ORIGINAL ARTICLE

Electrocardiographic algorithms to guide the management strategy of idiopathic outflow tract ventricular arrhythmias

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KEY WORDS

electrocardiographic
criteria, outflow tract,
ventricular arrhythmia

ABSTRACT

INTRODUCTION   The current guidelines of the European Society of Cardiology outlined electrocardiographic (ECG) differentiation of the site of origin (SoO) in patients with idiopathic ventricular arrhythmias (IVAs).
OBJECTIVES   The aim of this study was to compare 3 ECG algorithms for differentiating the SoO and to determine their diagnostic value for the management of outflow tract IVA.
PATIENTS AND METHODS   We analyzed 202 patients (mean age [SD]: 45 [16.7] years; 133 women [66%]) with IVAs with the inferior axis (130 premature ventricular contractions or ventricular tachycardias from the right ventricular outflow tract [RVOT]; 72, from the left ventricular outflow tract [LVOT]), who underwent successful radiofrequency catheter ablation (RFCA) using the 3-dimensional electroanatomical system. The ECGs before ablation were analyzed using custom-developed software. Automated measurements were performed for the 3 algorithms: 1) novel transitional zone (TZ) index, 2) V_2S/V_3R, and 3) V_2 transition ratio. The results were compared with the SoO of acutely successful RFCA.
RESULTS   The V_2S/V_3R algorithm predicted the left-sided SoO with a sensitivity and specificity close to 90%. The TZ index showed higher sensitivity (93%) with lower specificity (85%). In the subgroup with the transition zone in lead V_3 (n = 44, 15 from the LVOT) the sensitivity and specificity of the V_2– transition-ratio algorithm were 100% and 45%, respectively. The combined TZ index $+ V_2S/V_3R$ algorithm (LVOT was considered only when both algorithms suggested the LVOT SoO) can increase the specificity of the LVOT SoO prediction to 98% with a sensitivity of 88%.
CONCLUSIONS   The combined TZ-index and V_2S/V_3R algorithm allowed an accurate and simple identification of the SoO of IVA. A prospective study is needed to determine the strategy for skipping the RVOT mapping in patients with LVOT arrhythmias indicated by the 2 combined algorithms.

INTRODUCTION   Idiopathic ventricular arrhythmias (IVAs) in the form of premature ventricular contractions (PVCs) or ventricular tachycardia (VT) with an inferior-axis QRS morphology usually originate from either the right or the left ventricular outflow tract (RVOT and LVOT, respectively). Radiofrequency catheter ablation (RFCA) is an effective treatment method for arrhythmia in adults and children,[1,2] but the strategy is slightly different depending on the IVA site of origin (SoO). The current guidelines recommend the use of Ic agents before referring

a patient with the LVOT origin of arrhythmia for ablation. The ablation of left-sided arrhythmias usually necessitates the use of the transaortic approach and an antithrombotic treatment, and could be associated with a more complex procedure requiring a more experienced electrophysiologist.[1] Although several electrocardiographic (ECG) algorithms have been proposed for differentiating an LVOT from an RVOT origin,[3-6] these drawbacks make many electrophysiologists first map the RVOT, and the LVOT is mapped only in the case of failure.

Three new algorithms have recently been published: 1) V_2S/V_3R index, 2) novel transitional zone (TZ) index, and 3) V_2 transition ratio.[7-9] The aim of this study was to retrospectively compare these algorithms and to check the possibility of their combined use to improve their specificity and to develop a strategy of skipping the RVOT mapping in patients with LVOT arrhythmias as indicated by the combined algorithms.

PATIENTS AND METHODS **Study population**
The study population consisted of patients from the multicenter "Electra" registry who had symptomatic IVA and underwent an acutely successful RFCA of the LVOT or RVOT IVA between September 2009 and November 2016. In all patients, the surface ECG of the PVCs/VT with a left bundle branch block (LBBB) or right bundle branch block (RBBB) morphology and inferior axis was observed. Standard precordial and limb leads were carefully positioned. We included only patients without structural heart diseases based on history, typical clinical features, and echocardiography, which was available in most patients.

Patients with pacemakers, LBBB/RBBB during sinus rhythm (SR), chest anomalies, ischemic or organic heart disease, and uncontrolled chronic, systemic, or endocrine diseases were excluded. Patients underwent a follow-up assessment to confirm the effectiveness of treatment. Participants with inadequate results in the follow-up were excluded. Some patients required a repeat procedure. In this case, only the last successful procedure was analyzed. To equalize the number of patients in both groups, the RVOT group (potentially larger) was reduced only to patients with available follow-up results.

All patients gave written informed consent for the procedure, and the study analysis was performed according to the protocols approved by an institutional review board.

Electrocardiography We analyzed the ECG data from a clinical spontaneous IVA recorded by electrophysiological recording systems (Ep-Tracer CardioTek, Maastricht, the Netherlands) in the initial phase of the procedure. Twelve-lead ECG data selected by a physician were exported in the form of a bitmap to custom-developed software. We used a sweep speed of 50 mm/s and a scale of 5 mm/mV to avoid overlapping of the ECG lines. Due to the pixel size, the resulting resolution allowed a semiautomatic analysis with a measurement accuracy of 2 ms in the interval and 0.017 mV of amplitude. Compatibility analysis was carried out by the system and was tested on sample records by 2 independent physicians.

The measurement procedure was not totally automatic. The physician had to direct the system where the isoelectric line and approximate beginning and end points of the QRS complexes for arrhythmia and SR were located. Next, the system drew the ECG waveforms and calculated the amplitudes and wave surfaces. It then suggested the hypothetical SoO based on the 3 algorithms: 1) novel TZ index, 2) V_2S/V_3R index, and 3) V_2 transition ratio. The process is illustrated in **FIGURES 1–4**. The system recorded parameters required by these algorithms, including the amplitude of the R- and S-waves in lead V_2 for SR and PVC/VT, R in lead V_3 for PVC/VT, the position of the TZ in SR and arrhythmia, and appropriate TZ scores. For additional analysis, the area of the appropriate waves was also recorded. The analysis was performed for the default criteria: the cut-off value for the V_2S/V_3R index was 1.5, and for V_2 transition ratio, −0.6.[7-9] A manual correction was possible when the system incorrectly identified the isoelectric line position. The localization of the isoelectric line was the only parameter determined by the physician, which may have contributed to the difference in the results obtained in separate measurements of the same QRS complex. In some cases, its location was modified manually for single leads. In the case of the discrepancies between the results of individual algorithms, the analysis was performed several times for different records. During the procedures, particular attention was paid to the determination of lead position in all precordial leads, with a check-up of the crucial position of leads V_1 to V_4 by the first operator. Four limb leads were placed on the distal parts of the extremities: the left and right wrist, and the left and right ankle. Physicians were blinded to the SoO reported after ablation.

The V_2S/V_3R and TZ-index algorithms are explained in **FIGURES 5** and **6**.

Mapping and ablation protocol For the RFCA, local anesthesia and light conscious sedation were used. The ablation catheter was introduced percutaneously into the femoral vein and positioned in the right ventricle. In most cases, a standard decapolar diagnostic catheter was introduced into the coronary sinus or the right ventricle under fluoroscopic guidance or, without an X-ray technique, using the 3-dimensional electroanatomical mapping system (Ensite Velocity NavX, St Jude Medical, St. Paul, Minnesota, United States). First, a programmed ventricular stimulation was carried out to assess the propensity for sustained ventricular arrhythmia. Then, classic mapping was performed to localize the optimal site of ablation according to pace mapping and local activation mapping. The decision to extend the mapping to the LVOT was made if no adequate RVOT

FIGURE 1 Initial indication of the position of the isoelectric line, beginning and end of the QRS complex at once for all leads
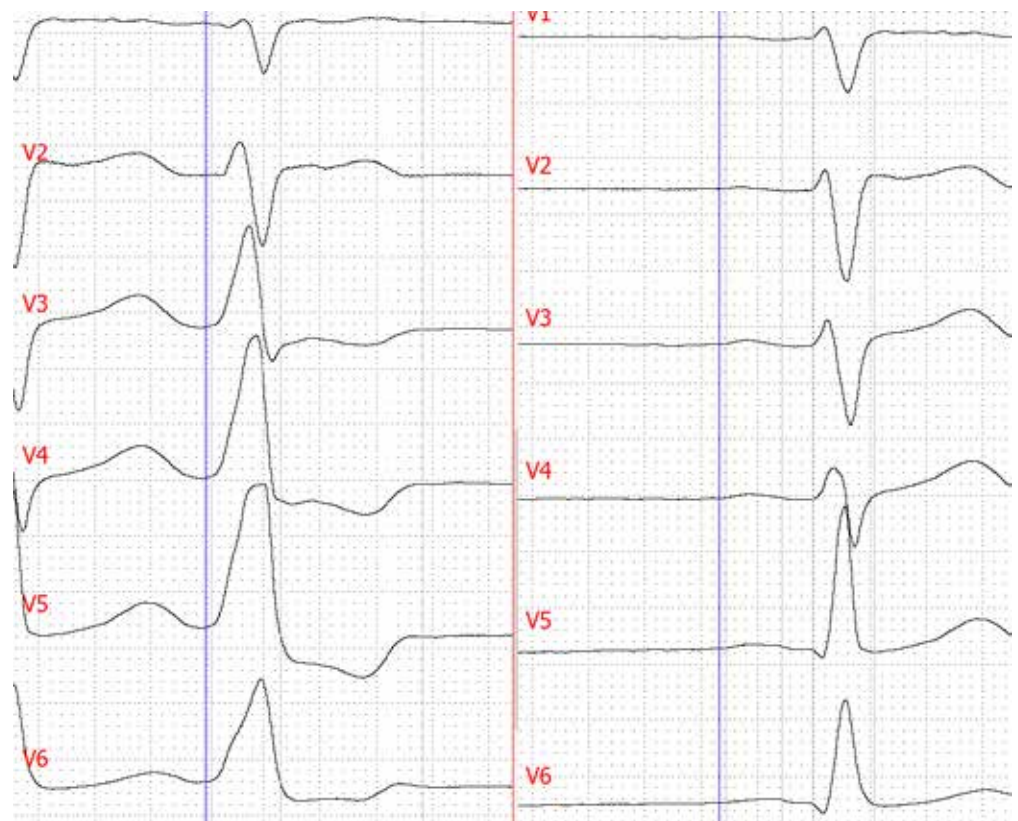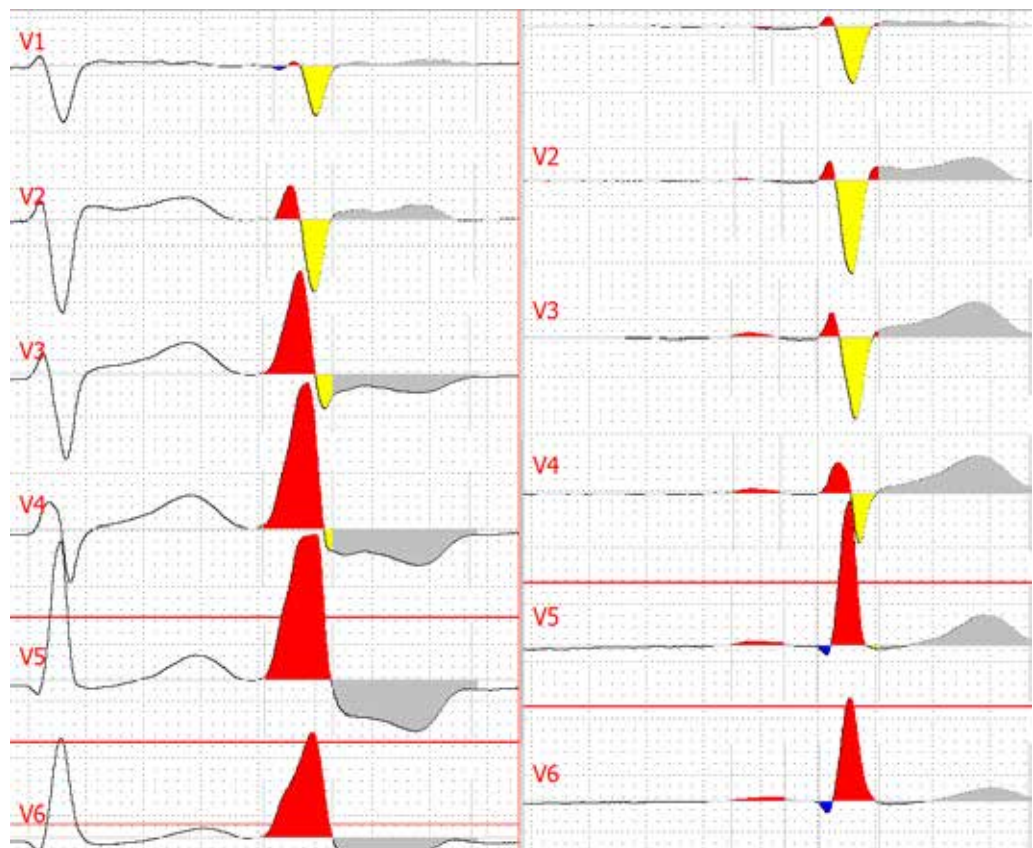

FIGURE 2 Positions can be adjusted for each lead separately.

sites were identified or if RFCA in the RVOT was unsuccessful.

The LVOT sites were mapped via a retrograde aortic approach. All mappings in the LVOT were performed after a heparin bolus. Moreover, when the LVOT mapping was insufficient, a mapping catheter was also inserted into the coronary sinus and followed into the great cardiac vein in order to validate the signals from the epicardial region of the LVOT covered by the great cardiac vein and anterior interventricular vein. The radiofrequency applications were set at 50–60 W and
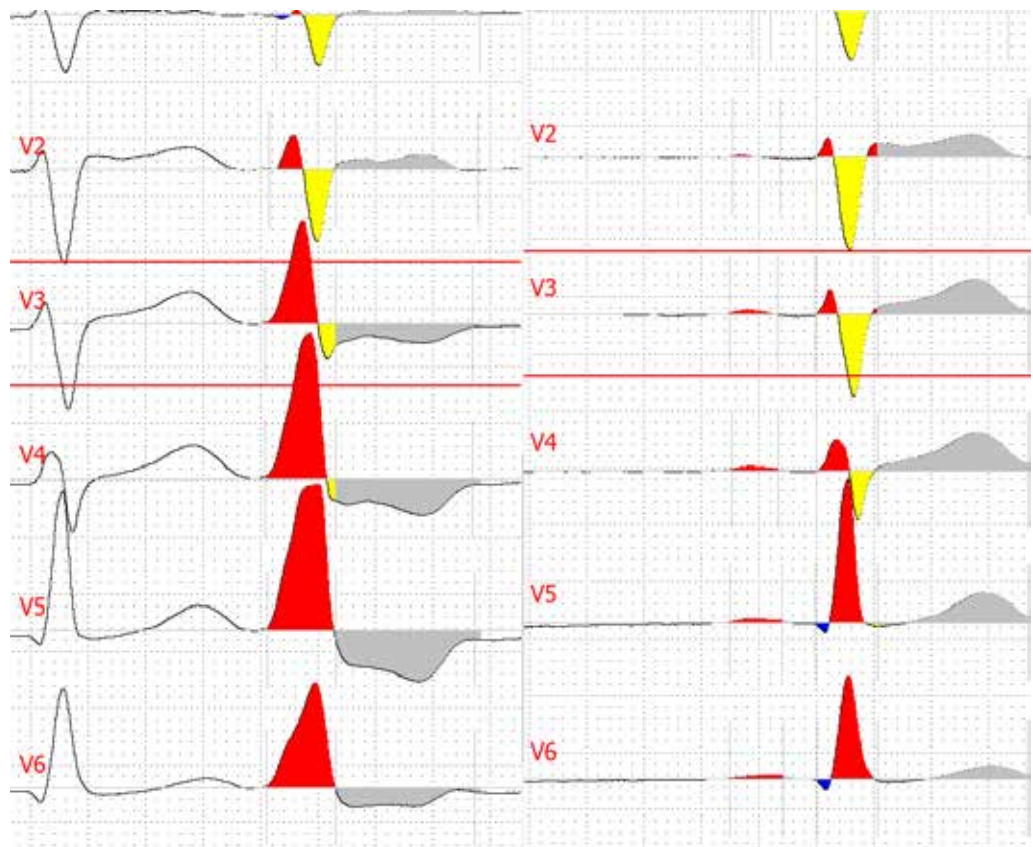
VT/PVC		
Sinus rhythm – TZ score	4.5	
VT – TZ score	2.5	
VT – transition zone (lead number)	5	
VT – transition zone (lead number)	3	
Sinus rhythm – R-wave in V_2	0.324	
Sinus rhythm – S-wave in V_2	1.639	
VT – R-wave in V_2	0.598	
VT – S-wave in V_2	1.263	
VT – R-wave in V_3	1.810	

VT/V_2 1.94 LVOT
Transition ratio 1.94 ≥0.6

V_2S/V_3R 0.698113 LVOT
V_2S/V_3R index 0.7 ≤1.5

TZ index −2 LVOT
TZ index −2.0 <0

FIGURE 4 Original computed study calculator screen view. Suggested origin of idiopathic ventricular arrhythmias based on electrocardiographic algorithms. The combined use of indexes indicates the left ventricular outflow tract (LVOT) site of origin only when both indexes (V_2S/V_3R and transitional zone [TZ] index) indicate the LVOT site of origin.
Abbreviations: PVC, premature ventricular contractions; VT, ventricular tachycardia

50–60°C. A power setting of 30 W was used for irrigated catheters. The control coronary angiography and a limited value of radiofrequency settings (30–50 W and 50°C for nonirrigated catheters) were used during application in the aortic cusps. The endpoint of the RFCA was complete disappearance of spontaneous PVCs/VT for more than 20 minutes after the last application. In patients without spontaneous ectopy at the time of the intracardiac mapping, pacing or isoproterenol infusion (or both) were used to induce PVCs or VT.

Statistical analysis Data were expressed as mean (SD). Continuous variables between the groups were compared using the unpaired t test or the Mann–Whitney test, as appropriate. Categorical variables were compared by the χ^2 test. Statistical significance was set at a P value of less than 0.05.

RESULTS The study involved 202 patients with IVA (mean age [SD], 45 [16.7] years, 133 [66%] women), including 130 PVCs/VT originating from the RVOT and 72 PVCs/VT originating from the LVOT. Patient characteristics and the results of analyses are shown in TABLE 1.

The SoO in the LVOT group included the left aortic cusp (n = 26), right aortic cusp (n = 1), junction of the left and right aortic cusp (n = 4), noncoronary aortic cusp (n = 2), aorto-mitral

FIGURE 5 Electronic caliper measurements can be obtained manually. The V_2S/V_3R index is calculated by dividing the S-wave amplitude in lead V_2 by the R-wave amplitude in lead V_3 in premature ventricular contractions. The results below 1.5 indicate left ventricular outflow tract.[7]
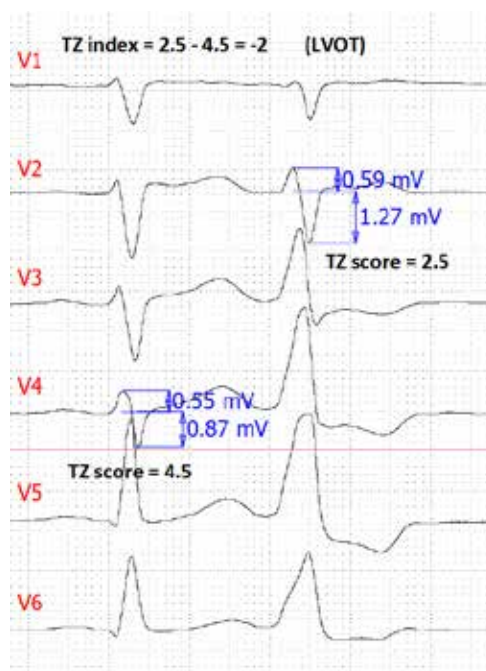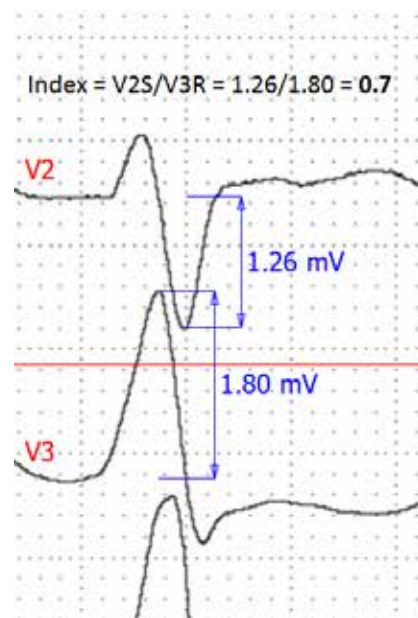

Index = V2S/V3R = 1.26/1.80 = **0.7**

V2

1.26 mV

1.80 mV

V3

TZ index = 2.5 - 4.5 = -2   (LVOT)

V1

V2

0.59 mV

1.27 mV

V3   TZ score = 2.5

V4

0.55 mV

0.87 mV

V5

TZ score = 4.5

V6

FIGURE 6

The transitional zone (TZ) index is calculated as follows[8]: the TZ score of the premature ventricular contractions/ventricular tachycardia minus the TZ score of the sinus beat. The TZ score is graded with 0.5 increments according to the site of the R-wave transition (eg, TZ in V_3 = 3 points, between V_3 and V_4 = 3.5 points, V_4 = 4 points. The TZ score is equal to the lead number when the R-wave amplitude divided by the S-wave amplitude is between 0.9 and 1.1. A TZ index value below zero suggests the left ventricular outflow tract site of origin.

continuity (n = 25), superior mitral annulus (n = 10), epicardial great cardiac vein close to the superior mitral annulus (n = 2), and other subaortic SoOs (n = 2). In terms of the parameters analyzed, patients with arrhythmias of the RVOT and LVOT

origins did not differ in tems of the ECG presentation in SR, and significant differences were noted in PVC/VT in the range of R- and S-wave amplitudes in lead V_2 and R-wave amplitude in lead V_3, transition zone, and in the values of indices of the analyzed algorithms.

The V_2S/V_3R algorithm in the whole study group predicted the left SoO with a sensitivity and specificity of 90% and 92%, respectively. The TZ-index algorithm was slightly more sensitive (93%), but less specific (85%). The V_2–transition-ratio algorithm applies only to patients with TZ in V_3 (44 patients, 15 with the LVOT SoO). The sensitivity of the algorithm in this subgroup was 100% at low specificity (45%). A trial use of this algorithm for all patients also showed a sensitivity of 100% at a specificity of 65%.

The algorithms were independently analyzed for the subgroups and were limited to patients with TZ in lead V_3 and with features of heart rotation determined based on the TZ in SR, assuming that the heart was rotated when the TZ in SR was not in leads V_3 and V_4. The results are shown in TABLE 2.

The combined use of the algorithms assumes that the arrhythmia has the SoO in the LVOT only when all algorithms indicate LVOT. This indicates the location with a sensitivity of 88% and high specificity (98%). Identical results were achieved based only on the TZ-index and V_2S/V_3R algorithms (excluding V_2 transition ratio). Assessing the absolute values, a hypothetical combined use of the algorithms correctly identified the location of the LVOT in 63 patients and incorrectly, only in 3 patients; 9 patients with a left-sided location were classified as originating from the RVOT.

The standard cut-off value for the LVOT location by the V_2S/V_3R index is ≤1.5. Next, we studied what happened when we analyzed the combined index with different cut-off values. A cut-off value for the V_2S/V_3R index of 1.1 yielded different results. This reduced the number of incorrectly classified patients for ablation in the LVOT from 3 to 2, which was associated with increased specificity, but this increased the number of incorrect RVOT indications to 10. Further reductions in the cut-off value to 1.0 yielded incorrect RVOT indications in 13 cases and decreased the sensitivity to 82%.

All algorithms are based on wave amplitudes. The usefulness of the waves' surface-based variant in the V_2S/V_3R algorithm was also analyzed. The index was defined as the surface of the S-wave in lead V_2 divided by the surface of R-wave in lead V_3. This yielded a sensitivity of 92% and a specificity of 87% at a cut-off value of 1.5. The cut-off value of 1.2 produced the same sensitivity as the amplitude algorithm version (90%) and a worse specificity (89%).

DISCUSSION   The study revealed high sensitivity and specificity for the TZ-index and V_2S/V_3R-index algorithms for a differential diagnosis of the SoO of IVA originating from the LVOT. Using

TABLE 1 Characteristics of the study groups depending on the site of radiofrequency catheter ablation

Parameter	Site of successful radiofrequency catheter ablation		P value
	LVOT (n = 72)	RVOT (n = 130)	
Age, y	48.7 (20.1)	42.6 (14.0)	<0.05
Number of PVCs	25 708 (13 967)	21 243 (16 520)	<0.05
Hypertension, n (%)	35 (49)	47 (36)	NS
Diabetes mellitus, n (%)	8 (11)	6 (5)	NS
Smoking, n (%)	17 (24)	19 (15)	NS
Total procedure duration, min	66.8 (27.6)	56.7 (25.8)	<0.05
Total fluoroscopy duration, min	6.0 (7.7)	3.8 (6.9)	<0.05
Complete zero-fluoroscopy approach, n (%)	19 (26)	66 (51)	<0.001
Ejection fraction, %	60.6 (6.8)	62.3 (6.8)	NS
BMI, kg/m²	27.1 (4.5)	26.3 (4.7)	NS
TZ index	−1.9 (1.2)	0.2 (0.8)	<0.001
V_2 transition ratio	2.8 (1.9)	9.9 (46.7)	<0.001
V_2S/V_3R index	0.7 (1.0)	7.1 (11.8)	<0.001
SR: Transitional zone	3.8 (1.0)	3.7 (0.9)	NS
SR: V_2 R-wave amplitude, mV	0.3 (0.2)	0.3 (0.2)	NS
SR: V_2 S-wave amplitude, mV	1.0 (0.5)	1.0 (0.4)	NS
PVC/VT: Transitional zone	1.9 (1.0)	4.0 (0.7)	<0.001
PVC/VT: V_2 R-wave amplitude, mV	1.0 (0.5)	0.3 (0.2)	<0.001
PVC/VT: V_2 S-wave amplitude, mV	0.8 (0.6)	1.7 (0.6)	<0.001
PVC/VT: V_3 R-wave amplitude, mV	1.6 (0.6)	0.5 (0.3)	<0.001

Data are presented as mean (SD) unless otherwise stated.

Abbreviations: BMI, body mass index; LVOT, left ventricular outflow tract; RVOT, right ventricular outflow tract; SR, sinus rhythm; others, see **FIGURE 4**

TABLE 2 Results for the whole study group and specific subgroups

Algorithm	LVOT indication	RVOT indication	Sensitivity	Specificity	PPV	NPV
All patients						
TZ index	87	115	93.1	84.6	77.0	95.7
V_2S/V_3R	76	126	90.3	91.5	85.5	94.4
TZ-index + V_2S/V_3R	66	136	87.5	97.7	95.5	93.4
Outflow tract IVAs with TZ in lead V_3						
V_2-transition ratio	31	13	100.0	44.8	48.4	100.0
TZ index	20	24	86.7	75.9	65.0	91.7
V_2S/V_3R	20	24	80.0	72.4	60.0	87.5
TZ-index + V_2S/V_3R	11	33	66.7	96.6	90.9	84.8
Normal TZ in SR						
TZ index	65	104	91.7	90.8	84.6	95.2
V_2S/V_3R	62	107	90.0	92.7	87.1	94.4
Heart rotated (TZ in SR >4 or <3)						
TZ index	22	11	100.0	52.4	54.5	100.0
V_2S/V_3R	14	19	91.7	85.7	78.6	94.7
Surface-based variant of the V_2S/V_3R algorithm depending on the cut-off level						
Cut-off level, 1.5	83	119	91.7	86.9	79.5	95.0
Cut-off level, 1.2	79	123	90.3	89.2	82.3	94.3

Abbreviations: IVA, idiopathic ventricular arrhythmia; NPV, negative predictive value; PPV, positive predictive value; TZ, transitional zone; others, see **TABLE 1**

both algorithms, the physician may accurately guide noninvasive and invasive management strategy in outflow tract ventricular arrhythmias. Moreover, the software developed for this study could provide easy and valuable information for clinical practitioners.

The authors of the TZ index emphasized the importance of the heart rotation for ECG analysis. In patients with normal TZ (usually between leads V_3 and V_4), both algorithms had high sensitivity and specificity; however, patients with a rotated heart showed a significant decrease in the specificity of the TZ index to 52% with a sensitivity of 100%. The corresponding values for V_2S/V_3R were 86% and 92%, respectively. This proves a high reliability of the V_2S/V_3R index also in patients with a rotated heart, which was also suggested by the authors of the index.[7]

Of the 202 enrolled patients, 44 (22% of the whole study group, including 15 from the LVOT group) had TZ in lead V_3. Similarly to a previous work, we observed that this is a difficult group to assess.[9] While the V_2–transition-ratio algorithm was designed specifically for this subgroup of patients, the results had low specificity. In the same subgroup, the TZ-index algorithm predicted the left-sided SoO with a higher sensitivity and specificity (87% and 76%, respectively) as compared with the V_2S/V_3R index (80% and 72%, respectively). The cited data indicate a high diagnostic value of the TZ-index and V_2S/V_3R-index algorithms in all analyzed subgroups.

One of the main objectives of the study was to evaluate the possibility of using the algorithms to select patients who can adopt a strategy of starting IVA mapping directly in the LVOT without mapping in the RVOT. Therefore, a broad group of patients with an LBBB- and RBBB-like pattern of PVCs/VT was intentionally included. Since the mapping and RFCA in the LVOT have additional drawbacks associated with the need to puncture the artery and the use of anticoagulation, we analyzed the possibility of the combined use of the algorithms in order to exclude the maximum number of patients potentially erroneously referred for LVOT mapping accepting any redundant RVOT mapping. A very high specificity (98%) with a sensitivity of 88% in the combined use of the TZ-index and V_2S/V_3R-index algorithms with a small amount of incorrect classification as the left-sided SoO (3 patients; 1.5% of the whole study group) seems to confirm the usefulness of this strategy versus the algorithms used separately.

To simplify the analyses, we used a computer-aided measurement integrated with the database. This greatly reduced the time needed to collect ECG parameters and calculate the indices. It also reduced the number of sites that could generate measurement errors. The algorithms were adopted for semiautomatic measurements. The original measurements were performed using electronic calipers, which are also possible in the application but were not used in this study. As mentioned earlier, the measurements were intentionally repeated only in the case of disagreement between the algorithms. The idea underlying this protocol was to check the accuracy and usability of the fastest and easiest way of performing the measurements that could be utilized in clinical practice. On the other hand, the wave surface-based version of the V_2S/V_3R algorithm was not superior to the amplitude-based version that can be easily used manually by physicians.[7-9]

One of the interesting modalities used for the SoO location is ECG imaging. Some authors reported lead repositioning (synthesized right-sided leads, posterior leads V_7 to V_9, or superior and inferior precordial leads) or using the high-resolution ECG to increase the diagnostic ECG performance for the RVOT or LVOT). However, there are limited data on prospective validation of these techniques, and ECG imaging is not widely available.[10-13] On the other hand, practical application of these methods in routine procedures is more complicated.

As noted above, the superior and inferior precordial lead placement has a significant effect on the results.[12] Hence, the correct location of the electrodes is crucial in determining the location of the arrhythmia.

Our study may have a significant importance for accumulating evidence on the zero-fluoroscopy approach to IVA and supraventricular arrhythmias.[14-17] In a large series of 188 patients managed with the zero-fluoroscopy approach to supraventricular arrhythmias, 5 cases of double tachycardia syndrome were diagnosed (ablation of supraventricular arrhythmia combined with PVCs or VT).[18] A preprocedural ECG analysis allowed additional cardiac magnetic resonance or computed tomography to validate the anatomy of the outflow tracts, aortic cusps, and coronary arteries and to integrate it into the 3-dimensional mapping system. Moreover, intracardiac echocardiography could be used to monitor the procedure. The majority of patients with the SoO in the RVOT can be treated with the complete zero-fluoroscopy approach, but in the aortic cusps, PVC/VT ablation usually requires mapping of the coronary ostia by coronary angiography or intracardiac echocardiography. In our study, more than 50% of the patients with the RVOT origin were treated with the zero-fluoroscopy approach. The current guidelines emphasized that the procedure should be performed by experienced cardiologists or a specialist center, which has additional clinical value when referring patients for an invasive procedure.[1,19]

A pharmacological treatment of IVA remains unsatisfactory, with only about 40% of patients with effective and well-tolerated treatment by one of the 3 evaluated antiarrhythmic drugs (verapamil, propafenone, and metoprolol). However, even patients with drug intolerance or not willing to use them permanently are often referred for an invasive procedure.[1,20] Moreover, some of the patients may have 2 separate focuses of IVA

that require mapping of 2 or more SoOs of arrhythmia.[21] Therefore, a precise and easy determination of the SoO of IVA has clinical importance as a noninvasive and invasive strategy.

Clinical implication Arrhythmias and conduction disturbances without atrial fibrillation constitute less than 7% of all causes of hospitalization among patients with cardiovascular diseases.[22] Although IVAs constitute only a small subgroup of them, they are still a real clinical challenge. The current guidelines of the European Society of Cardiology outlined ECG differentiation of the SoO in patients with IVAs. Patients with the LVOT origin with a potentially higher periprocedural risk should be treated invasively after failed antiarrhythmic therapy (with preference for class Ic agents). The combination of algorithms could facilitate a selection of patients for medical treatment. Our study demonstrated the ability to use computer-assisted, semiautomatic determination of the IVA SoO, which could be utilized in commercially available ECG recorders to perform an automatic analysis of records and support physicians who are not electrophysiologists in making initial treatment decisions. In addition, the possibility of selecting patients reliably with the SoO in the LVOT could help optimize the RFCA procedure, reduce the number of unnecessary venous punctures, and shorten the procedure duration.

Study limitations This study is limited by its retrospective design. A prospective study is needed to enhance the credibility of the results. Because of the need to assess the TZ in SR, it was necessary to exclude patients with active ventricular pacing, bundle branch blocks, and chest anomalies. In stimulated patients, the V_2S/V_3R index can be used, but its use in this group was not analyzed in our study.

Moreover, we excluded small children and patients with suspected PVC-induced cardiomyopathy. Therefore, the validation of these criteria cannot be generalized to those populations and will be performed in our ongoing trial.

Finally, some patients may have been successfully ablated with late recurrences of the same focus or late remission after a primary unsuccessful ablation.

Conclusions A combined TZ-index and V_2S/V_3R-index algorithm allowed an accurate and simple identification of the location of ventricular arrhythmia in patients without organic heart disease. Those parameters can be used as a pharmacological and nonpharmacological management strategy. A prospective study can determine the strategy of skipping the RVOT mapping in patients with LVOT arrhythmias indicated by the 2 combined algorithms.

Contribution statement BL and SS conceived the idea for the study. BL, KD, and SS contributed to the design of the research. BL created the dedicated computer application for ECG analysis. All authors were involved in data collection. BL, SS, and KD analyzed the data. BL and SS drafted the manuscript. All authors edited, reviewed, and approved the final version of the manuscript.

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