Automatic Prediction of the Origin in Outflow Tract Ventricular Arrhythmias with Machine Learning Combining Clinical Data and Electrocardiogram Analysis

Álvaro José Bocanegra[1], Diego Penela[2], Rafael Sebastian[3], Guillermo Jimenez-Perez[1], Andrea Saglietto, David Soto-Iglesias[4], Antonio Berruezo[4], Gemma Piella[1], Oscar Camara[1]

[1] Universitat Pompeu Fabra, Barcelona, Spain
[2] Humanitas Research Hospital, Milan, Italy
[3] University of Valencia, Valencia, Spain
[4] Teknon Medical Centre, Barcelona, Spain

Abstract

Identifying the site of origin in outflow tract ventricular arrhythmias (OTVAs) is crucial for the success of radiofrequency ablation procedures. Despite recent progress, this task remains challenging and too dependent on clinician's expertise, since origin estimation merely relied on visual inspection of the electrocardiogram (ECG).

This study presents an automatic system to identify the ventricular origin in OTVA with machine learning algorithms. The system comprises two cascading classifier models that utilize raw electrocardiogram (ECG) signals, relevant ECG signal features, and clinical data. It was trained using data from four different databases.

The final model achieved an accuracy of 95.45%. Furthermore, we identified specific regions in the ECG signal, such as the transition between the R and the S waves in V3 and V4 and the beginning of the QRS complex in V2, which are key when estimating the OTVA origin.

1. Introduction

Ventricular Tachycardia (VT) plays a significant role in sudden cardiac death, accounting for nearly 80% of cases, underscoring the critical importance of accurate VT treatment [1]. Within the spectrum of VT, idiopathic ventricular arrhythmias pose a unique challenge, as the underlying mechanisms triggering these arrhythmias remain unclear. Furthermore, the most common type originates from the outflow tracts, and the structural and functional complexity of these structures intensifies the difficulty in diagnosing and planning treatment for OTVAs. This type of arrhythmia can be treated with drugs or Radiofrequency Ablation (RFA) [2].

However, the implementation of RFA has proven to be suboptimal, leading to excessively high recurrence rates [3]. To enhance the performance of the RFA procedure, pre-operative planning is crucial. The goal is to identify the optimal ablation site, known as the ectopic foci or the site of origin (SOO) of the OTVA before the procedure. The primary source of information for this analysis is the ECG, as its morphology is affected in patients with OTVA [2]. Visual inspection provides an estimate of the SOO; specifically, it is used to determine whether the origin is in the right or left ventricle. An incorrect estimation can lead to a suboptimal intervention approach, increasing the interventional time. Relying solely on ECG visual inspection may prove insufficient for SOO prediction. Recently, advanced methods have been developed to predict the right or left ventricle outflow tract (RVOT or LVOT, respectively) origin.

These methods include ECG visual morphology analysis along with patient data, such as the one described by Penela et. al [4], this algorithm incorporates clinical features such as sex, hypertension, and age, and conducts an ECG analysis based on the precordial R/S transition (defined as the first precordial lead with a dominant R wave) as well as the amplitude in V3 if the precordial transition occurs in this lead. However, this method includes manual thresholds when including the age and the V3 amplitude, also, it depends on the clinician's expertise to determine the R/S transition.

Since premature ventricular contraction (PVC) are present in OTVA cases [2], other methods include R/S transition of the sinus rhythm along with the transition in the PVC to differentiate RVOT and LVOT origins [5, 6].

Doste et. al used machine learning to classify the OTVA origin using real and simulated ECG signals [7]. Nevertheless, this approach did not include any patient data.

In the following sections, we introduce our novel pro-

posal—a comprehensive ML methodology that integrates signal analysis methods for both simulated and real data, patient-specific information, and an exploration of the most relevant features. This integrated approach not only enhances classification accuracy but also provides valuable interpretability, empowering clinicians with insights into the critical factors influencing treatment decisions.

2. Methods

We propose a two-stage classification system. In the first stage, we trained a classifier model using the QRS complexes of the different leads, following the findings of Doste et al. [8]. In the second stage, the resulting probabilities of the previous classifier are combined with patient information (as proposed by Penela et. al [4]) to refine the prediction. After training, feature relevance was analyzed in both models to improve the performance and interpret the results.

2.1. Databases

We used multi-centric 4 ECG databases: 1) DS-2496, composed by 2496 simulated ECGs created to imitate OTVA patients following Doste's pipeline [9]; 2) DS-31, which consisted on 31 cases from Hospital Clinic, Barcelona; 3) DS-334, corresponding to an open source database published by Zheng et al. [10]; and 4) DS-111, which was retrieved from Hospital Teknon, Barcelona. The latter was partially used by Penela et al. [4], and consisted on 111 cases. All the data was collected according to internal ethical committee regulations, and with written informed consent from every patient.

DS-31, DS-334 and DS-2496 included 12-lead ECG signals and the outcome of the patient (RVOT or LVOT origin). DS-111 included additional information, specifically, multiple beats from each patient, including the PVC, and the clinical information used to predict the SOO in [4].

Considering the lack of standardization in the available databases, we adopted a two-step approach. Initially, we used the first three databases for training the first-stage classifier, utilizing solely the QRS morphology as input. Following this, we applied the first classifier to extract features from DS-111 and used these extracted features to train the second classifier. In essence, the output of the first classifier served as the input for the second classifier. The overall model was tested using a subset of DS-111, because it was the only database that had both QRS complex and patient data.

We divided the dataset into training (80%) and test (20%) using a stratified splitting to maintain the proportion on both subsets since RVOT is more common [11]. We split each database individually, and then we merged the respective subsets of DS-2496, DS-31 and DS-334 for the first model. Then, we used 5-fold cross-validation and performed grid search for hyperparameters optimization in both models.

2.2. Classification system

The classification system consists of 2 classifier models connected in cascade. The first was trained following the guidelines set in [7]. The QRS complexes of each lead were resampled to 10 samples and concatenated in a vector. To analyze the relevance of each QRS complex in every lead, we used all 12 leads rather than the most relevant leads previously reported, we made this decision because we wanted to include in the morphological analysis all leads.

We tested support vector machines (SVM), multiple layer perceptron (MLP), extra trees (ET) and random forest (RF) algorithms offered by scikit-learn [12]; and the XGBoost solution for python by dmlc [13], and we compared their performance using the test subset.

The design of the second model drew inspiration from the weighted hybrid algorithm proposed by Penela et al. [4]. To enhance the model's ability to generalize and prevent overfitting, we computed the precordial transition rather than relying on clinician-reported values. Additionally, we removed any age or V3 amplitude-related thresholds.

We predicted the outcome of the training dataset with the first model and used the probability per class as an input for the second model, along with the amplitude of the V3 lead, the calculated R/S transition, and the clinical features of the patient. Then, we followed the same procedure as for the first model to train the second model.

Since the precordial transition lead depends on the cardiac electrical axis in the horizontal plane and the clinical features of the patient [14], we used the information of the sinus rhythm to standardized the R/S transition. We calculated the R/S transition for both beats and then computed them as a single feature with the subtraction of both values.

To calculate both R/S transitions, we delineated the ECG signal of each patient using the delineation convolutional neural network designed by Jimenez-Perez et al. [15]. Then, the cardiac cycles were separated, , extracting the PVC beat and the immediately preceding one. From here, we segmented the QRS complexes and calculated the R/S ratios on the precordial leads for both beats.

Subsequently, we analyzed the relevance of the features in the first model to improve the classification process by identifying, and keeping the most relevant features that had clinical sense. We used RF models and calculated the relevance of each feature using the Gini's coefficient. Given that each feature represented a 10% of the original signal, we were able to determine which sections of the ECG

were the most relevant for the classification. These sections were used to train the second model.

3. Results

The accuracies obtained in the testing subset for the first-stage models are reported in Table 1.

Table 1. Accuracies obtained for the first model using different ML algorithms. The test set was composed by 20% of DS-2496, DS-31 and DS-334.

Model	Accuracy	LVOT recall	RVOT recall
RF	98.39%	99.02%	98.35%
SVM	92.10%	93.39%	89.43%
MLP	95.73%	98.82%	96.00%
ET	98.93%	99.21%	98.59%
XGBoost	98.59%	99.06%	98.06%

Feature relevance from RF was analyzed per lead and per individual section. Precordial leads showed the highest relevance, accumulating 80% between V1 and V6. Among them, V2, V3 and V4 were the most relevant. When analyzing the different sections of these leads, we found that the most relevant part of the QRS complexes in V3 and V4 was the section between 60% and 70% of the QRS length, which correspond to the R/S section, while in V2 the most relevant section was between 10% and 20% of the QRS complex, which corresponded to the beginning of the Q wave, as shown in Figure 1.

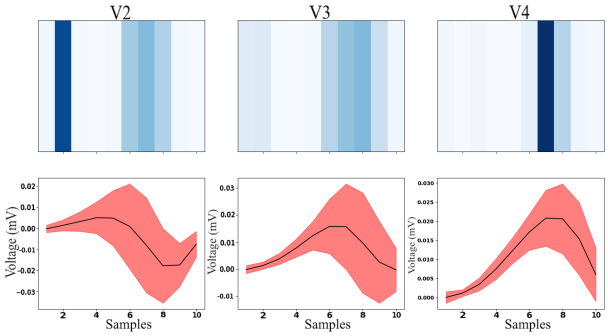

Figure 1. Feature relevance for leads V2, V3 and V4. Top row: Relevance colormap (darker blue means higher relevance). Bottom row: average signal per lead (black) and the corresponding standard deviation (red).

These amplitudes were included as additional features in the second-stage classifier model. Also, we tested the DS-111 using RF, ET and XGBoost, since these algorithms achieved the best performance. The best results in the second model were obtained when using XGBoost as the first model. We got 73% of accuracy when testing the first model on DS-111. The second model included the inference of the first model, the clinical features and the relevant amplitudes found after the feature relevance analysis, the overall model achieved 95.45% of accuracy. The accuracies obtained in the test subset for the second-stage models are reported in Table 2.

Table 2. Accuracies obtained for the overall model using different ML algorithms. The test set was composed by 20% of DS-111.

Model	Accuracy	LVOT recall	RVOT recall
RF	68.18%	50.0%	75.0%
SVM	86.36%	50.0%	100.0%
MLP	95.45%	83.33%	100.0%
ET	77.27%	50.0%	87.50%
XGBoost	81.81%	83.33%	81.25%

When analyzing the feature relevance in the RF model, we found that the most relevant feature was the amplitude in V2 with 15.36%. Amplitudes accumulated 43% of the relevance, R/S transition accumulated 11.08%, the clinical features reached 19.9% (being age the most relevant feature with 11.9%) and the class probability obtained from the first model got 25.28%.

4. Discussion and conclusions

We developed a classification algorithm to identify the site of origin (left/right ventricle) in OTVA cases. After training multiple models, and analyzing the partial results to improve the outcome we reached an accuracy of 95.45%.

The analysis of the first model showed that the most relevant features were in V2, V3 and V4, which aligns with consistent with findings in previous works [4, 7, 8]. We went a step further and analyzed the feature relevance on segments of 10% of the signal, finding that the most relevant segments were located on the transition between the R and the S waves in V3 and V4 and the beginning of the QRS complex in V2. This is an important outcome since most of the algorithms developed to find OTVA SOO consider the central zone of the precordial leads as the most problematic to differentiate RVOT and LVOT [4–8, 11, 14].

For the second model, we included clinical features previously reported [4], avoiding threshold choices or data that depends on the clinician expertise to maximize the generalization power of the algorithm. We avoid thresholds by directly using age and we prevent human error by calculating the R/S transition using both sinus rhythm and PVC beat transitions.

The posterior feature relevance analysis showed how the

inclusion of the amplitudes boosted the performance of the model, while the R/S transition was less relevant. The clinical features reached 19.9% of relevance with just 3 features, which shows the potential of including clinical features for the classification. Finally, class probability from the first model reached 25.28% of the total relevance, being the second most relevant group. This suggests that working on previous weaker classifiers may increase the performance of the final model.

This system was designed with simple and interpretable models and the analysis of the feature importance allowed us to enhance the performance in classification while preserving the clinical validity. However, this approach has some limitations on its different stages. First, when downsampling the signals to 10 samples, most of the high frequency components were discarded. Furthermore, the time information may not be accurately represented since when concatenating the different leads, simultaneously ocurring events may be lost. Second, the feature relevance analysis may depend on the performance of the RF algorithm, which is relatively low in the second stage when comparing with the other classifier models. Finally, the system was tested in a dataset acquired in a unique center. To assess the robustness of the system, it should be tested on a multicenter dataset, despite these limitations, the approach seems promising, and the methodology could be extended to find specific SOO with a high accuracy and interpretability.

References

[1] Koplan BA, Stevenson WG. Ventricular tachycardia and sudden cardiac death. In Mayo Clinic Proceedings, volume 84. Elsevier, 2009; 289–297.

[2] Lerman BB. Mechanism, diagnosis, and treatment of outflow tract tachycardia. Nature Reviews Cardiology 2015; 12(10):597–608.

[3] Marrouche NF, Wilber D, Hindricks G, Jais P, Akoum N, Marchlinski F, Kholmovski E, Burgon N, Hu N, Mont L, et al. Association of atrial tissue fibrosis identified by delayed enhancement MRI and atrial fibrillation catheter ablation: the DECAAF study. Jama 2014;311(5):498–506.

[4] Penela D, Falasconi G, Carreño JM, Soto-Iglesias D, Fernández-Armenta J, Acosta J, Martí-Almor J, Benito B, Bellido A, Chauca A, et al. A hybrid clinical and electrocardiographic score to predict the origin of outflow tract ventricular arrhythmias. Journal of Interventional Cardiac Electrophysiology 2023;1–12.

[5] Betensky BP, Park RE, Marchlinski FE, Hutchinson MD, Garcia FC, Dixit S, Callans DJ, Cooper JM, Bala R, Lin D, et al. The V2 transition ratio: a new electrocardiographic criterion for distinguishing left from right ventricular outflow tract tachycardia origin. Journal of the American College of Cardiology 2011;57(22):2255–2262.

[6] Efremidis M, Vlachos K, Kyriakopoulou M, Mililis P, Martin CA, Bazoukis G, Dragasis S, Megarisiotou A, Unger P, Frontera A, et al. The RV1-v3 transition ratio: A novel electrocardiographic criterion for the differentiation of right versus left outflow tract premature ventricular complexes. Heart Rhythm O2 2021;2(5):521–528.

[7] Doste R, Lozano M, Jimenez-Perez G, Mont L, Berruezo A, Penela D, Camara O, Sebastian R. Training machine learning models with synthetic data improves the prediction of ventricular origin in outflow tract ventricular arrhythmias. Frontiers in Physiology 2022;13:909372.

[8] Doste R, Lozano M, Gomez JF, Alcaine A, Mont L, Berruezo A, Camara O, Sebastian R. Predicting the origin of outflow tract ventricular arrhythmias using machine learning techniques trained with patient-specific electrophysiological simulations. In 2019 Computing in Cardiology (CinC). IEEE, 2019; Page–1.

[9] Doste R, Sebastian R, Gomez JF, Soto-Iglesias D, Alcaine A, Mont L, Berruezo A, Penela D, Camara O. In silico pace-mapping: prediction of left vs. right outflow tract origin in idiopathic ventricular arrhythmias with patient-specific electrophysiological simulations. EP Europace 2020;22(9):1419–1430.

[10] Zheng J, Fu G, Anderson K, Chu H, Rakovski C. A 12-Lead ECG database to identify origins of idiopathic ventricular arrhythmia containing 334 patients. Scientific Data 2020; 7(1):98.

[11] Anderson RD, Kumar S, Parameswaran R, Wong G, Voskoboinik A, Sugumar H, Watts T, Sparks PB, Morton JB, McLellan A, et al. Differentiating right-and left-sided outflow tract ventricular arrhythmias: classical ECG signatures and prediction algorithms. Circulation Arrhythmia and Electrophysiology 2019;12(6):e007392.

[12] Pedregosa F, Varoquaux G, Gramfort A, Michel V, Thirion B, Grisel O, Blondel M, Prettenhofer P, Weiss R, Dubourg V, Vanderplas J, Passos A, Cournapeau D, Brucher M, Perrot M, Duchesnay E. Scikit-learn: Machine Learning in Python. Journal of Machine Learning Research 2011; 12:2825–2830.

[13] Chen T, Guestrin C. XGBoost: A Scalable Tree Boosting System. In Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining, KDD '16. New York, NY, USA: ACM. ISBN 978-1-4503-4232-2, 2016; 785–794. URL http://doi.acm.org/10.1145/2939672.2939785.

[14] Mariani MV, Piro A, Della Rocca DG, Forleo GB, Pothineni NV, Romero J, Di Biase L, Fedele F, Lavalle C. Electrocardiographic criteria for differentiating left from right idiopathic outflow tract ventricular arrhythmias. Arrhythmia Electrophysiology Review 2021;10(1):10.

[15] Jimenez-Perez G, Alcaine A, Camara O. Delineation of the electrocardiogram with a mixed-quality-annotations dataset using convolutional neural networks. Scientific Reports 2021;11(1):863.

Address for correspondence:

Álvaro José Bocanegra Pérez
Physense, Universitat Pompeu Fabra, Barcelona, Spain
alvaro.bocanegra@upf.edu