

# Increased preexcitation on electrocardiography improves accuracy of algorithms for accessory pathway localization in Wolff–Parkinson–White syndrome

Paweł Moskal<sup>1</sup>, Adam Bednarski<sup>2</sup>, Grzegorz Kiełbasa<sup>1</sup>, Danuta Czarnecka<sup>1</sup>, Marek Jastrzębski<sup>1</sup>

<sup>1</sup> 1st Department of Cardiology, Interventional Electrophysiology and Hypertension, Institute of Cardiology, Jagiellonian University Medical College, Kraków, Poland

<sup>2</sup> 1st Department of Cardiology, Interventional Electrophysiology and Hypertension, University Hospital, Kraków, Poland

## KEY WORDS

accessory pathway, algorithms, maximal preexcitation, preexcitation, Wolf–Parkinson–White syndrome

## ABSTRACT

**BACKGROUND** Several electrocardiographic (ECG) algorithms have been developed for predicting accessory pathway (AP) location in Wolff–Parkinson–White syndrome. However, their accuracy may be related to the manifested degree of preexcitation on ECG.

**AIMS** Our goal was to assess the effect of the degree of preexcitation on the accuracy of 4 traditional AP localization algorithms and to compare them with the algorithm specifically designed for ECGs with maximal preexcitation (Pambrun).

**METHODS** The study included 300 patients who underwent successful ablation of an overt atrioventricular AP. Resting and maximally preexcited ECGs obtained during incremental atrial pacing were assessed using 4 traditional AP localization algorithms: Xie, d’Avila, Iturralde, and Taguchi. Maximally preexcited ECGs were additionally assessed with the Pambrun algorithm. We compared the precision of the algorithms to predict accurate or anatomically adjacent AP location.

**RESULTS** The overall accuracy of traditional AP localization algorithms using resting ECG ranged between 26% and 53.7% and improved to a range of 47.3% to 69.7% when adjacent locations were accepted. When used with maximal preexcitation, all algorithms had significantly higher accuracy, with a mean improvement of 14.3 and 15.6 percentage points for precise and adjacent sites, respectively. The Pambrun algorithm for maximally preexcited ECGs had the highest precision for both accurate and adjacent locations of the APs (89.7% and 97%, respectively).

**CONCLUSIONS** Greater preexcitation on ECG improved the accuracy of the traditional AP localization algorithms. The algorithm designed to use maximally preexcited ECGs has the best accuracy. Maximally preexcited ECG recordings should preferably be used in clinical practice to facilitate the ablation procedure.

**Correspondence to:**  
Paweł Moskal, MD,  
1st Department of Cardiology,  
Interventional Electrophysiology  
and Hypertension, Institute  
of Cardiology, Jagiellonian  
University Medical College,  
ul. Jakubowskiego 2,  
30-688 Kraków, Poland,  
phone: +48 12 400 2150,  
email: pawel@moskal.in  
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**INTRODUCTION** Ventricular preexcitation caused by an accessory pathway (AP) is a typical feature of Wolff–Parkinson–White syndrome. The electrocardiographic (ECG) hallmark of preexcitation is the QRS complex that is distorted, prolonged, and often with altered polarity. The radiofrequency catheter ablation of an AP is a standard treatment in Wolff–Parkinson–White syndrome.<sup>1</sup> Preprocedural prediction of

the AP location facilitates the success of ablation and allows for preprocedural risk assessment. Over 20 different algorithms were created to predict the AP location based on the following resting 12-lead ECG features: delta wave morphology, QRS polarity, or the R/S amplitude ratio of QRS complexes. However, most of these algorithms had low accuracy in validation studies.<sup>2-6</sup> This discrepancy might be

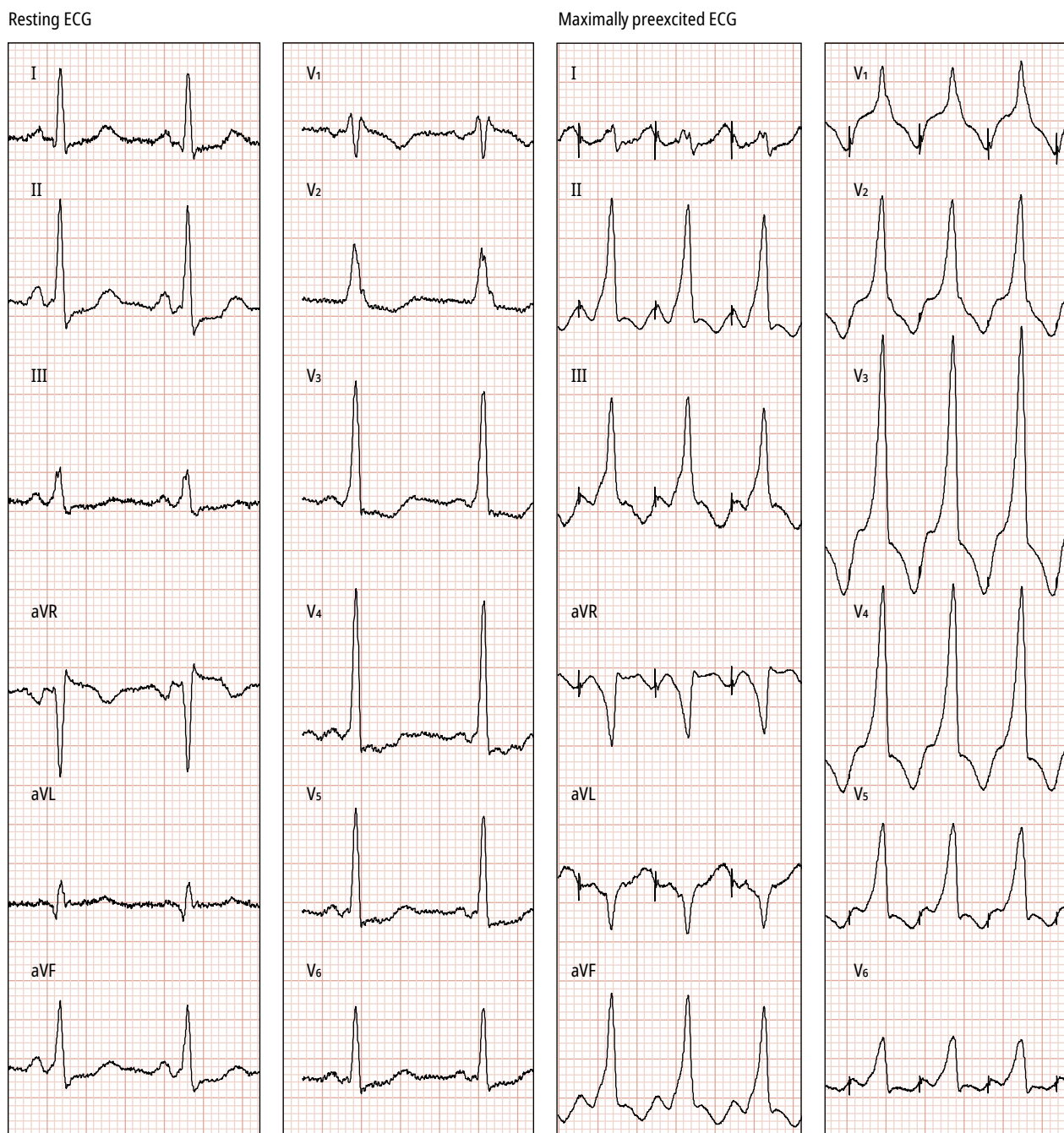
## WHAT'S NEW?

This study assessed the accuracy of 5 algorithms to predict accessory pathway location using resting and maximally preexcited 12-lead electrocardiogram (ECG). We found that the increased preexcitation improved the accuracy of all the algorithms. The Pambrun algorithm, based on maximally preexcited ECGs, was shown to have the best accuracy. Our main finding is that the use of maximally preexcited ECG recordings is preferable in clinical practice to facilitate the ablation procedure.

related to a different degree of preexcitation in the initial sets of ECGs and in the validation cohorts. The majority of the AP localization algorithms were designed to be used with resting

ECG, where QRS morphology results from a fusion of ventricular activation through the His-Purkinje conduction system and an AP.<sup>7</sup> Fused QRS morphology is influenced mainly by 2 factors: 1) conduction via atrioventricular node, His bundle, and bundle branches, and 2) AP localization. However, during provoked or spontaneous maximal preexcitation, ventricular activation accomplished almost exclusively by the AP is observed, with the QRS morphology almost completely depending on the AP location (FIGURE 1).<sup>8</sup>

Variability in the degree of preexcitation in the QRS morphology can explain the difficulty



**FIGURE 1** Examples of resting and maximally preexcited electrocardiograms (ECGs) recorded in a patient with a left lateral accessory pathway. The predictions of traditional algorithms were as follows: right lateral by Xie et al,<sup>12</sup> anteroseptal by d'Ávila et al,<sup>13</sup> midseptal / posteroseptal by Taguchi et al,<sup>14</sup> and right anterosuperior paraseptal by Iturralde et al.<sup>15</sup> Using maximally preexcited ECG, Pambrun et al<sup>9</sup> and all traditional algorithms correctly predicted the left lateral location.

in creating an accurate and universal algorithm. Pambrun et al<sup>9</sup> proposed a new AP localization algorithm designed for ECGs with maximal pre-excitation that aims to have a better predictive value; however, it has not been validated by independent studies so far.

This study aimed to assess the effect of the degree of preexcitation on resting ECG on the accuracy of 4 AP localization algorithms designed for resting ECGs, and to compare them to the recently introduced algorithm specifically designed for ECGs with maximal preexcitation.

**METHODS** We retrospectively analyzed 340 consecutive ablation procedures from 2002 to 2019 in patients with overt preexcitation. The ablation outcomes, success rates, and risk factors for malignant arrhythmias in this cohort were reported previously.<sup>10,11</sup> For the current study, we excluded patients with structural heart disease, multiple APs, atriofascicular (“Mahaim”) and fasciculoventricular pathways, failed ablation, and without high-quality 12-lead ECGs with resting and maximally preexcited patterns.

From the electrophysiological recording system, we printed a 12-lead surface ECG (25 mm/s) with baseline preexcitation (observed at the beginning of the procedure). The second ECG recording was obtained during the electrophysiological study when maximal preexcitation was provoked by incremental fast atrial pacing, induction of antidromic antidromic atrioventricular reentry tachycardia, or induction of rapid atrial fibrillation. The AP location was assessed using the right and left anterior oblique views according to the position of the ablation catheter at the successful ablation site.

To compare the accuracy of AP prediction, we analyzed each pair of resting and maximally preexcited ECGs with 4 traditional algorithms developed by Xie et al,<sup>12</sup> d’Avila et al,<sup>13</sup> Iturralde et al,<sup>14</sup> and Taguchi et al.<sup>15</sup> They were designed to use with resting 12-lead ECG and do not require subjective delta wave assessment. The Iturralde, d’Avila, and Xie algorithms predict the AP location at 5 to 9 sites along the mitral and tricuspid annulus, using mainly the polarity and morphology of the QRS complexes in leads II, III, aVF, aVL, V<sub>1</sub>, and V<sub>2</sub>. The Taguchi algorithm uses the R/S ratio in leads V<sub>1</sub>, V<sub>2</sub>, and aVF to predict the location of the AP at 5 sites.

In addition, we assessed maximally preexcited ECGs with the recently published algorithm by Pambrun et al.<sup>9</sup> To localize the AP at 9 sites, it uses the polarity of leads V<sub>1</sub> and V<sub>3</sub>, the number of overall positive inferior leads (II, III, aVF), the ratio of R waves in leads V<sub>1</sub> and lead I, and the morphology of lead II. Algorithm criteria are summarized in Supplementary material, *Table S1*.

The number of possible AP locations in the selected algorithms ranges from 5 to 9, and different terminology was used to describe them. To facilitate the comparison of the algorithms, we adapted a unified classification of AP locations, as it was done in previous studies.<sup>4,6</sup> We used the AP sites reported by Pambrun et al<sup>9</sup> as a reference and translated locations provided in other algorithms, as described in *TABLE 1*.

We defined the predictions of the algorithm as: 1) accurate (predictions matched precisely the AP location established during the electrophysiological study); 2) adjacent (predictions were anatomically adjacent to the actual AP location); and 3) inaccurate (predictions did not match the above definitions).

**TABLE 1** Unified classification of accessory pathway nomenclature between algorithms

AP location in the Pambrun algorithm, reference	Algorithms			
	Xie et al <sup>12</sup>	d’Avila et al <sup>13</sup>	Iturralde et al <sup>14</sup>	Taguchi et al <sup>15</sup>
Right anterior	RAS	AS	RA	RAS/RA/RL
Right lateral	RL	RL		
Right posterior	RP	RPS	RIP/RI	RPL/RP
Right paraseptal	RPS	PS		MS/PS
Deep coronary sinus				
Nodo-Hisian	MS	MS	RASP	
Left paraseptal	LPS	LPS	LIP/LI	
Left posterolateral	LP/LPL	LP	LPL/LAS	LP/LPL
Left lateral	LAL	LL		LA/LL

Abbreviations: AP, accessory pathway; AS, antero-septal; DCS, deep coronary sinus; LA, left anterior; LAL, left anterolateral; LI, left inferior; LIP, left inferior paraseptal; LL, left lateral; LP, left posterior; LPL, left posterolateral; LPL, left posterolateral; LAS, left anterosuperior; LPS, left posteroseptal; MS, midseptal; PS, posteroseptal; RA, right anterior; RAS, right antero-septal; RASP, right anterosuperior paraseptal; RI, right inferior; RIP, right inferior paraseptal; RL, right lateral; RP, right posterior; RPL, right posterolateral; RPS, right posteroseptal

In the secondary analysis, we aimed to investigate the performance of traditional algorithms in patients divided according to the degree of preexcitation on resting ECG. We measured resting QRS duration (QRSd) with the global QRS method<sup>16</sup> and used terciles to classify ECGs into 3 groups according to the manifested preexcitation: 1) low, QRSd <123 ms (n = 109); 2) moderate, QRSd = 123–138 ms (n = 92); and 3) high, QRSd >138 ms (n = 99).

The study protocol was approved by the local ethics committee. Patient consent was not required in this study.

**Statistical analysis** The accuracy of the algorithm was defined as the percentage of patients with a correct prediction of a successful ablation site. The  $\chi^2$  and McNemar tests were used to compare categorical variables and algorithm accuracy, respectively, between baseline and maximally preexcited ECGs. The Mann–Whitney test was used to compare the median QRS duration between left- and right-sided APs. A *P* value of less than 0.05 was considered significant. The analysis was performed using STATA 16.1 (StataCorp, College Station, Texas, United States).

**RESULTS** The final study group included 300 patients. The demographic data and AP locations according to the successful ablation site during the electrophysiological study are presented in TABLE 2. Left free-wall APs were more prevalent than septal or right free-wall APs (44%, 38%, and 18%, respectively). On resting ECG, the median QRS duration for left-sided APs was

significantly shorter than for right-sided APs (127 ms vs 132 ms; *P* = 0.01).

**Accuracy of algorithms for resting and maximally preexcited electrocardiograms**

The overall accuracy of the algorithms is presented in TABLE 3. For the ECGs with resting preexcitation, the Taguchi and Iturralde algorithms had the most accurate predictions (53.7% and 53.3%, respectively). When adjacent locations were accepted, the accuracy of all the algorithms improved, but the d’Avila, Iturralde, and Taguchi algorithms outperformed the Xie algorithm (*P* <0.001).

For the ECGs with maximal preexcitation, all traditional algorithms showed an increase in accuracy, with a mean improvement of 14.3 percentage points for precise locations and 15.6 percentage points for adjacent locations. The Pambrun algorithm achieved the most accurate predictions for precise and adjacent sites.

**Performance of algorithms according to the degree of preexcitation on resting electrocardiograms**

The accuracy of the algorithms in patients with low, moderate, and high resting preexcitation is presented in FIGURE 2. The precision of all traditional algorithms improved with the increase of preexcitation, with a mean improvement from low to high resting preexcitation of 14.3 percentage points for accurate locations and 10 percentage points for adjacent sites. The Xie algorithm showed the lowest accuracy independently of the degree of preexcitation.

**Accuracy in distinguishing between left- and right-sided accessory pathways**

The accuracy of the traditional algorithms in predicting

**TABLE 2** Clinical characteristics of the study group (n = 300)

Parameter			Value
Age, y, mean (SD)			32 (18.4)
Male sex			178 (59.2)
QRS duration on resting ECG, ms, mean (SD)			130.4 (21)
AP location	Left free-wall	Left lateral	71 (23.67)
		Left posterolateral	61 (20.33)
Septal		Left paraseptal	17 (5.67)
		Right paraseptal	64 (21.33)
		Parahisian / midseptal (nodo-Hisian)	29 (9.67)
		Epicardial (deep coronary sinus)	4 (1.33)
Right free-wall		Right anterior	24 (8)
		Right posterior	19 (6.33)
		Right lateral	11 (3.67)

Data are presented as number (percentage) of patients unless otherwise indicated.

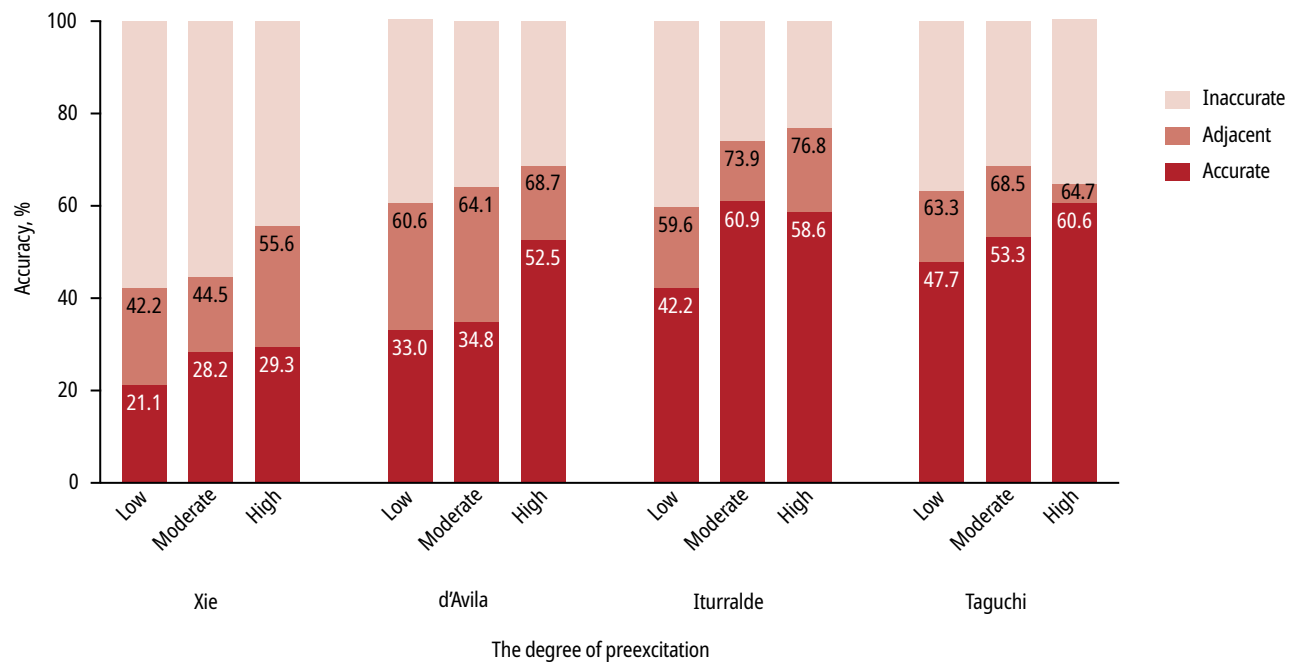
Abbreviations: see TABLE 1

**TABLE 3** Overall accuracy of the accessory pathway localization algorithms on resting and maximally preexcited electrocardiograms

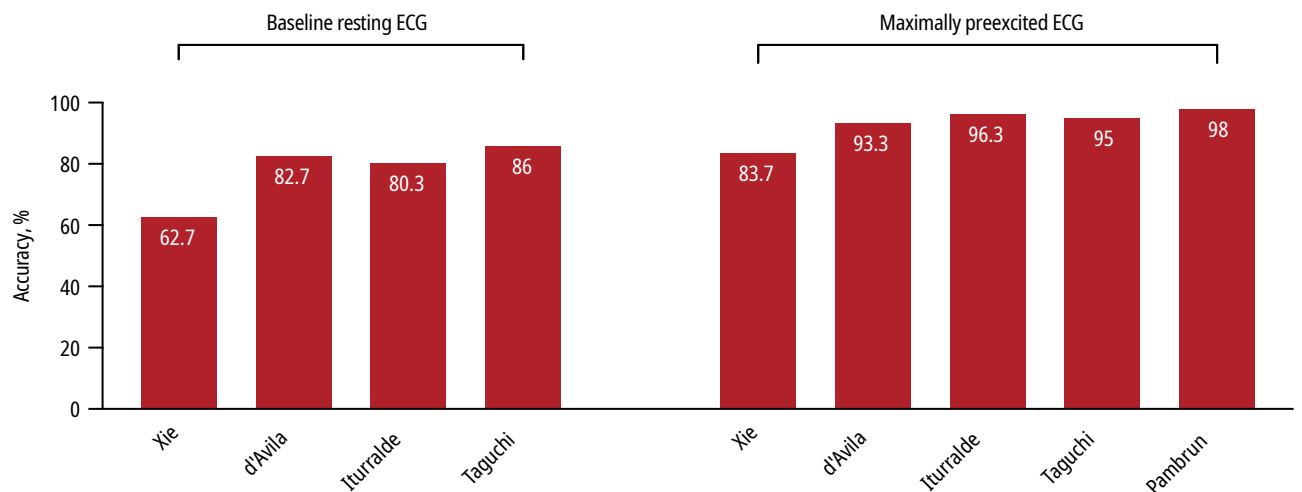
Algorithm	Resting ECG		ECG with maximal preexcitation		P value (resting vs maximal preexcitation)	
	Accuracy, %	Adjusted accuracy <sup>a</sup> , %	Accuracy, %	Adjusted accuracy <sup>a</sup> , %	Accuracy	Adjusted accuracy
Xie et al <sup>12</sup>	26	47.3	32.7	62.7	<0.001	<0.001
d'Avila et al <sup>13</sup>	40	64.3	54.7	79	<0.001	<0.001
Iturralde et al <sup>14</sup>	53.3	69.7	67.7	86.3	<0.001	<0.001
Taguchi et al <sup>15</sup>	53.7	65.3	75	81	<0.001	<0.001
Pambrun et al <sup>9</sup>	—	—	89.7	97	—	—

a Predictions were anatomically adjacent to the actual AP location.

Abbreviations: ECG, electrocardiogram; others, see TABLE 1



**FIGURE 2** Accuracy of traditional algorithms according to the degree of manifested preexcitation on resting electrocardiogram (low, resting QRS duration [QRSd] <123 ms; moderate, QRSd = 123–138 ms; high, QRSd >138 ms)



**FIGURE 3** Accuracy of the algorithms to predict left- and right-sided accessory pathways using baseline and maximally preexcited electrocardiogram (ECG)

left- and right-sided locations of APs using resting ECG ranged from 62.7% to 86% (FIGURE 3). Using the maximally preexcited ECGs, the accuracy of the Xie, d'Avila, Iturralde, and Taguchi algorithms increased to a range of 83.7% to 95%. The Pambrun algorithm was the most accurate (98%).

#### Analysis of errors in the Pambrun algorithm

In our cohort, 33% of parahisian APs manifested the overall negative polarity of the QRS complex in lead  $V_3$  during maximal preexcitation and were subsequently incorrectly predicted as a right anterior or right lateral AP. There were 4 epicardial or deep coronary sinus APs. None of them met the criteria of the Pambrun algorithm (Supplementary material, Table S1). In 3 cases, the QRS pattern was typical for right paraseptal AP. In one case, there were notched QS complexes in lead II. The fourth case had positive QRS complex in lead  $V_1$  but did not have a notched QS complex in lead II.

**DISCUSSION** Our analysis of a large cohort of patients with Wolff–Parkinson–White syndrome showed that the accuracy of traditional algorithms in predicting AP location improved with the increase of preexcitation on resting ECG. Moreover, the traditional algorithms had better accuracy when applied to a maximally preexcited ECG obtained at the beginning of the electrophysiological study. In line with this, we found that the Pambrun algorithm, specifically designed for maximally preexcited ECGs, had the highest accuracy among all analyzed algorithms.

In our study, the Xie and Iturralde algorithms showed a similar accuracy in predicting AP locations as previous studies.<sup>2,5,6</sup> Teixeira et al<sup>6</sup> and Maden et al<sup>5</sup> reported that the d'Avila algorithm was significantly worse than other algorithms, but in our research, its performance was comparable. The Taguchi algorithm has not been validated so far. We found that it was not better than the Iturralde algorithm, which is similarly designed to predict AP at 3 sites with only 3 criteria. The performance of all 4 traditional algorithms in discriminating a left-sided from right-sided AP was poor, with an error rate of 14% to 37.1%.

It is generally assumed that the degree of preexcitation is associated with the accuracy of the AP localization algorithms, although this relationship has not been proved so far. Our study confirmed this clinical assumption. Low preexcitation on resting ECG hampered the predictive value of the traditional algorithms. On the other hand, the accuracy of the algorithms was significantly better when applied to ECGs with maximal preexcitation. For over 2 decades, the d'Avila algorithm has been routinely used in our electrophysiology laboratory, although with

a modification in that we used fully preexcited ECG obtained at the beginning of the electrophysiological study instead of required resting ECG. This study confirms that it was the right approach, as the accuracy of this algorithm increased from 64% to 79%. Similarly, about 15% more cases were correctly diagnosed by other algorithms when fully preexcited ECG was analyzed instead of ECG with baseline preexcitation. We believe that these results are firmly rooted in basic electrophysiology and ECG. A more preexcited QRS complex contains more information on the impact of an AP on ventricular depolarization. More information translates to a more accurate ECG analysis in terms of predicting the AP location around mitral and tricuspid annuli.

In the secondary analysis, we observed that the performance of the algorithms depended on the degree of preexcitation on resting ECG. This could be explained by the fact that the sensitivity of the algorithms varies between different AP locations, which, in turn, is the primary determinant of the degree of preexcitation.<sup>4-6</sup> The algorithms have the worst ability to locate an AP at low preexcitation. Therefore, particular caution is needed when trying to predict the AP location in this group of patients.

Our study provides the first external validation of the Pambrun algorithm using a large cohort. We confirmed the high accuracy of the algorithm for precise localization of APs (89.7%), which is in line with the accuracy reported by Pambrun et al (90%).<sup>9</sup> However, we found 2 recurring errors in nodo-Hisian (midseptal and parahisian area) and deep coronary sinus AP locations that need to be addressed. First, Pambrun et al<sup>9</sup> reported that they did not have enough cases of AP localized in the coronary sinus diverticulum to fully assess the criterion for the deep coronary sinus location (notched QS complex in lead II). In our cohort, there were 4 epicardial APs, 3 of which were localized in the coronary sinus diverticulum. In all cases, the maximal preexcitation pattern was similar to the right paraseptal AP, with deep negative QS complexes in leads II, III, and aVF. Interestingly, in one of these cases, the criterion for deep coronary sinus location was present. We believe that this feature should also be assessed for the right paraseptal location to predict a location closer to the epicardium. Second, Pambrun et al<sup>9</sup> used positive QRS complex in lead  $V_3$  as a criterion to differentiate the mid-septal and parahisian AP location (or nodo-Hisian using Pambrun's terminology) from the right lateral and right anterior AP. However, in our cohort, we found that almost 33% of true parahisian APs had overall negative QRS complex in lead  $V_3$  during maximal preexcitation; therefore, this feature cannot be reliably used to exclude this particular location.

Although the prediction of an AP location is better when based on maximally preexcited

ECG, usually only resting ECG is available to clinicians. However, more preexcited ECG can be easily obtained, either using vagal maneuvers, short-acting drugs that slow conduction in the atrioventricular node, or by assessing 12-lead Holter monitoring, as the degree of preexcitation on ECG often changes during the day. During the electrophysiological study, maximally preexcited ECG should be obtained at the beginning of the procedure to verify resting ECG data.

Our study has several limitations. First, this was a single-center retrospective study. Despite a large number of patients, population-related differences could influence the accuracy of the tested algorithms. Second, resting ECGs were acquired at the beginning of the procedure, and the altered sympathetic/parasympathetic tone could affect the degree of baseline preexcitation.

In conclusion, our study confirms that the accuracy of traditional algorithms is related to the degree of preexcitation on resting ECG. Among all the investigated algorithms, the Pambrun algorithm, designed explicitly for maximally preexcited ECG, had the best accuracy for predicting AP location and should be preferably used for this purpose. When other algorithms are used, the fully preexcited ECG should be assessed to maximize their performance.

## SUPPLEMENTARY MATERIAL

Supplementary material is available at [www.mp.pl/kardiologiapolska](http://www.mp.pl/kardiologiapolska).

## ARTICLE INFORMATION

**CONFLICT OF INTEREST** None declared.

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