Additionally, PWD of the first P-wave part (PWD_1), corresponding to the activation of the RA and of the second part (PWD_2), corresponding to the activation of the LA were calculated.

P-wave to R-peak distance: Distance from P-wave onset to R-peak ($P_{on} - R$) is called P-R interval and calculates the time from the initiation of the RA depolarization in the sinus node to the conduction of the electrical impulse to the Purkinje-muscle junction [18]. P-R interval has been connected to AF incidence due to its association with PWD. The interval from the P-wave offset, symbolizing the depolarization of the last particle of the LA until the R-peak ($P_{off} - R$), when ventricles are being depolarized, is the component of the P-R interval that provides measurements independent from the atrial depolarization. Calculation of the aforementioned features is illustrated in figure 1.

Since temporal P-wave features are influenced by the variable heart rate (HR) observed throughout the PVI procedure [19], all features were multiplied by

$$N_i^x = \frac{1000}{R_i - R_{i-1}}, \quad (1)$$

where N_i^x is the normalized value of the i -th sample of the x feature and $R_i - R_{i-1}$ is the interbeat interval that this

TABLE I
FIRST TWO COLUMNS: MEDIAN VALUES (INTERQUARTILE RANGE) OF FEATURES BEFORE AND AFTER PVI. THIRD COLUMN: THEIR VARIATION (Δ) AS A PERCENTAGE. LAST COLUMN: p -VALUE FROM THE COMPARISON OF THE PRE-POST RESULTS. STATISTICALLY SIGNIFICANT RESULTS CAN BE SEEN IN BOLD.

Feature	Median values (IQR)		Δ [%]	p
	pre-PVI	post-PV		
PWD	122.00 (12.00)	110.00 (11.00)	-9.84	0.0085
PWD_1	67.00 (14.00)	61.00 (11.00)	-8.96	0.5289
PWD_2	59.00 (8.00)	46.00 (7.00)	-22.03	0.0250
$P_{on} - R$	246.00 (10.00)	244.00 (11.00)	-0.81	0.5585
$P_{off} - R$	127.00 (8.00)	140.00 (7.00)	10.24	0.3519
N(PWD)	123.63 (15.08)	101.42 (12.15)	-17.96	0.0442
$N(PWD_1)$	64.59 (13.00)	60.19 (10.97)	-6.81	0.3651
$N(PWD_2)$	59.89 (8.55)	43.26 (7.55)	-27.77	0.0268
$N(P_{on} - R)$	264.96 (14.11)	262.19 (12.73)	-1.04	0.3924
$N(P_{off} - R)$	130.47 (9.00)	139.11 (9.62)	6.62	0.6507

sample belongs to.

Given that PWD is the most employed feature, its correlation with the rest of the features was investigated in order to define their relevance in atrial substrate analysis. Firstly, correlation between each PWD and the rest of the calculated features was performed by Pearson correlation (PC) and then averaged, providing one value for each recording and feature combination. Afterwards, the effect that PVI has had on PWD with respect to the PVI effect on the remaining features was also calculated by Pearson correlation. Given feature x , the variation (Δ) due to PVI is calculated by the following equation

$$\Delta = \left(\frac{x_{post-PVI}}{x_{pre-PVI}} - 1 \right) \times 100\%. \quad (2)$$

Finally, features before and after PVI were compared with Mann-Whitney U-test, as indicated from the normality test and their median values were calculated.

III. RESULTS

The median values of all features before and after PVI as well as the variation that PVI provoked can be seen in table I. When measured as a uniform value, PWD shortened significantly after PVI. Getting deeper into the variation, it can be seen that the second part of the P-wave, which reflects the LA depolarization, was the one to provoke the shortening, as it was significantly reduced by $\Delta_{PWD_2} = -22.03\%$. The corresponding change in RA depolarization time showed a non-significant shortening of just $\Delta_{PWD_1} = -8.96\%$. Normalization maintained the observed effects in P-wave and P-wave LA part alterations. Moreover, while variation for PWD was intensified, statistical power was weakened after normalization. On the contrary, the effect of PVI on PWD_2 was not significantly altered after normalization, with both variation and statistical power being quite close to the non-normalized values. As for P-R interval calculations, none of the calculated components varied significantly as a function of the PVI effect, regardless of normalization ($p > 0.05$).

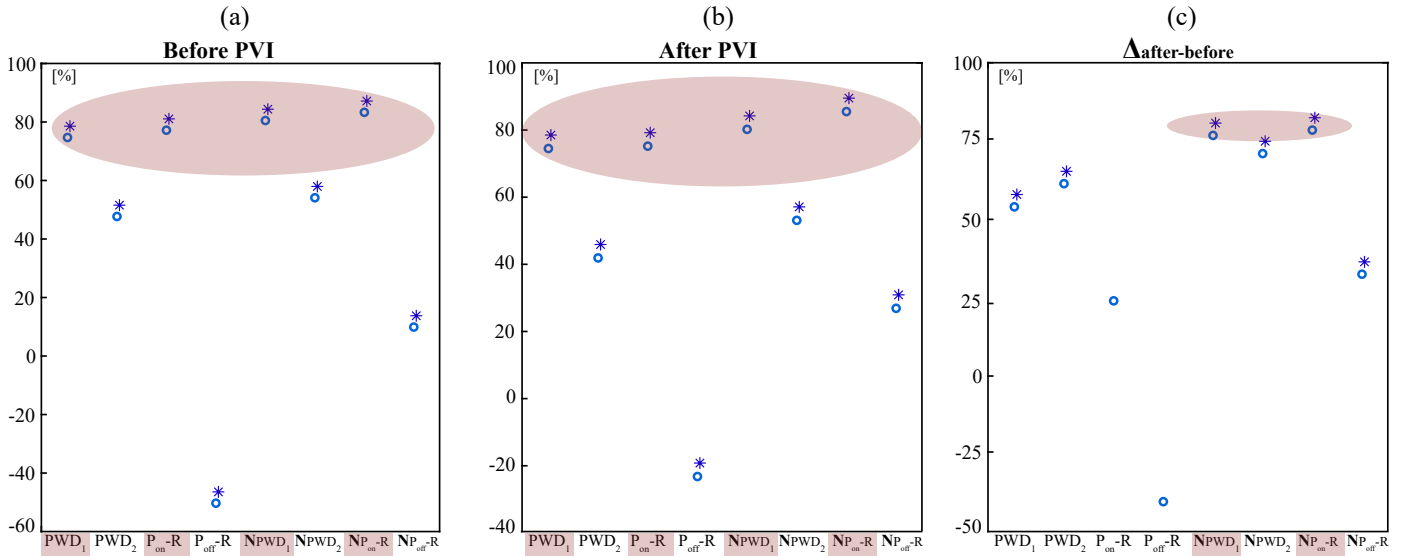


Fig. 2. Correlations between PWD and the rest of the features. Correlations $> 75\%$ and their corresponding features are shown in shaded area. Statistically significant results are marked with an asterisk.

Figure 2 shows the correlations between PWD and the rest of the features at each ablation point (before and after PVI) as well as how PVI has affected PWD with respect to the effect of PVI on the remaining features. While correlation between PWD and all the features is statistically significant, the highest values in P-waves analysis are observed between PWD and PWD_1 , that is the RA depolarization. However, when the PVI effect is investigated, PWD alteration seems to be more in line with the alterations of the LA before normalization, as can be observed from figure 2.c. After normalization, though, PWD and PWD_1 correlation becomes slightly higher than PWD and PWD_2 correlation.

The highest correlations were observed between PWD and $P_{on} - R$ at all analysis cases, regardless of normalization. However, the PVI effect on PWD did not correlate significantly with the PVI effect on $P_{on} - R$ ($p > 0.05$), a fact which was altered after normalization, where again PWD and $P_{on} - R$ correlation was the highest. Correlation between PWD and $P_{off} - R$ was negative when recordings before or after PVI were analyzed and low, showing no statistical significance for the effect of PVI without normalization. Although the effect of normalization was once more favorable for the study of the correlation between PWD and $P_{off} - R$, the resulting relationships were rather weak.

IV. DISCUSSION

While PWD analysis is an established technique of observing the atrial substrate condition after PVI, studies are limited to a uniform perception of the P-wave corresponding to the entire atria [6], [7], [10], [20]. Despite the fact that RA and LA contribution to the atrial substrate has been investigated in the past and atrial volume has been correlated with P-waves, the PVI effect on RA and LA separately remains an unknown field [3]–[5], [21].

In the present study, the analysis has been focused on the separate effect that PVI can have on RA and LA. The knowledge obtained from this investigation can optimize future studies, by focusing and prioritizing the side that is more characteristic of the substrate alterations and providing a more detailed perspective of the mechanisms activated after PVI. Temporal characteristics have been recruited for this purpose, as they have been utilized by a plethora of studies orientated on the same scope [6], [7], [9], [10], [20], [22].

The P-wave part corresponding to LA depolarization has been found to be shortened significantly after PVI. The fact that PVs, the main object of intervention during a PVI process, are found proximal to the LA may be the explanation for this finding. Spatial proximity of LA sites to PVs possibly contributes to the elimination of fibrotic phenomena to a higher degree than the RA substrate alteration, which did not seem to be significantly affected by PVI. Moreover, normalization has affected to a higher degree the overall PWD study than partial PWD analysis. Specially, the effect of PVI on LA depolarization time did not alter in statistical power or magnitude after normalization, whereas overall PWD analysis seemed to be dependent on this adjustment.

It should be noted, however, that regardless of the PVI effect, depolarization time of RA was more in line with the depolarization time of the entire atria with respect to LA depolarization time. Found in RA, sinus node (SN) is the first atrial site to be depolarized and its normal function is crucial for the sinus rhythm maintenance [11], [12]. Hence, overall atrial depolarization time strongly depends on the proper SN function, a fact that may cause higher PWD and PWD_1 correlations. Additionally, RA depolarization time lasts longer than LA depolarization time, showing higher connection between RA and overall depolarization time, expressed by PWD.

Finally, the high correlations observed between PWD and

$P_{on} - R$ are in line with previous studies [18] and can be explained from the fact that a $P_{on} - R$ interval constitutes of PWD in the most part and the interval from the end of the atrial depolarization to the ventricular depolarization. Consequently, studies focusing on the propagation time of the wavefront from the end of the atria towards the ventricles should perform calculations without considering features including the P-wave component or parts of it. $P_{off} - R$ is the index that represents this interval. In the present study, no significant alterations have been observed as a function of the PVI procedure on $P_{off} - R$. PWD and $P_{off} - R$ correlation has been reported as rather weak as well.

V. CONCLUSIONS

LA substrate alteration is more prominent than RA substrate alteration and describes to a higher level the PWD modifications observed after PVI. Additionally, the effect of PVI on LA depolarization remained unaltered. Therefore, partial PWD analysis is highly recommended for a more detailed substrate analysis and the study on PWD corresponding to LA depolarization should be prioritized.

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