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Independent predictive accuracy of classical electrocardiographic criteria in the diagnosis of paroxysmal atrioventricular reciprocating tachycardias in patients without pre-excitation

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KEYWORDS
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Aims In patients without pre-excitation, the differential diagnosis of paroxysmal atrioventricular (AV) reciprocating tachycardias consists mainly of atrioventricular nodal re-entrant tachycardias (AVNRTs) and AV reciprocating tachycardias (AVRTs) through a concealed bypass. Our purpose was to validate the diagnostic accuracy of a predictive logistic model using classical electrocardiographic (ECG) criteria.
Methods and results We included 470 patients who underwent an electrophysiological study for paroxysmal, regular, and narrow-QRS complex tachycardia without pre-excitation in sinus rhythm. The ECG recordings were reviewed for the presence of the following: (i) pseudo r′ deflection (V1) and/or pseudo s-wave (inferior leads), (ii) identifiable P-wave after the QRS complex, (iii) QRS alternans, and (iv) repolarization abnormalities during tachycardia. We performed a cross-validation method using the first 300 patients to develop a logistic model to predict the tachycardia diagnosis. The model was validated through the remaining 170 patients. The invasive study demonstrated AVNRT in 314 patients and AVRT in 156 patients. The presence of pseudo r′ deflection and/or pseudo s-wave, a visible P-wave after the QRS complex, and QRS alternans were selected by a stepwise multiple logistic regression analysis as predictors for the diagnosis of AVNRT. The application of the model in the validation group showed a shrinkage prediction factor of 3%. Diagnostic probabilities for both tachycardia mechanisms depending on every combination of selected ECG criteria were >75% in 70% of the patients.
Conclusion The presence of pseudo r′ deflection and/or pseudo s-wave, an identifiable P-wave after the QRS, and QRS alternans during tachycardia permit us to derive a reliable logistic model to predict the mechanism of paroxysmal AVRT in patients without pre-excitation. Precise probabilities for a correct diagnosis associated with every combination of those classical ECG criteria are presented.

Introduction

In patients without pre-excitation in sinus rhythm, the differential diagnosis of paroxysmal supraventricular tachycardias consists mainly of atrioventricular nodal re-entrant tachycardias (AVNRTs) and atrioventricular reciprocating tachycardias (AVRTs) through a concealed accessory pathway (AP). The non-invasive differentiation of both tachycardia mechanisms is clinically important, as it helps in counselling and potentially facilitates different ablation procedures. Several electrocardiographic (ECG) criteria have been classically proposed to distinguish both tachycardia mechanisms.[1–14] However, there are no previous studies to validate the adjusted, independent predictive accuracy of these ECG criteria in a large series of consecutive patients with regular, paroxysmal, and narrow-QRS complex tachycardia without pre-excitation during sinus rhythm. In addition, the diagnostic accuracy of different combinations of those classical ECG findings is not well known. The objective of the present study was, therefore, to analyse the independent diagnostic accuracy of those ECG classical findings and their possible combinations, as well as to validate the resulting predictive logistic model in order to determine its accuracy prospectively.

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Methods

We included 470 consecutive patients (296 females and 174 males; 46 ± 18 years, range: 1–89 years) who underwent an electrophysiological study for paroxysmal, regular, and narrow-QRS complex tachycardia without pre-excitation in sinus rhythm. The documented arrhythmias occurred either spontaneously (342 patients, 73%) or induced during the electrophysiological study; the former was preferred for analysis. The patients were not receiving anti-arrhythmic drugs at the time of the clinical tachycardia documentation. Patients with atrial tachycardias without prior non-invasive diagnosis (nine patients) or one or more tachycardia mechanism (six patients) were excluded. No significant structural heart disease was observed in all but nine cases (hypertensive, four patients; valvular, three patients; and coronary, two patients).

The 12-lead ECGs were recorded at a paper speed of 25 mm/s and a gain setting of 10 mm/mV. Filter settings were 0.05–50 Hz for clinical recordings and 0.05–150 Hz for laboratory recordings. The ECG recordings during tachycardia and sinus rhythm were reviewed for the presence of the following criteria: (i) pseudo r′ deflection in V1 and/or pseudo s-wave in inferior leads, defined as an apparent r′ deflection in V1 and/or an apparent s-wave present during tachycardia and absent during sinus rhythm[5]; (ii) the presence of a discrete deflection consistent with a P-wave after the QRS complex[5]; (iii) QRS alternans defined as a beat-to-beat oscillation in QRS amplitude of ≥1 mm in at least one lead[3,5]; and (iv) ST-segment depression (≥2 mm) and/or T-wave inversion during tachycardia.[6,9] Comparing the sinus rhythm ECGs helped identify the possible retrograde P-wave and assess the repolarization abnormalities during tachycardia. All ECGs were reviewed independently by two experienced electrophysiologists (E.G.-T. and S.d.C.) who were blinded to patient information and tachycardia mechanism. In the case of discordant judgement, the final diagnosis was reached by consensus. Great care was taken in using ECG criteria consistent with those applied in previous studies. A random subset of 50 ECGs were selected to determine the inter- and intra-observer concordance for categorical variables. In every patient, the mechanism of arrhythmia was defined during the electrophysiological study using standard criteria[8] and confirmed by the efficacy of radiofrequency ablation or cryoablation.

Statistical analysis

Continuous and categorical variables are expressed as mean value ± SD and as percentages, respectively. Normally distributed continuous variables were compared using Student's *t*-test. Differences between categorical variables were analysed using the χ^2 test. We performed a cross-validation method using the first 300 patients to develop a binary multiple logistic model through stepwise regression to predict the tachycardia diagnosis using the mentioned ECG criteria as candidate-independent variables with a forward-entry stepping algorithm (derivation group). Predicted probabilities were calculated for each patient in the derivation group in order to construct the predicted diagnostic probability for every combination of selected ECG criteria. Interactions among covariates were tested. The predictive model was validated through the remaining 170 patients (validation group) and a shrinkage prediction factor was calculated as an index of the reliability of the logistic model.[15] This index is based on the difference $R_d^2 - R_v^2$ between the squared coefficient of correlation in the multiple correlation in the derivation set (R_d^2) and the squared coefficient of correlation in the simple correlation between the dependent variable *Y* and the predicted value Y′ after applying the regression model in the validation set (R_v^2). Intra- and inter-observer agreement in analysing the presence of the ECG criteria and the subjective ECG diagnosis were calculated through the kappa statistic. Statistical analyses were performed using SPSS software, version 12 (SPSS, Inc., Chicago, IL, USA). A two-tailed *P*-value of less than 0.05 was considered statistically significant.

Results

Descriptive results and univariate comparisons

The invasive study demonstrated AVNRT in 314 patients and AVRT in 156 patients. Atrioventricular nodal re-entrant tachycardias were classified as atypical (VA interval >100 ms) in 31 patients (posterior type in 27 patients and uncommon forms in 4 patients). The concealed AP had a septal location in 49 AVRT patients (inferoparaseptal: 26 patients and superoparaseptal: 16 patients; 9 of them with a parahisian location; and mid-septal: 7 patients). In the remaining 107 patients with AVRT, the AP had a free-wall location: left lateral (67 patients), left superior (9 patients), left inferior (28 patients), and right free-wall (3 patients). Two concealed APs were found in three patients, both with a left free-wall location.

Table 1 illustrates the demographic and ECG differences in both groups of tachycardias in the total study group. There were significant differences in every classical ECG criterion. In contrast, no significant differences were found between derivation and validation groups of patients. An accurate subjective ECG diagnosis (68% for total study population) was obtained more frequently in the AVRT group. The Cohen's kappa values for the inter-observer

Table 1 Demographic and electrocardiographic characteristics of the study population

	AVNRT ($n = 314$)	AVRT ($n = 156$)	*P*-value
Age at inclusion (years)	49 ± 17	39 ± 19	0.0001
Age at onset of symptoms (years)	37 ± 17	26 ± 16	0.0001
Sex (M/F)	89/225	83/73	0.0001
Tachycardia R-R interval (ms)	344 ± 51	336 ± 53	ns
Identifiable P-wave after QRS complex	77 (25)	113 (72)	0.0001
RP > PR	12 (4)	22 (14)	ns
Pseudo r′/s-waves	140 (45)	7 (5)	0.0001
Pseudo r′-wave in lead V1	116 (37)	5 (3)	0.0001
Pseudo s-wave in inferior leads	37 (12)	2 (1.3)	0.001
QRS alternans	32 (10)	31 (20)	0.018
Repolarization abnormalities	116 (37)	82 (53)	0.002
T-wave inversion	57 (18)	67 (43)	0.001
ST depression ≥2 mm	72 (23)	57 (37)	0.04
Limb leads ST-T changes	106 (34)	94 (60)	0.001
Precordial ST-T changes	67 (21)	45 (29)	ns
Correct subjective ECG diagnosis	194 (62)	126 (81)	0.0001

Figures in parenthesis are percentages. AVNRT: atrioventricular nodal re-entrant tachycardia; AVRT: atrioventricular reciprocating tachycardia.

concordance in the detection of visible P-waves, pseudo r′/s-waves, QRS alternans, and repolarization abnormalities were 0.72, 0.83, 0.81, and 0.73, respectively (all $p < 0.01$).

Multivariate analysis

The presence of pseudo r’ deflection in V1 and/or pseudo s-wave in inferior leads (adjusted OR: 17; 95% CI: 5.7–48.7; $P = 0.0001$), an identifiable P-wave after the QRS complex (adjusted OR: 0.18; 95% CI: 0.09–0.31; $P = 0.0001$), and QRS alternans (adjusted OR: 0.4; 95% CI: 0.18–0.91; $P = 0.029$) were selected by a stepwise multiple logistic regression analysis as independent predictors for the diagnosis of AVNRT in the derivation group (*Table 2*).

Table 2 Multivariate logistic regression results for the diagnosis of atrioventricular nodal re-entrant tachycardia (vs. atrioventricular reciprocating tachycardia) in the derivation group ($N = 300$)

ECG finding	OR (95% CI)	Wald χ^2	*P*-value
Visible P-wave after QRS complex	0.18 (0.09–0.31)	34.2	0.0001
Pseudo r′ (V1)/s-waves (inferior leads)	16.6 (5.7–48.7)	26.2	0.0001
QRS alternans	0.4 (0.18–0.91)	4.7	0.029

Constant: exp(ß) = 3.05 (SE = 0.22); $P = 0.0001$. Hosmer–Lemeshow’s goodness of fit test: $P = 0.972$.

No significant interactions were found including those between the R-R interval during tachycardia and the selected variables. *Figure 1* shows the predicted probabilities obtained from the derivation group for both tachycardia mechanisms depending on every combination of selected ECG parameters. Diagnostic probabilities >75% were found for nearly 70% of the patients. Repolarization abnormalities during tachycardia were not selected as independent covariates of the tachycardia mechanism (*Figure 2D–E*).

Model validation

The application of the obtained model in the validation group showed a shrinkage prediction factor of only 3%. The sensitivity and specificity obtained by the predictive logistic model in the validation group were 77 and 85%, respectively, with an overall correct classification rate of 82%. In the validation group, 10/12 false-positive cases for the diagnosis of AVNRT were without independent positive ECG findings (*Figure 2A–C*). Similarly, 13/17 false-negative cases corresponded to patients with atypical or uncommon forms of AVNRT (*Figure 3*).

Discussion

To the best of our knowledge, this is the largest series of consecutive patients validating the independent accuracy of classical ECG criteria and their combinations for the differential diagnosis of paroxysmal AVRT in patients without pre-excitation during sinus rhythm. The presence of pseudo r′ deflection in V1 and/or pseudo s-wave in

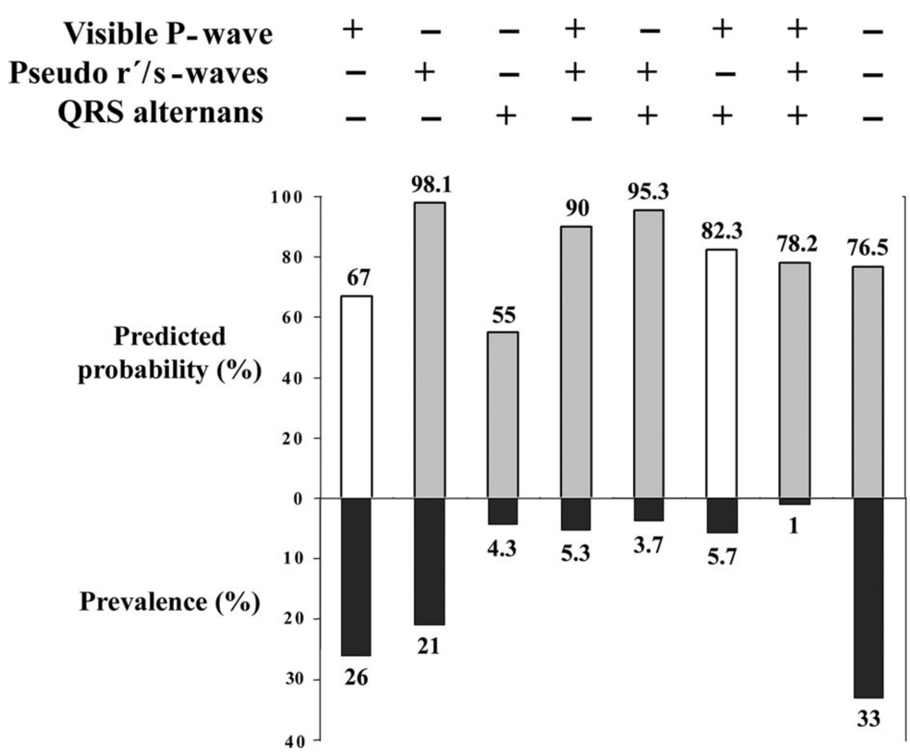

Figure 1 Predicted probabilities for the diagnosis of atrioventricular nodal re-entrant tachycardia (gray bars) or atrioventricular reciprocating tachycardia (white bars) depending on every combination of selected electrocardiographic parameters. The corresponding prevalences of every combination of electrocardiographic criteria (present: +; absent: −) in the derivation group are shown as dark gray bars. Figures are percentages. Diagnostic probabilities for both tachycardias depending on every combination of selected electrocardiographic signs were >75% in 70% of the patients.

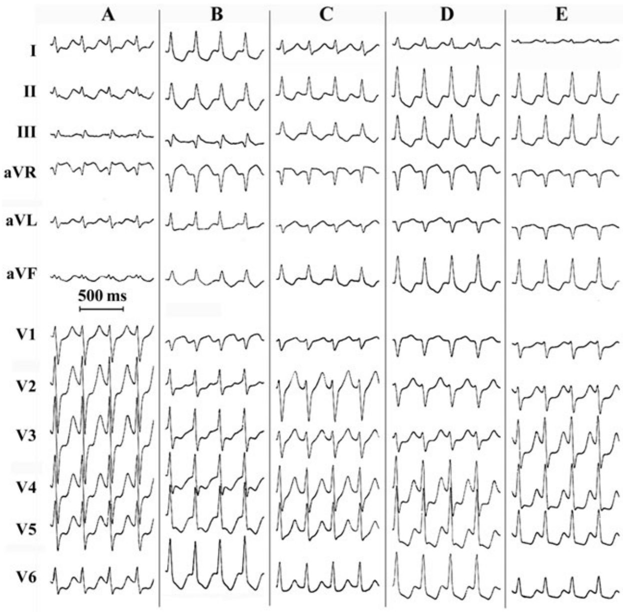

Figure 2 (A–C)Twelve-lead electrocardiographs from three atrioventricular reciprocating tachycardia patients without clearly identifiable P-wave misclassified as atrioventricular nodal re-entrant tachycardia. (D and E) Twelve-lead electrocardiographs from two patients with demonstrated atrioventricular nodal re-entrant tachycardia and clear repolarization abnormalities. The presence of repolarization changes during tachyardia was not selected as independent predictor of the tachycardia mechanism.

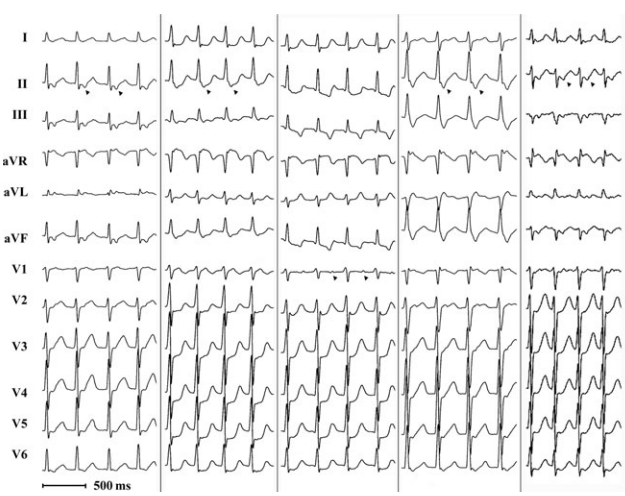

Figure 3 Twelve-lead electrocardiographs from five patients with atypical atrioventricular nodal re-entrant tachycardia misclassified as atrioventricular reciprocating tachycardia after subjective electrocardiographic interpretation of identifiable P-waves (arrowheads).

inferior leads, a visible P-wave after the QRS complex, and QRS alternans during tachycardia permit us to derive a reliable logistic regression model to predict the major mechanisms of paroxysmal supraventricular tachycardias in patients without pre-excitation in sinus rhythm. The presence of repolarization abnormalities during tachycardia was not selected by the predictive model. These criteria correctly assigned the tachycardia type in 82% of the validation cases. However, a correct subjective ECG interpretation was obtained in 68% of these patients. In addition, the predictive diagnostic probabilities of useful combinations of both positive and negative significant ECG findings have been analysed for the first time in our study.

Although our results are in close agreement with those of Kalbfleisch *et al.*[5] in their multivariate analysis on 178 patients without pre-excitation during sinus rhythm, no previous external validation of these classical ECG criteria has been reported in a large sample of patients. Furthermore, in a large series of Tai *et al.*,[7] 12-lead ECG tracings without discernible P-waves during tachycardia were excluded from the analysis. Interestingly, the absence of a visible P-wave after the QRS complex during tachycardia was observed in 62% of the patients in the derivation group and was associated with predicted probabilities for AVNRT diagnosis ranging from 76 to 98% in prevalent groups of patients (*Figure 1*). In fact, a diagnostic probability for AVNRT greater than 76% is predicted when all selected ECG criteria are lacking, thus highlighting the value of negative ECG findings.

Previous studies evaluating the significance of QRS alternans have shown conflicting results.[16] According to our results, QRS alternans is independently associated with tachycardia type occurring more frequently with AVRT by unexplained mechanisms.[1,5] In addition, our study does not demonstrate an adjusted rate dependence of the phenomenon as previously found by others,[2,3,5] as the corresponding test for interaction was non-significant. However, previous analysis of this possible association has merely been univariate by comparisons of means.

Previous univariate analyses have shown that the presence of certain repolarization changes during narrow-QRS complex tachycardia may be a useful adjunct to determine the arrhythmia mechanism.[6,9] A distinct pattern of retrograde atrial activation during AVRT, combining a longer ventriculoatrial interval and a retrograde P-wave of longer duration overlapping ST-segment, can explain this finding.[6] It is therefore possible that the presence of clearly identifiable retrograde P-wave on 12-lead ECG could offset the diagnostic value of associated repolarization changes, thus preventing its predictive influence on the multivariate logistic model. In fact, other authors do use the presence of ST-segment depression as a final step of their diagnostic algorithm when patients with visible P-waves or P-waves with an RP interval $<$100 ms have been ruled out.[9,13] It may be possible that a deeper ST-segment depression cut-off point could lead to stronger discrimination power. The impaired diagnostic value of ST-segment depression in adult patients,[13,14] the difficult assessment of negative findings in the ECG interpretation, and the misleading influence of ECG tracings of patients with atypical AVNRT could all explain the lower subjective diagnostic accuracy of the ECG in AVNRT patients. Finally, in recent guidelines,[11] the algorithm for the differential diagnosis of these tachycardias ultimately relies on the identification of visible P-waves and the measurement of the RP interval during tachycardia. Other findings such as the presence of pseudo r'-wave in V1 are commented but excluded from the diagnostic algorithm.

Limitations

The reproduciblity in the identification of ECG features is a major limitation of our study and an inherent drawback of the subjective interpretation of surface electrocardiography. Our study is based on a binary logistic regression analysis excluding patients with atrial tachycardia who are a minority in previous consecutive series of cases with paroxysmal, regular supraventricular tachycardias. In addition, non-invasive manoeuvres modifying AV nodal conduction are more frequently diagnostic in these patients. In fact, patients with atrial tachycardias without prior non-invasive diagnosis would constitute only 2% of our study population. Other reported ECG findings are not included in our analysis that was restricted to the most renowned ECG criteria in order to obtain a more robust statistical evaluation of these parameters and clinically useful results with their combinations. In fact, the analysis of R-P differences between V1 and inferior leads could be helpful in diagnosing atypical AVNRT patients,[10] a subset of cases that concentrate on most of the misdiagnosis. Finally, the possible influence of the different band-pass filter settings on ECG pattern recognition is a limitation of our study.

Conclusions

The presence of pseudo r' deflection in V1 and/or pseudo s-wave in inferior leads, an identifiable P-wave after the QRS complex, and QRS alternans during tachycardia permit us to derive a reliable logistic model to predict the two major mechanisms of paroxysmal AVRT in 82% of the patients with these arrhythmias and absence of pre-excitation during sinus rhythm. This model of classical ECG criteria is prospectively validated for the first time. Precise probabilities for the correct diagnosis associated with every combination of those classical ECG signs were found to be $>$75% in 70% of the patients.

Conflict of interest: none declared.

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