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Prognostic value of physical activity, gender, and age versus ECG in localizing the idiopathic ventricular outflow tract arrhythmias

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Abstract: Background: The idiopathic ventricular outflow tract arrhythmias may arise either from the right ventricular outflow tract or the left ventricular outflow tract. It is paramount to establish the precise location, based on the 12 lead ECG, to recommend the proper treatment for the patients. Methods: Based on the 12 lead ECG evaluation, the origin of the arrhythmias was established to be either in the RVOT or LVOT. The level of physical activity, gender, and sex were noted for each patient. Further, we evaluated the accuracy of the arrhythmia's location based on ECG versus the patient characteristics described earlier. Results: The clinical score based on these parameters presented a 71% sensitivity level and, 69% specificity level. The overall accuracy of predicting the right versus left outflow tract origin of arrhythmias based on the QRS morphology in lead V1 and the subsequent R wave transition in the precordial leads was 96.72%, with a 100% sensitivity and 88.89% specificity. Conclusion: Our clinical score, encompassing older age, sedentarism, and hypertension for the prediction of OT origin presents a lower sensitivity and specificity when compared to the ECG for differentiating the right versus left OT arrhythmias.

Keywords: age, sedentarism, arterial hypertension, idiopathic ventricular outflow tract, ventricular arrhythmias, ECG, radiofrequency ablation, QRS morphology.

1. Introduction

Idiopathic ventricular tachycardias (VTs) include various subtypes that are differentiated by their pathophysiological mechanism, VT-QRS morphology, and their origin. The idiopathic ventricular outflow tract arrhythmias (OTA) include the spectrum of premature ventricular contractions (PVCs) and non-sustained or sustained VTs.

Even though they occur in structurally normal hearts, and have a benign prognosis, the risk of developing left ventricular systolic dysfunction, and next, cardiomyopathy, exists, especially for the patients presenting a high ventricular burden. At the same time, PVCs originating in the ventricular outflow tract may be a trigger for idiopathic ventricular fibrillation.

The most frequent mechanism involved in the OTA is related to the calcium-dependent triggered activity - cAMP-mediated, causing delayed afterdepolarizations (1). There is an activation of the protein kinase A that enhances the slow inward of Ca2+ current and, next, the calcium release from the sarcoplasmic reticulum through phosphorylation, which further activates the Na+/Ca2+ exchanger, resulting in a delayed afterdepolarization (2). Other mechanisms involved in other forms of idiopathic VT, such as verapamil-sensitive VTs (3) and idiopathic ventricular fibrillation (4), remain unclear, although studies have shown that they originate from Purkinje fibers.

Despite a benign prognosis when compared to structural heart disease–associated VT, symptoms compromising the quality of life and even death in patients with OTA are reported. Most frequently, patients present palpitations, usually in the 2nd to the 5th decade, either presyncope or dizziness, and rarely true syncope. There is a high variation of symptoms, from the absence of symptoms (up to 20%) to sudden death (5).

Possible triggers of OT arrhythmias are thought to be exercise-related, stress, and caffeine. For women, the hormonal flux seems to be a trigger, as ventricular arrhythmias are observed mostly during pregnancy, in the perimenstrual or premenstrual period (6). The usual means of OT arrhythmias detection are the 12 leads ECG, the Holter monitoring system, and the long-term monitoring systems.

The Idiopathic OT arrhythmias may arise either from the right ventricular outflow tract (RVOT) in 60% of patients, more frequently from the septal wall compared to the free wall, and the left ventricular outflow tract (LVOT) in 20% of patients (7), and more precisely from the aorto-mitral continuity, the anterior aspect of the mitral annulus, the aortic cusps, or the epicardium.

It is paramount to distinguish between idiopathic OTA and the ventricular arrhythmias observed in structural cardiac diseases as arrhythmogenic right ventricular dysplasia (ARVD). The ECG analysis, as well as the cardiac imaging – transthoracic echocardiography, cardiac MRI, or CT, are extremely important, besides the medical and the family history of the patients. Despite the results of some studies that have noticed anomalies such as focal thinning, focal adipose infiltration, or abnormal contraction in the RV (8,9), there are no clear findings to suggest a relationship between structural abnormalities and idiopathic RVOTA (10).

A therapeutic intervention is requested when patients are symptomatic or present a deterioration of the cardiac function. The recommendations for using antiarrhythmic drugs are based on either small or non-controlled studies, with β blockers and calcium–channel blockers (11) being the most studied, and with less evidence for flecainide (12). Because of the systemic toxicity, amiodarone is recommended for cases where either drugs or ablation fail (13).

The European Society of Cardiology recommendations (2022) for the treatment of patients with idiopathic ventricular arrhythmias [14] are presented in Table 1.

Table 1. The European Society of Cardiology recommendations (2022) for the treatment of patients with idiopathic arrhythmias. I - Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective; IIa - Weight of evidence/opinion is in favor of usefulness/efficacy; IIb - Usefulness/efficacy is less well established by evidence/opinion; III - Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.

Arrhythmias	Ablation	β blockers	Ca blockers	Flecainide	Amiodarone
RVOT ≥10% burden – symptomatic patients, normal LV function	I	IIa	IIa	IIa	III
LVOT ≥10% burden- symptomatic patients, normal LV function	IIa	I	I	IIa	III
RVOT with LV dysfunction	I	IIa	III	IIa	IIa
LVOT with LV dysfunction	I	IIa	III	IIa	IIa
Asymptomatic patients with ≥20% buden	IIb				III

Catheter ablation is recommended as the first-line therapy for RVOT arrhythmias with rare complications [15], but when it comes to LVOT arrhythmias, the rate of success is lower and associated with a higher level of recurrences and procedural complications [16].

In the last decades, we have observed overwhelming data regarding the multiple forms of VT occurring in patients without structural heart disease, which account for 10 to 20% of all VTs. Therefore, it is paramount to establish the OT's precise location, right or left, based on the 12 lead ECG, to correctly detect patients who are prone to have structural or genetic diseases. Also, establishing the origin of arrhythmias is extremely important for guiding the proper management of the patients – wait and see approach, a proper antiarrhythmic therapy selection, or transcatheter ablation.

This study aims to establish the feasibility of using a clinical score based on physical activity, age, and gender to determine the origin of outflow tract arrhythmias when compared to the origin obtained at the 3-D mapping at the electrophysiological study. As secondary endpoints of this study, we evaluated the accuracy of two simple criteria from the 12 lead ECG – the QRS morphology in lead V1 and the R wave transition in the precordial leads when compared to the origin obtained at the 3-D mapping, and next, we compared the accuracy between the clinical score and the ECG approach.

2. Material and Methods

2.1. Study population

117 patients were retrospectively evaluated in our Cardiology Department for ventricular outflow tract arrhythmias. Based on the 12 lead ECG evaluation, the origin of the arrhythmias was established to be either in the RVOT or LVOT. Based on the echocardiography, cardiac CT, and/or MRI, an underlying structural heart disease was excluded or confirmed.

If patients presented a high ventricular burden on the 24-hour ECG monitoring (>10000 PVCs/24h), with arrhythmias supposed to originate in the RVOT, and were either symptomatic or had LV systolic dysfunction, they were scheduled for radiofrequency catheter ablation. If patients were symptomatic and presented a high ventricular burden with arrhythmias supposed to originate in the LVOT, antiarrhythmic therapy with β or Calcium blockers was started. After 1 month, a 24-hour ECG monitoring was performed. In case of persistence of a high ventricular burden, therapy with flecainide was started and another 24-hour ECG monitoring after 1 month was performed. For the patients with persistent high ventricular burden despite flecainide treatment and for the patients presenting LV dysfunction, catheter ablation was scheduled.

Data such as gender, age, level of physical activity, clinical ECG, and echocardiography parameters were registered for each patient. Regarding the level of physical activity of each patient, a simple classification was used as follows: sedentary for patients getting little or no exercise daily (as working in an office), moderately active for patients running one hour daily or work based on moderate physical activity, vigorously active for patients with moderate to intense physical activity more than two hours daily, and finally extremely active as in the case of the athlete patients.

The ECG represents a critical component of the evaluation of patients with arrhythmias. The ECG tracings were performed using a BTL ECG, analyzed at a paper speed of 25 mm/s, and reviewed by one cardiologist each. No ECG software was used for interpretation. For each ECG, the PVC-QRS morphology in lead V1 and the precordial lead transition were evaluated. If the PVC -QRS presented an LBBB morphology, an inferior axis, and a late transition ≥V4, the origin was established to be in the RVOT. If the PVC -QRS had an RBBB morphology or an LBBB morphology but with an early precordial transition < V3, and an inferior axis, the location was set to be in the LVOT. Next, the concordance between the arrhythmia origin based on the 12 lead ECG and 3D mapping system site was evaluated.

The RVOT arrhythmias usually present a left bundle branch block (LBBB) morphology, an inferior frontal QRS axis, and a leftward R wave transition (the first precordial lead where R≥S) in the precordial leads. Other parameters considered highly suggestive of RVOT origin are an R wave transition ratio in V2<0.6, and a delayed R wave transition compared to the transition in sinus rhythm [17]. Several features allow a more detailed location of the arrhythmias such as:

1. A QS aspect in lead I predict an anterior location.
2. A R or qR aspect in lead I predicts a posterior location.
3. The presence of the R wave notching and wider PVC - QRS in the inferior leads predicts a free wall location.
4. A narrow PVC–QRS is suggestive of a septal origin.
5. A positive or isoelectric PVC – QRS in lead AVL predicts a proximal location.
6. A negative PVC – QRS in lead AVL suggests a distal location.

The LVOT arrhythmias may present a right bundle branch (RBBB) morphology, as well as LBBB morphology, and an inferior QRS axis. In the case of a right coronary cusp (RCC) origin, which lies posterior to the RVOT wall, the morphology is predominantly LBBB. For arrhythmias originating from the lateral mitral annulus, a rightward R wave transition is observed, with a QRS morphology shifting from LBBB to RBBB. An RBBB morphology associated with a right inferior axis is more frequently observed in left coronary cusp (LCC) arrhythmias, while the presence of an R-wave in lead aVL is suggestive of non-coronary cusp (NCC) origin. The R-wave amplitude from the inferior leads is usually higher for the LCC compared to the RCC origin.

Because arrhythmias with an LB morphology and inferior axis are challenging in differentiating between an RV versus an LV OT origin, our purpose was to determine the accuracy of the 12 lead ECG in predicting a right versus left origin of the OT arrhythmias (Figure 1) based on the QRS morphology in V1 and the R wave transition in the precordial leads compared to the one obtained from the 3D mapping system.

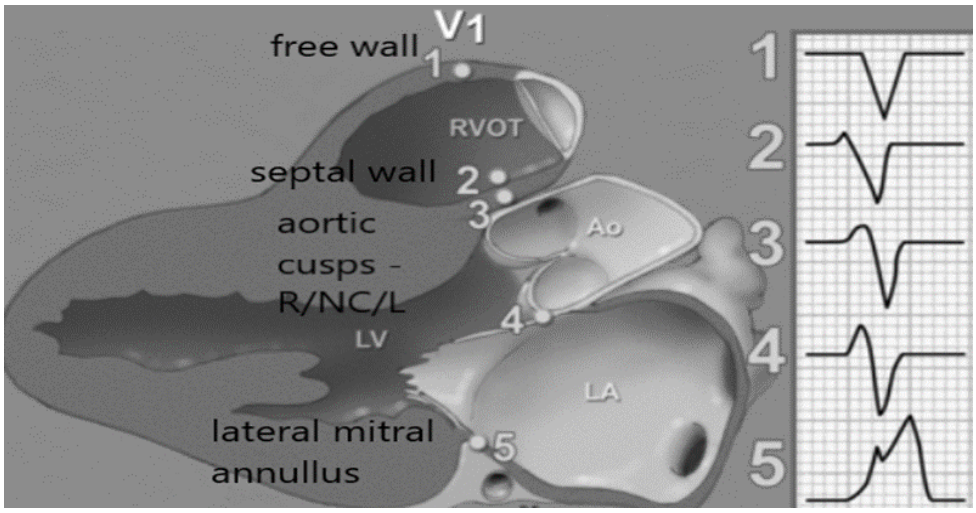


Figure 1. The QRS morphology in the lead V1 depends on the location of the arrhythmias originating in the outflow tract.

2.2. Electrophysiological procedure

Anti-arrhythmic therapy was interrupted five half-lives before the procedure. Through the femoral vein, a quadripolar electrode catheter was inserted and, next, positioned in the RV. If the origin was suspected to be in the RVOT, an 8F quadripolar catheter with a 4 mm distal electrode, sensor-enabled interelectrode spacing of 1-4-1mm, and a flexible tip (Abbott Laboratories, Abbott Park, IL, USA) was inserted through the femoral vein. If the origin was suspected to be in the LVOT, the mapping catheter was inserted through the femoral artery and positioned in the LVOT.

The 12-lead ECG and the bipolar and unipolar intracardiac electrograms were recorded with a filter setting for the intracardiac electrograms (EGM) set at 30 –500 Hz.

The 3D geometry of RVOT/LVOT was reconstructed by navigating the mapping catheter within the suspected chamber using the non-contact electro-anatomical mapping system (Ensite system, Abbott Laboratories). The arrhythmias, either premature ventricular contractions (PVC) or ventricular tachycardia (VT) at baseline and during isoprenaline infusion (1 –4 μg/min) were registered.

The earliest activation (EA) site was identified by using a broad color setting with a high pass filter set at 2 Hz while stepping back in time where the red color area turns to blue. The EA zones were targeted by radiofrequency (RF) catheter ablation. RF energy was delivered through the ablation catheter in a temperature-control mode (Stockert, Biosense Webster, Diamond Bar, CA, USA) with a power output of 30 up to 40 W to achieve a temperature of 45-48°C for 60 s. A waiting period of 30 min was applied for all procedures. If the arrhythmias were not eliminated, the adjacent zones were further investigated by activation mapping to discover other ablation zones and subsequent RF ablations were applied in those areas. Success was considered if the clinical arrhythmia disappeared during RF and didn't reoccur within 30 minutes after the last RF firing, and if arrhythmia was non-inducible after Isoproterenol infusion (1-10 μg/min) [16].

2.3. Statistical analysis

IBM SPSS Statistics for Windows (version 20.0; IBM Corp., Armonk, NY, USA) was used for analysis, with continuous variables presented as median and mean ± standard deviation (SD) and categorical variables presented as counts and percentages. Continuous variables were analyzed with a paired t-test. Results were reported also as odds ratios (OR) with 95% confidence interval (CI). The OR is a measure of how strongly a parameter is associated with the final result, in our case the true origin of the arrhythmia. When an OR >1, as the continuous variable increases, the parameter is more likely to be linked with the true origin. When the CI for the OR includes the number 1 then the calculated OR would not be considered statistically significant. A P-value <0.05 was considered statistically significant.

3. Results

3.1. General results

Among the 117 patients evaluated in our Cardiology Department, one patient, RV arrhythmogenic dysplasia was diagnosed. After analyzing the 24-hour ECG monitoring for the ventricular burden calculation, only 72 patients presented a significant ventricular burden ≥10%. Ventricular dysfunction was not detected in any of the patients. After starting the antiarrhythmic treatment, we observed a significant decrease in the ventricular burden for 11 patients. Finally, 61 patients were enrolled in this study. The clinical, ECG, and echocardiographic parameters of the patients are presented in Table 2.

Table 2. Clinical, ECG, and echocardiographic parameters. RVOT, right ventricular outflow tract; LVOT, left ventricular outflow tract; PVC, premature ventricular contraction; LVEF, left ventricular ejection fraction; SD, standard deviation.

Age (years; mean ± SD)	48 ± 19.5
Female/ Male (n)	37/24 patients
Use of antiarrhythmic drugs (%) - β blockers - Ca blockers - Flecainide - Amiodarone	34.42% (21/61 patients) 26.22% (16/61 patients) 1.63% (1/61 patients) 3.27% (2/61 patients) 3.27% (2/61 patients)
ECG based origin - RVOT - LVOT	 73.77% (45/61 patients) 26.22% (16/61 patients)
PVC burden (%; mean ± SD)	19 ± 9.1
LVEF (%;mean ± SD)	59 ± 5.5
History of Hypertension (n)	23/61
History of Diabetes (n)	6/61
Hypercolesterolemia (n)	14/61

3.2. Localizing the arrhythmia site during the electrophysiological procedure

The 3D electroanatomic maps were created for all patients. In one patient with RVOT suspected origin, the true location was identified in the LVOT (right coronary cusp) and was successfully ablated. In 2 patients, an LV epicardial origin of the arrhythmia was detected and ablation was not performed.

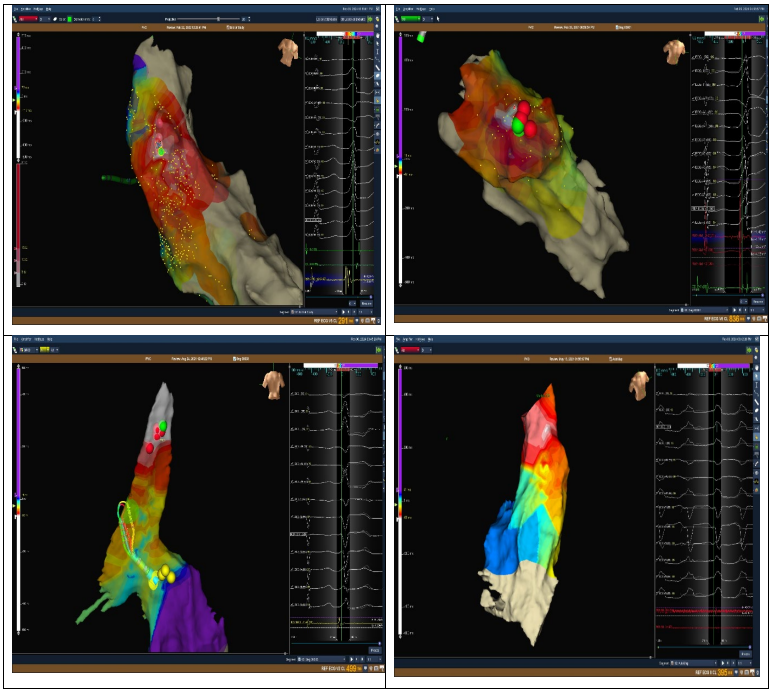
Acute procedural success was obtained for 58 out of 61 patients (95.08%), 43 out of 44 patients with true RVOT arrhythmias (97.72%), and 15 out of 17 patients with true LVOT arrhythmias (88.23%) (Figure 2). Ablation was delivered at the RVOT and LVOT sites as it is shown in Table 3. For one patient with RVOT-origin ectopies, after RF applications in the earliest activation site located in the septal wall, ectopies disappeared for 20 minutes, and after this period, ectopies with a slightly similar morphology reappeared (9 out of 12 lead ECG similarity). After 3-D mapping of the new ectopy, the activation map revealed an EA site a region close to the first EA zone. RF applications in the new EA zone were not successful in suppressing the ectopy.

During a mean follow-up of 15 ± 11 months after the procedure, recurrence of arrhythmias with the same QRS morphology was observed in 2 patients from the RVOT group (4.65%) and in 2 patients from the LVOT group (12.5%). There were no significant differences in the procedural parameters such as the earliest activation time (p=0.71), the amplitude of the ventricular electrograms (EGM) at the successful ablation area (p=0.66), or in terms of duration (p=0.76) or number of RF firing (p=0.8) between the RVOT and LVOT sites.

Table 3. The earliest activation zone detected on the 3-D mapping compared to the ECG-based origin of arrhythmias originating in the outflow tract.

	RVOT	LVOT
Location detected during the EP procedure	43/61 patients	18/61 patients
Location-based on the ECG	45/61 patients	16/61 patients

Figure 2. 3-D origin of arrhythmias detected my mapping with the Ensite system (left) and the 12 lead ECG of the PVC (right). Left upper image – the 3D origin of the PVC is located in the LVOT, in the right coronary cusp, and the ECG reveals an RB morphology with the inferior axis. Right upper image - the 3D origin of the PVC is in the LVOT, in the left coronary cusp or left/ right coronary junction, and the ECG reveals an RBBB morphology with the inferior axis. Left lower image - the 3D origin of the PVC is in the RVOT, in the septal wall, and the ECG reveals an LBBB morphology with the inferior axis. Right lower image - the 3D origin of the PVC is located in the RVOT, in the free wall, and the ECG reveals an LBBB morphology, with late transition of the R wave in the precordial leads, and with notching of the RS in the inferior leads. The white zone surrounded by red represents the earliest activation zone. The green dots represent the successful sites where RF application induced the warming-up phenomenon and then, suppression of the arrhythmia.



3.3. Predictive value of the clinical parameters

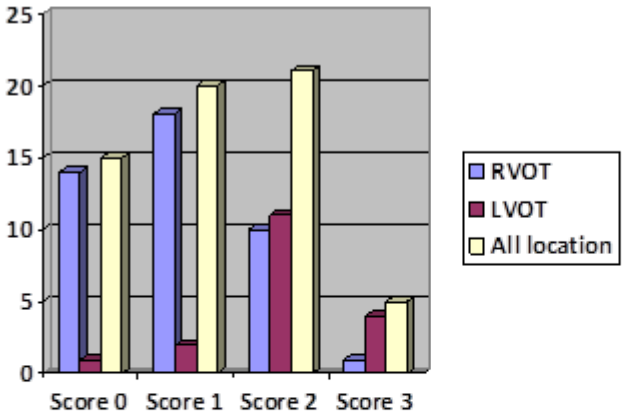
When the analysis of the clinical predictors was performed (Table 4), an LVOT origin was associated with age over 52 years (OR 54.8, CI 2.1−10.6), as well as a lower physical activity level (OR 2.3, CI 1.3−4.2), and the presence of arterial hypertension (OR 3.5, CI 1.9−6.7). The gender presented no significant predictive value. After performing a multivariable analysis, we observed that the age over 52 years is a powerful predictor for LVOT origin (OR of 3.3 (1.5−7.5, p = 0.002), and the activity level and the presence of hypertension are not independent predictors.

Based on a clinical score including the age, the sedentarism, and the presence of arterial hypertension, with 1 point for each clinical parameter, we observed a score of 0 for 15/61 patients (24.56%), a score of 1 for 20/61 patients (32.78%), a score of 2 for 21/61 patients (34.42%) and a score of 3 for 5 out of 61 patients (8.19%). A score of 0 or 1 was suggestive of an RVOT origin, and a score of 2 or 3 for a LVOT origin. Next, a positive predictive value for LVOT origin was established as: score 0 – 12%, score 1 – 26%, score 2 – 51%, and score 3 – 58% (Figure 3). This clinical score presented a 71% sensitivity level and a 69% specificity level. We did not observe significant differences in sensitivity and specificity between the RVOT versus LVOT groups.

Table 4. Parameters evaluated between the RVOT and LVOT groups.

Parameters	RVOT true location	LVOT true location	P value
Age (years; mean ± SD)	44 ± 18.5	52 ± 20	0.02
Female (n)	26/43 patients (60.46%)	11/18 (61.11%)	0.6
Level of physical activity			
- Sedentary	33 (76.74%)	16 (88.8%)	0.01
- Moderately active	7 (16.27%)	2 (11.11%)	
- Vigorously active	2 (4.65%)	0	
- Extremely active	1 (2.32%)	0	
History of Hypertension (n)	11	12	0.001
History of Diabetes (n)	4	2	0.71
Hypercolesterolemia (n)	8	6	0.68

Figure 3. Clinical score distribution related to the arrhythmia location



3.4. Predictive value of ECG parameters

Based on the ECG parameters as QRS morphology in lead V1, inferior axis, and the precordial lead transition, the origin of arrhythmias was established to be in the RVOT for 45 patients compared to 43 true EP locations and in the LVOT for 16 patients compared to 18 true origins (Figure 4). The overall accuracy of predicting the right versus left outflow tract origin of arrhythmias based on the ECG parameters was 96.72%, with a 100% sensitivity and 88.89% specificity. The accuracy for detecting the RVOT arrhythmias was 95.55% accuracy and 100% for the LVOT arrhythmias (p=0.7) (Table 5).

Figure 4. Comparison between the true locations detected during the electropysiological (EP) study and the ECG based location.

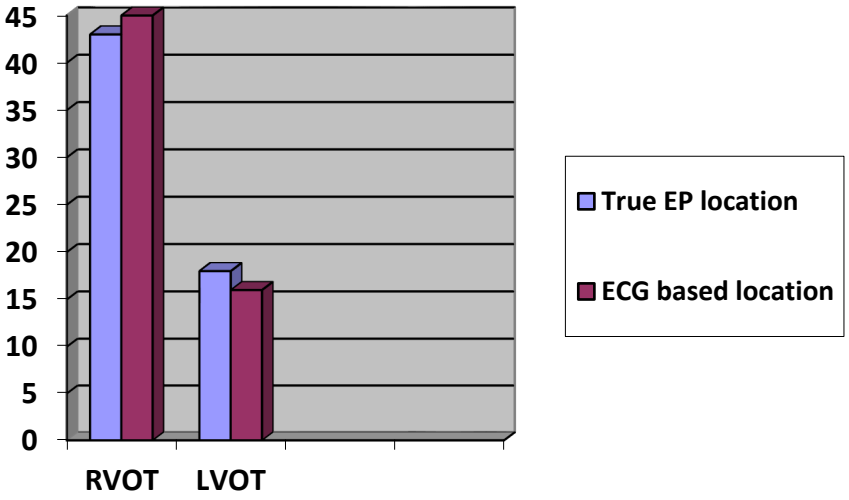


Table 5. Statistical parameters: accuracy, sensitivity, and specificity for predicting the RV versus LV OTA of the 12 lead ECG evaluation.

Parameters	Value	95% CI
Sensitivity	100.00%	91.78% to 100.00%
Specificity	88.89%	65.29% to 98.62%
Positive Likelihood Ratio	9.00	2.44 to 33.24
Negative Likelihood Ratio	0.00	
Positive Predictive Valu	95.56%	85.34% to 98.76%
Negative Predictive Value	100.00%	79.41% to 100.00%
Accuracy	96.72%	88.65% to 99.60%

4. Discussion

This study reveals the fact that an LVOT origin is associated with an advanced age, and arterial hypertension, clinical predictors that were also previously described [19,20], with age being an independent predictor. The incidence of cardiovascular diseases increases significantly with age due to the presence of hypertrophy, dysfunctions such as fibrosis, protein accumulation, or abnormal mitochondria that contribute to the heart's susceptibility to stress. The macroautophagy mechanism described as a lysosome degradation process decreases with aging and the murine macroautophagy loss-of-function models are associated with exacerbated cardiac dysfunction and next with deposits of misfolded proteins and dysfunctions [21].

No significant association between the gender and the location of arrhythmias was observed. A low activity level is also associated with an LVOT origin. This fact can be explained by the fact that sedentarism is associated with an increased age, and other comorbidities like hypertension, diabetes, etc. It is known that aging and pressure overload can lead to cardiac fibrosis and next to arrhythmias. Also, the association between arterial hypertension and ventricular arrhythmia is generally known [22]. Hypertension is an established risk factor for sudden cardiac death, and this risk increases in hypertensive patients who develop LV hypertrophy.

The most frequent location of the arrhythmias was noted RVOT, as already described in other studies [23]. Multiple ECG algorithms have been developed to predict the OTA origin, to guide the vascular access – venous or arterial, to increase the success rate of the ablation procedures, and to minimize the complication rate. Most of these algorithms were created especially for differentiating RVOT versus LVOT origin as it is shown in Table 6.

These algorithms [24-38] have a complex structure, usually based on a step-by-step analysis, and are difficult to memorize. The ECG algorithms based on the R wave transition zone (TZ) like Cheng, Betenski, Yoshida, He, Li, and Tada present a sensitivity that varies from 60 to 100% and a specificity that varies from 82 to 100%, similar to data obtained in our study. Those differences may be explained by the inter–assessors and the developer's heterogeneity, as well as the discrepancies in the studied population. A possible explanation for the high levels of accuracy, sensitivity, and specificity from our study might be the fact that this study only searched to differentiate right versus left OT, and not to precisely locate the origin in the RVOT (free wall versus septal wall) or in the LVOT (aortic cusps, AMV, mitral annulus) as compared to other studies.

Table 6. ECG algorithms published for differentiating RVOT versus LVOT origin.

Algorithm	Location	Number of patients	Criteria	Sensitivity (%)	Specificity (%)
Yang et al [24]	RVOT versus LVOT	45	The early beginning of QRS and peak/nadir in V2 predict the RVOT origin.	92	88
Cheng et al [25]	RVOT versus LVOT	42	R wave transition in V3 R wave deflection interval in V3 R wave deflection interval in V3 (>80 ms) and R wave amplitude index in V1 (>0.3) predicts the LVOT origin.	100	83
Ito et al [26]	RVOT versus LVOT	168	S wave in V6 R wave transition in V4 S wave in lead I R/S index and R wave duration in lead I	Septal RVOT 68% Free wall RVOT 81% His region 73%	-
Betensky et al [27]	RVOT versus LVOT	61	R wave transition index in V2 ≥0.6 predicts LVOT origin	95	100
Yoshida et al [28]	RVOT versus LVOT	112	R wave transition zone <0 predicts LVOT origin	88	82
He et al [29]	RVOT versus LVOT	695	TZ index and V_2S/V_3R, $Y=-1.15\times(TZ)-0.494\times(V_2S/V_3R)$. If ≥−0.76 predicts LVOT origin	90	87
Kaypakli et al [30]	RVOT versus LVOT	123	S-R difference in $V_1-V_2=(V_1S+V_2S)-(V_1R+V_2R)$. If >1.625 predicts RVOT origin	95	85
Joshi et al [31]	Septal versus free wall RVOT	46	QRS duration ≥140 ms and R notching in the inferior leads and R/S index ≤1 predict the origin in the free wall QRS morphology in lead I (anterior versus posterior) and AVL (caudal versus cranial)	74	93

Dixit et al [32]	RVOT – septal, His, free wall	14	The presence of R wave notching in the inferior leads R≥S in V4 predicts the origin in the septal wall	Septum 41%; Free wall 72% His 53%	
Zhang et al [33]	RVOT - septum vs free wall	65	LBBB morphology, inferior axis R wave transition ≥V4 Absence of RR' sau RSR' morphology in lead AVL QRS duration PVC/ QRS sinus rhythm ≥1.9 predicts free wall origin	Septum 79%; Free wall 92% His 88%	
Yamada et al [34]	LV Summit	27	RBBB morphology R wave index in AVL/AVR >1.1 and S wave in V5 or V6	87	100
Ouyang et al [35]	LVOT	15	R/S amplitude index (>0.5) and R wave duration index (>0.3) predicts LVOT origin		
Li et al [36]	LVOT	7	RBBB morphology R wave transition in V2 Superior axis A small S wave in V6 suggests an inferior septal process origin		
Tada et al [37]	Mitral annullus - antero lateral location	19	R wave transition in precordial leads <V2 and R sau Rs in V2 till V5	60	99.7
Kumagai et al [38]	Mitral annulus - antero lateral	35	R wave transition in V1 or V2 S wave in V6 Positive R waves in the inferior leads and R amplitude ≥1.6 mV in AVF	85	

Another issue to be discussed is the fact that some studies established the origin of the arrhythmia using only pace mapping and not using 3-D activation maps or a combination, while pace mapping in the outflow tracts exhibits a low spatial resolution. Other studies predicted the arrhythmia origin only based on fluoroscopy, without the use of pace mapping and activation mapping. This fact may lead to errors in localizing correctly the origin of the arrhythmias as compared to the use of 3-D activation maps.

Our approach based only on the QRS morphology in lead V1 and the transition zone from the precordial leads presents excellent accuracy, sensitivity, and specificity, and can simplify the mapping and ablation procedure by selecting the proper vascular approach. Meanwhile, it is easy- to memorize and has a simple design compared to other algorithms. The complex algorithms may also lessen inaccurate results through the stepwise and discriminating analysis of the ECGs. Most of the time, they are difficult to memorize, so the ECG analysis is most of the time challenging when they are used. In our study, in the case of an erroneous prediction of the RVOT origin, the effectiveness of the ablation was not affected, but a change in the vascular access, causing this way a prolongation of the total procedural time.

The clinical score we propose may lessen the prediction of an LVOT origin of the arrhythmias when combined with ECG algorithms. Also, many patients presenting ventricular arrhythmias suffer from a lot of comorbidities and structural heart diseases. Aging and pressure overload can lead to cardiac fibrosis. Similarly, the association between hypertension and ventricular arrhythmias is well established.

Also, a high clinical score suggesting an LVOT origin might be useful in selecting an antiarrhythmic treatment as the first-line therapy, especially for elderly patients or those with significant comorbidities. For this category, catheter ablation should be scheduled only for cases with limited or no response to antiarrhythmic drugs, or for those presenting LV dysfunction, as the risk of periprocedural complications rises with increased age and

a high burden of comorbidities. A low clinical score suggesting an RVOT origin could direct the first-line therapy to catheter ablation, especially for younger patients who do not want to receive long-term antiarrhythmic therapy or who already present side effects of this therapy. Concerning the impact of the clinical score on the patient outcome, the OTAs usually have a benign prognosis.

The ECG-based approach can also be useful for guiding first-line therapy depending on whether the true origin is in the RVOT or LVOT to catheter ablation, respectively to antiarrhythmic drugs. On top of that, the ECG parameters might be useful in selecting the proper vascular approach – venous for RVOT locations versus arterial for LVOT sites, to shorten the total procedural time.

However, the combination of both clinical and ECG parameters could increase the prediction of the site of origin before the procedure. Further prospective studies involving a higher number of patients with OTAs are needed to increase the prediction of the exact location of these arrhythmias. Meanwhile, cardiologists and not only should also be aware of these results and use the ECG parameters together with the clinical score to enhance diagnostic accuracy and guide the proper first-line therapy.

It is known that idiopathic OTAs occur in patients with structurally normal hearts and that the ventricular burden in the general population is unknown. What this study adds is the fact that not only the OTA's incidence increases with aging as is noted in previous studies, but also the fact that the arrhythmias originating from the LVOT are more prone to appear in elderly patients. The age over 52 years was a powerful predictor for LVOT origin, while the activity level and the presence of hypertension are not independent predictors. So far, the studies have shown that the incidence of VT is similar across sexes, while that of PVCs is more frequent among women. In our study, gender had no significant predictive value for OT origin.

Limitations

Being a retrospective study, some data might be missing, as this study relies on others for accurate clinical parameters, ECGs, and electrophysiological procedure recordkeeping. The number of patients included in this study is relatively small and we did not include pediatric or older patients, so the relationship between the age and the arrhythmia morphology cannot be discussed. Other limitations reported also by other studies are the variability of lead placement, as well as the spatial relationship of the heart–thorax, which can create misinterpretation of the ECGs [39,40,41]. Also, during ablation. some foci from one side might have been ablated from the opposite side, especially in cases of VA originating from the aortic root or posterior RVOT, this chamber being adjacent structures. More studies are needed to correctly evaluate the accuracy and usefulness of the ECG algorithm and the proposed clinical score.

5. Conclusion

Our clinical score, encompassing older age, sedentarism, and the presence of arterial hypertension, for prediction of LVOT origin, presents a lower sensitivity and specificity when compared to the ECG approach based on the QRS morphology in lead V1 and the transition zone in the precordial leads for differentiating the right versus left outflow tract arrhythmias origine. However, the combination of both clinical and ECG parameters could increase the prediction of the site of origin before the procedure.

Ethical considerations- patient confidentiality was maintained although this is a retrospective study.

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