A novel electrocardiography algorithm to differentiate between ventricular arrhythmia and right ventricular outflow tract versus left ventricular outflow tract

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Abstract

Aim: To evaluate the accuracy of the diagnostic criteria for determining the origin of outflow tract ventricular arrhythmia (OTVA) and develop an electrocardiography (ECG) algorithm to predict its origin. **Method:** We analyzed the ECGs of 100 patients with OTVA who underwent successful ablation. The QRS complex was measured during sinus rhythm and ventricular arrhythmia (VA). After the ECG algorithm was developed, it was validated in an additional 100 patients from two different hospitals. **Results:** In this retrospective study, among the parameters without restrictions in the transition lead, the V2S/V3R index (AUC = 0.89) was significantly better in predicting VA originating from the right ventricular outflow tract (RVOT). Further, the larger ISA in V1 and V2 (AUC = 0.90) was significantly better in predicting VAs originating from the left ventricular outflow tract (LVOT). Among the parameters with the transition lead in V3, the V2S/V3R index (AUC = 0.82) was significantly better in predicting VAs originating from the RVOT. On the other hand, the V3 R-wave deflection interval (AUC = 0.81) was significantly better in predicting VAs originating from the LVOT. The algorithm combining the V2S/V3R index and the larger ISA in V1 and V2 could predict OTVA origin with an accuracy of 85.00%, a sensitivity of 75.68%, a specificity of 90.48%, a positive predictive value (PPV) of 82.35%, and a negative predictive value (NPV) of 86.36%. In the validation study, the algorithm exhibited excellent accuracy (95.00%) and AUC (AUC = 0.95), with a sensitivity of 94.12%, a specificity of 95.45%, a PPV of 91.43%, and an NPV of 96.92%. **Conclusion:** Our developed algorithm can reliably predict OTVA origin without restrictions in the transition lead.

Introduction

Outflow tract ventricular arrhythmia (OTVA) is one of the most common subgroups of idiopathic ventricular arrhythmia (VA) that typically occurs in healthy patients without any structural heart diseases. Radiofrequency catheter ablation (RFCA) is considered the curative therapy for OTVA, with a high success rate. Further, with the development of new techniques, the success rate is extremely high in experienced centers (>95%)[1]. Therefore, RFCA is suggested as Class I, level B for VA arising from the right ventricular outflow tract (RVOT), and Class IIa, level B for that arising from the left ventricular outflow tract (LVOT)[2]. Notably, it is clinically important to accurately predict OTVA origin before ablation as it reduces the risk of exposure to radiation, duration of the ablation, and the number of vascular access sites. Further, timely identification of the origin of the OTVA can improve the safety and efficacy of the ablation procedure. By accurately predicting OTVA origin, the physician can customize the ablation strategy to accurately target the arrhythmia source, thereby improving patient outcomes. Typically, VA originating in the RVOT manifests as a left bundle branch block (LBBB) configuration. In contrast, VA originating in the LVOT usually

manifests either as a right bundle branch block or an LBBB. Considering the overlap between precordial transition lead and morphological similarity, it is difficult to determine the origin of OTVAs. Rapid developments in the past two decades have resulted in the identification of several ECG parameters to distinguish between the origins of RVOT and LVOT. However, the use of these mentioned parameters may lead to different predictions of the VA origin and confuse the physician. To the best of our knowledge, this is the first study to systematically investigate the accuracy of these parameters. Further, we developed the algorithm for reliably predicting OTVA origin and validated it in an additional 100 patients.

Methods

Patients

We reviewed the procedural records of 105 consecutive patients who underwent ablation of idiopathic OTVA between May 2020 and October 2022 at our institutions. After exclusion, we reviewed the records of the remaining 100 patients (48 men, mean age 62.77 ±14.10 years, and 52 women, mean age 60.00 ±13.15 years) who successfully underwent ablation in either the RVOT or LVOT. No evidence of any structural heart disease was observed. Before the procedures, written informed consent was obtained from the patients, and antiarrhythmic drugs were discontinued for at least five half-lives, except for amiodarone. Electrophysiological studies and catheter ablation were performed under local anesthesia.

ECG measurement protocol

The Carto 3 Version 6 electrophysiological mapping system was used to measure the parameters of the QRS morphology during sinus rhythm (SR) and VA. The lead gain was uniform with a paper speed of 100 mm/s. Several parameters were obtained similar to previous studies: (1) R-wave and QRS complex amplitudes in lead V1–V3 during SR and VA, measured from the peak of the QRS complex to the isoelectric line and the nadir of the QRS complex; (2) R-wave duration in leads V1–V2 during VA, measured from the onset of the QRS complex to the transection point between the R-wave and isoelectric line; (3) total QRS duration during VA, measured from the earliest onset of the QRS complex to the time of the latest activation in any lead; (4) the precordial transition lead was defined as the position in which the amplitudes of the R- and S-waves were equal. The precordial transition zone (TZ) score was defined as the lead in which the R/S-wave amplitude ratio was 0.9–1.1. If the ratio was >1.1, the TZ score was graded in decrements of 0.5 points. On the other hand, if it was <0.9, the TZ score was graded in increments of 0.5 points; (5) R-wave deflection interval, measured from the initiation to the peak of the QRS complex in leads V2 and V3 during VA; and (6) amplitude of the QRS complex within the initial 40 ms in lead V2. The ECG parameters[3–11] proposed to predict the origin of the VA from the RVOT or LVOT are presented in Table 1. For all cases, quantitative measurements were performed by two observers. If there was apparent discordance between the two observers, Dr. Jiang was consulted. In our validation study, all 100 patients were selected from two different hospitals, and ECG measurements were performed by observers different from the previous study. Calculation of the parameters and statistical analysis were performed by the Tianjin Institute of Cardiovascular Diseases; they were blinded to the procedure. Our study protocol was approved by the ethics committee of the hospital. Owing to the retrospective observational nature of the study, it was not registered on ClinicalTrials.gov.

Inclusion criterion

Patients with symptomatic idiopathic monomorphic OTVA who underwent successful RFCA

Those with intramural VA[12] that was eliminated from either the RVOT or LVOT via ablation

Exclusion criterion

- Patients with significant structural heart anomalies
- Those with intramural VA[13] that was eliminated from both the RVOT and LVOT via bipolar ablation
- Those with VA with two or more similar QRS morphologies but one origin caused by preferential conduction[14]
- Those with a secondary VAs such as electrolyte disturbance or thyroid dysfunction

- Those without OTVA
- Those with a failed RFCA

Mapping and RFCA

Bipolar and unipolar intracardiac electrograms were filtered at 30–400 and 0.05–400 Hz, respectively, and the surface ECG was filtered at 0.05–30 Hz. If patients had sufficient VA with or without isoproterenol (2–4 μg/min), local activation time mapping was performed to identify the earliest bipolar ventricular electrograms, accompanied by a unipolar QS pattern wave. On the other hand, if patients had an insufficient VA, pace mapping was performed at a pacing cycle length of 500 ms. Then, the paced and the spontaneous VAs were closely compared to determine the target for RFCA. The site of VA origin was determined using the electroanatomic maps from the RAO and LAO views.

Radiofrequency energy was delivered to the distal electrode of the irrigated 3.5-mm tip catheter at a temperature limit of 55°C and power setting of 30 W. In cases where the target was within the great cardiac vein near the anterior interventricular vein (GCV-AIV), the power was started from 15 W and increased up to 30 W. In other cases where the target was adjacent to the intense fibrous structures or there was suppression and recurrence of VA, a power of up to 40 W was used. The ablation duration of each site was approximately 60 s, with a maximum duration of 120 s.

Successful ablation success was achieved when (1) clinical VA was eliminated at the end of the procedure; (2) clinical VA was absent after 24 h of continuous ECG monitoring without antiarrhythmic drugs; and (3) there was no recurrence of clinical VA during >3 months of follow-up. All of these predescribed criteria should be satisfied to achieve successful ablation.

Validation study

After developing the algorithm for predicting OTVA origin, we validated it by including another 100 patients from two different hospitals between June 2020 and October 2022.

Statistical analysis

Continuous variables were presented as mean ±SD. Categorical variables were presented as counts (percentages). After measuring each variable, the accuracy and features of all of the pre-existing parameters were calculated via receiver operating characteristic (ROC) curve analysis. The optimal cutoff was selected based on the Youden index. Statistical analysis was performed using SPSS 23.0. A two-tailed p-value of <0.05 was considered statistically significant.

Results

Baseline characteristics

In this study, 100 patients (48 men, mean age 62.77 ±14.10 years, and 52 women, mean age 60.00 ±13.15 years) who underwent successful ablation in either the RVOT or the LVOT were enrolled. All these patients had taken at least one antiarrhythmic drug, including metoprolol, propafenone, or amiodarone. According to the successful ablation site, in 63 (63.00%) patients, the VA had originated in the RVOT, and in 37 (37.00%) patients, it had originated in the LVOT. The LVOT group comprised 14 (37.84%) patients with left coronary cusp (LCC), 9 (24.32%) patients with right coronary cusp (RCC), 10 (27.03%) patients with left ventricular endocardium below the aortic sinus cusp (ASC), and 4 (10.81%) patients with GCV-AIV.

Comparison of the previous ECG parameterswithout restrictions in thetransition lead

In the previous ECG parameters, the V2 transition ratio, V3 R-wave deflection interval, and V1–V3 transition index were used in the OTVAs, with the transition lead in V3. The other seven parameters could be used in the OTVAs without restrictions in the transition lead. Therefore, the 100 patients with OTVAs were analyzed with the other seven parameters using ROC curve analysis (Figure 1A). The V2S/V3R index (AUC = 0.89, p = 0.00) was superior to S-R difference in leads V1 and V2 (AUC = 0.87, p = 0.00) and the TZ index (AUC = 0.75, p = 0.00) in predicting the origin of the RVOT. Further, the larger ISA in leads V1 and V2

(AUC = 0.90, p = 0.00) was superior to the larger R/S-wave amplitude index in leads V1 and V2 (AUC = 0.87, p = 0.00), the larger R-wave duration index in leads V1 and V2 (AUC = 0.84, p = 0.00), and the amplitude of the QRS complex in the initial 40 ms in V2 (AUC = 0.65, p = 0.04) in predicting the origin of the LVOT. Table 2 compares the accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the ECG parameters for predicting the origin of the LVOT.

Among the parameters, the V2S/V3R index was significantly greater for VAs originating from the RVOT. The Youden index was 0.65, and the optimal cutoff value was 1.5 (Figure 1B). Further, the accuracy was 81.00%, sensitivity was 79.37%, specificity was 83.78%, PPV was 89.29%, and NPV was 70.45%.

The larger ISA in leads V1 and V2 was significantly greater for VAs originating from the LVOT. The Youden index was 0.62, and the optimal cutoff value was 57 ms × mv (Figure 1C). The accuracy was 82.00%, sensitivity was 81.08%, specificity was 82.54%, PPV was 73.17%, and NPV was 88.14%.

Comparison of the previous ECG parameterswith the transition lead in V3

An additional ROC analysis (Figure 2A) for the previous 10 parameters was performed among 37 (37.00%) patients with the transition lead in V3. The V2S/V3R index (AUC = 0.82, p = 0.01) was better than the S-R difference in leads V1 and V2 (AUC = 0.78, p = 0.02) in predicting the origin of the RVOT. Further, the V3 R-wave deflection interval (AUC = 0.81, p = 0.01) was better than the larger ISA in leads V1 and V2 (AUC = 0.77, p = 0.02) and larger R/S-wave amplitude index in leads V1 and V2 (AUC = 0.77, p = 0.02) in predicting the origin of the LVOT. The other parameters in predicting the origin of VAs with the transition lead in V3 were not statistically significant (Table 3).

Among the parameters, the V2S/V3R index was significantly greater for VAs originating from the RVOT. The Youden index was 0.59, and the optimal cutoff value was 1.5. The accuracy was 72.97%, sensitivity was 75.00%, specificity was 72.00%, PPV was 56.25%, and NPV was 85.71%. On the other hand, the V3 R-wave deflection interval was significantly greater for VAs originating from the LVOT. The Youden index was 0.73, and the optimal cutoff value was 80 ms (Figure 2B–2D). The accuracy was 86.49%, sensitivity was 75.00%, specificity was 92.00%, PPV was 81.82%, and NPV was 88.46%.

Appropriate ECGalgorithm for reliably predicting VA origin

For VAs without restrictions in the transition lead, the algorithm (Figure 3) combining the V2S/V3R index and larger ISA index could predict VA origin with an accuracy of 85.00%, a sensitivity of 75.68%, a specificity of 90.48%, a PPV of 82.35%, and an NPV of 86.36%. For VAs with the transition lead in V3, no statistical significance was observed in the accuracy of predicting VA origin between the V3 R-wave deflection interval and the algorithm (86.49% vs. 85.00%, p = 0.528). Therefore, the algorithm can reliably determine OTVA origin without restrictions in the transition lead.

Results of the validation study

For the validation study, an additional 100 patients (54 men, mean age 57.63 ±11.44 years, and 46 women, mean age 63.54 ±9.55 years) who underwent successful ablation in either the RVOT or the LVOT were enrolled. According to the successful ablation site, in 66 (66.00%) patients, the VAs had originated in the RVOT, and in 34 (34.00%) patients, the VAs had originated in the LVOT. The LVOT group comprised 18 (52.94%) patients with LCC, 5 (14.71%) with RCC, 10 (29.41%) with left ventricular endocardium below the ASC, and 1 (2.94%) with GCV-AIV.

In the validation study, our ECG algorithm exhibited excellent accuracy (95.00%) and AUC (0.95), with a sensitivity of 94.12%, a specificity of 95.45%, a PPV of 91.43%, and an NPV of 96.92%.

Discussion

Major findings

In clinical settings, to determine the origin of OTVAs, we might get confused by different diagnostic criteria. This is the first systemic and comprehensive study that included 10 parameters to identify OTVA origin

between 2002 and 2020. The main findings of our study are summarized as follows. (1) Among the seven parameters without restrictions in the transition lead, the larger ISA in leads V1 and V2 exhibited the best predictive value in differentiating the VAs in the LVOT, with a cutoff value of 57 ms × mv, which was different from a previous study (cutoff value of 15 ms × mv)[10], and the V2S/V3R index exhibited the best predictive value in differentiating the VAs in the RVOT, with a cutoff value of 1.5. (2) The algorithm combining the larger ISA in V1 and V2 and the V2S/V3R index has the best predictive value in determining the origin of OTVAs without restrictions in the transition lead. (3) Among the 10 parameters with the transition lead in V3, the V3 R-wave deflection interval exhibited a greater power to predict the origin of VAs than the other parameters. It has an accuracy similar to the algorithm proposed by us. (4) In the validation study, the algorithm exhibited optimal accuracy (95%). Taken together, the findings suggest that the algorithm can reliably determine the origin of the OTVA without restrictions in the transition lead.

Need forreviewing and comparing the accuracy of different diagnostic criteria for determining OTVA origin

The criteria proposed to differentiate OTVA origin spanned nearly two decades, with considerable discrepancies among the studies. (1) Different cases were included in the studies. The outflow tract was classified into six subdivisions: RV septum, RV free wall, RV near the His-bundle region, LV endocardium, ASC, and LV epicardium remote from the LSV[15]. Ouyang et al.[3] and Yoshida et al.[5] just enrolled patients with VAs originating from the RVOT and ASC. Di et al.[9] and Cheng et al.[6] did not enroll patients with the OTVAs originating from the LV epicardium. However, patients with OTVAs originating from all six subdivisions were enrolled in other studies. These discrepancies in the included cases might inevitably lead to different diagnostic accuracies. (2) A considerable discrepancy was present in the number of participants among the different studies. Ouyang et al.[3] only enrolled 15 cases, whereas Xia et al.[11] enrolled 382 cases. (3) Considerable differences in sample capacity might lead to different diagnostic accuracies, whether or not accounting for sinus rhythm. Betensky et al.[4], Yoshida et al.[5], and Di et al.[9] performed QRS measurement during sinus rhythm. This measure takes into account variations in body habitus, cardiac rotation, respiration, and ECG lead position. (4) Precordial transition lead. The criteria established by Betensky et al.[4], Cheng et al.[6], and Di et al.[9] just included OTVAs with the transition lead in V3. However, other studies included OTVAs without restrictions in the precordial transition lead. Given the discrepancy among the studies mentioned above, we need to comprehensively review and compare these criteria. In our retrospective and validation study, 200 patients with OTVAs originating from all six subdivisions were enrolled. The precordial transition lead varied from V1 to V6. Given the anatomic complexity of the ventricular outflow tract, it may be difficult to differentiate the origin of PVCs using a single parameter. Therefore, it is better to combine several simple and credible parameters to predict OTVA origin.

Thelarger ISA in leads V1 and V2 and theV2S/V3R index have great power in predicting VA origin without restrictions in the transition lead

The precordial V1–V3 leads are adjacent to the LVOT and RVOT and are the best parameters to distinguish OTVA. As the focus moves far away from the lead, R-wave amplitude increases, and S-wave amplitude decreases. This results in a higher R-wave amplitude and lower S-wave amplitude in the V1–V3 leads during OTVAs originating from the LVOT than those originating from the RVOT. Therefore, VAs originating from the LVOT would have a larger ISA and a smaller V2S/V3R index than those originating from the RVOT.

The ablation targets of five patients who were misdiagnosed by the algorithm were analyzed. In three patients, the VA was located in the septum of the RVOT (misdiagnosed as in the LVOT), and in two, the VA was located in the LCC (misdiagnosed as in the RVOT). Anatomically, the location of the RVOT is more anterior and leftward of the LVOT, whereas that of the LVOT is more posterior and rightward of the RVOT. The intimate nature of these two structures explains why OTVAs from these two distinct locations can be morphologically similar on surface ECG and result in successful ablation in the RVOT with the origin in the LVOT, or vice versa[16, 17].

Cutoff values of the parameters

In our retrospective study, the cutoff values of V2S/V3R and the V3 R-wave deflection were the same as those in previous studies. However, compared with Nikoo et al.[10], the larger ISA in V1 and V2 (66.53 ±59.73 vs. 29.48 ±55.57) and the cutoff value of ISA (57 vs.15, P = 0.00) in our study were larger. After reviewing the data obtained from the previous study, we found that the duration of the R-wave in V1 (67.34 ±35.38 vs. 49.75 ±31.02) and V2 (71.09 ±25.26 vs. 53.08 ±27.72) and the amplitude of R-wave in V1 (0.38 ±0.31 vs. 0.20 ±0.26) and V2 (0.79 ±0.51 vs. 0.35 ±0.47) in our study were larger. This may be related to the inclusion of more patients with a transition lead in V1 (21.00% vs.10.00%) in our study. However, after excluding 21 patients with a transition lead in V1, the ISA (42.50 ±31.56 vs. 29.48 ±55.57) in our study was still larger than that in the previous study; the cutoff value remained unchanged (cutoff value = 57 and Youden index = 0.49). In addition, with a cutoff value of 57 in our validation study, we achieved satisfactory diagnostic accuracy (94.00%) and AUC (0.95), with a sensitivity of 97.06%, a specificity of 92.42%, a PPV of 86.84%, and an NPV of 98.39% (Table 4). Therefore, we believe that a cutoff value of 57 is more appropriate.

Improve the accuracy of OTVA localization and broaden clinical applications

Tanner et al.[18] reported that stepwise endocardial and epicardial mapping using up to six anatomic approaches could lead to successful RFCA. In all patients, activation mapping was performed from the RVOT, including the pulmonary cusp or trunk. If ablation was not achieved, epicardial mapping within the GCV-AIV was performed. If ablation still failed, mapping of the ASC and left ventricular endocardium below the ASC was performed via the femoral artery. Owing to its benefit–risk ratio, the subxiphoid approach was avoided.

The use of this simple ECG measurement algorithm can improve the accuracy of OTVA localization and has the advantage of procedural simplification. Moreover, our algorithm avoided complicated calculations and confusing diagnostic results acquired from different ECG parameters, keeping the diagnostic algorithm simple, and contributes to generalized clinical application.

Limitations

The present study has several limitations. First, we used the location of successful RFCA at the RVOT or LVOT as the PVC/VT site of origin. It is possible that PVCs/VTs with an LVOT origin could be abolished from the RVOT. Second, a study recently reported about preferential conduction across the ventricular outflow septum[19]. The presence of preferential conduction decreases the reliability of the accuracy of determining VA origin. Third, extremely rare VAs may have multiple exits, and during ablation, their exit pathways may change; therefore, an altered ablation target may be needed. Lastly, to increase the reliability of the algorithm, further prospective studies with a larger sample size are warranted.

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