ECG Images Analysis for the Prediction of Fatal Arrhythmic Events in Patients with Brugada Syndrome Based on a Vision Transformer Model

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Silvia Caligari, Vincenzo Randazzo, Carla Giustetto, Fiorenzo Gaita, and Eros Pasero

Abstract Brugada syndrome (BrS) is an inherited arrhythmogenic disease that is distinguished by an increased risk of sudden cardiac death due to the appearance of ventricular arrhythmias without any structural heart diseases.
There are distinct types of BrS electrocardiogram (ECG) patterns observed in the right precordial leads, but only Type 1, characterized by a coved shape, is considered a diagnostic indicator of Brugada syndrome. Patients with spontaneous Type 1 who have experienced ventricular fibrillation are generally recommended to undergo implantable cardioverter-defibrillator (ICD) placement to prevent sudden death, despite the associated complications. Nevertheless, risk stratification in Brugada syndrome remains challenging, particularly in cases where patients do not exhibit symptoms.
Due to limitations in experimental research involving human cardiac tissue, there is growing interest in alternative methods such as artificial intelligence (AI) based on deep learning. In this study, we present a Vision Transformer model that utilizes 12-lead ECG images as input to predict arrhythmic fatal events in patients with Brugada syndrome. The employed dataset is composed of 278 ECGs from the Piedmont Brugada Register, where 94 ECGs are connected to patients who have developed significant arrhythmic events and the remaining portion belongs to patients without any recorded arrhythmic events. The promising results obtained in negative predictive value and sensitivity may reveal the AI-based ECG analysis as an encouraging

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tool for risk stratification of Brugada Syndrome patients, offering helpful support for clinical decision-making, and possibly preventing sudden cardiac death (SCD).

Key words: Artificial Intelligence; Vision Transformer; Brugada syndrome; ViT; Risk Stratification; ECG; Sudden Cardiac Death.

1 Introduction

The Brugada syndrome (BrS), described for the first time by Josep and Pedro Brugada as a unique clinical entity in 1992 [3], has drawn increasing interest due to its high risk of sudden cardiac death and susceptibility to ventricular arrhythmias. A series of studies that aim at defining the clinical, biological, chemical, ionic, and genetic aspects of this disease have significantly increased knowledge on Brugada syndrome in recent years [14] [7]. The diagnosis is based on an electrocardiogram (ECG) analysis to identify a distinct pattern exhibited in the right precordial leads. However, these anomalies may not always be evident, and the use of specific drugs may be necessary to uncover these specific ECG signs. Electrocardiography is a crucial diagnostic tool to detect irregular heart rhythms. The ECG can accurately record the heart electrical activity regulated by the variations of cardiac action potential over time. In particular, the 12-lead ECG measures the heart's electrical potential from distinct views, referred to as "leads" through ten electrodes that are positioned on the patient limbs and chest surface.

The ECG, being a widely adopted and cost-effective cardiological tool, presents an ideal foundation for AI applications, achieving remarkable results in recent years. For instance, a convolutional neural network has been developed to detect the electrocardiographic signature of atrial fibrillation within normal sinus rhythm [2]. Additionally, deep learning techniques consisting on various neural network architectures have been employed to estimate arterial blood pressure non-invasively by utilizing photoplethysmogram (PPG) and electrocardiogram (ECG) signals [17] [16].

Optimized and adapted convolutional neural models have been developed for the automatic detection of heartbeats and the classification of cardiac diseases based on ECG data [6] [5]. These advancements have presented a promising opportunity to apply AI-based ECG analysis for the identification of Brugada syndrome [21] [10] but risk stratification remains a complex task.

Currently, the identification of patients at high risk of arrhythmia relies solely on clinical indicators, including a history of unexplained syncope, the presence of a spontaneous type 1 ECG pattern, and previous instances of sustained ventricular tachycardia (VT) [9]. An AI-enabled algorithm based on a convolutional neural network has been proposed for the prediction of previous or future ventricular fibrillation with a recall of 0.77 ± 0.14, a negative predictive value of 0.94 ± 0.11, and a positive predictive value of 0.44 ± 0.29 [12].

In this paper, we propose a novel AI-enhanced ECG analysis that uses the Vision Transformer (ViT) [4] to identify Brugada syndrome patients who are at high risk of developing fatal rhythmic events.

We provide a brief description of the Brugada syndrome in Section 2 while highlighting the challenges associated with diagnosis and risk stratification. In Section 3 the distribution of the population in the two classes is described and Section 4 sums up the architecture of Vision Transformer and the method adopted for the research of the optimized threshold useful for the classification process. In Section 5 a statistical analysis of the numerical experiments is provided, while the most prominent findings of this paper are summarized in the final section.

2 Diagnosis and risk stratification

Precise diagnostic criteria and specific ECGs patterns were described by a Consensus Report on Brugada Syndrome [1]. The first pattern, Type 1, is characterized by a coved-shaped ST-segment elevation (greater than 2 mm in one or more right ventricular precordial leads V1-V3) come behind a negative T wave and represents the unique diagnostic pattern of Brugada syndrome (see Fig.1). A second pattern, Type 2, exhibits an ST-segment elevation greater than 0.5mm (greater than 2mm in V2) in one or more right precordial leads (V1-V3), followed by a convex ST segment and, although non-diagnostic, it indicates the need for further investigations.

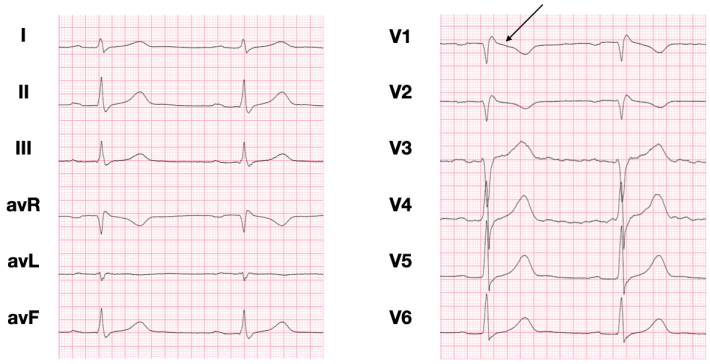

Fig. 1 Peripheral (left) and precordial (right) leads from a single ECG with a Brugada pattern of Type 1.

Diagnosing and risk-stratifying individuals with Brugada syndrome can be challenging due to several factors. The relative rarity of the disease does not permit to access large amounts of data for an exhaustive risk evaluation and precise statistical analysis. In addition, some individuals with Brugada syndrome may be asymptomatic and unaware of their condition until a sudden cardiac event occurs, such as cardiac

arrest or syncope. This makes it arduous to recognize those who have an high risk of incurring in a life-threatening arrhythmia.

Patients with spontaneous Type 1, who have previously experienced aborted cardiac arrest or arrhythmic syncope, are classified as being at higher risk of recurrence and may require therapeutic interventions such as ICD [11]. However, there are no clear instructions for asymptomatic for whom an electrophysiological study is suggested to determine the need for an ICD, despite the associated complications [19].

Ongoing research efforts focus on improving risk prediction models, exploring the role of genetic testing, investigating on additional clinical and ECG markers, and considering advanced techniques such as three-dimensional electroanatomic mapping of the abnormal substrate, which can be visualized by inducing sodium-channel blockade in the pericardium. This mapping allows for the identification of the affected tissue and subsequent epicardial ablation to eliminate it [13]. However, ablation procedures carry their risks and complications, and specialized centers capable of performing these procedures are not widely available.

3 Database description

The dataset used in this study consists of 278 12-lead electrocardiograms obtained from 210 patients collected in the Piedmont Brugada register [8] where two classes were defined: *event* and *no event*. The first class collects 94 ECGs that are associated with 62 patients who experienced arrhythmic events, specifically sustained ventricular tachycardia (VT) or ventricular fibrillation (VF), up to sudden cardiac death (SCD). For clarity, syncope cases were not included in the dataset due to the challenges in distinguishing them from neurally mediated syncope, which is unrelated to the Brugada Syndrome.

The remaining portion of the dataset includes 184 ECGs from 148 patients diagnosed with BrS but without any recorded arrhythmic events and assembles the *no event* class. To address the imbalance distribution of the dataset during training, where the *event* class is significantly smaller than the *no event* class, we reduced the size of the *no event* class to match the cardinality of the *event* class, resulting in a *balanced dataset* containing 94 ECGs from each class. The entire dataset was partitioned into training, validation, and test subsets.The former accounts for 85 *event* ECGs and 85 *no event* ECGs, while the validation set was created by selecting 10% of the ECGs from the balanced dataset (9-9). The remaining ECGs from the *no event* class (90), were combined with 30 *event* ECGs obtained from a single individual Holter recording to form the final test set.

4 Architecture of the AI model - Vision Transformer

Specific pre-processing methods are not necessary for the proposed models. The background region of the image is reduced by applying a manual cropping, which is the only pre-processing step involved. This cropping aims to highlight all 12 ECG leads without worrying about information loss or expensive computations and represents the input format for the Vision Transformer for each of the ECGs.

In the range of computer vision, the Vision Transformer (ViT) has gathered increasing significance thanks to its sophisticated architecture and the integration of the self-attention mechanism for processing visual data. ViT was first introduced in [20], and since then, it has demonstrated impressive performance in various vision tasks. In ViT the input consists of a one-dimensional sequence of tokens. The key contribution is the transformation of images into a sequence of two-dimensional fixed-size patches. These patches are flattened and mapped to a one-dimensional constant vector (embedded patch) through a trainable linear projection, ensuring the correct dimensionality for input into the transformer. To retain positional information, learned vectors with the same dimension as the patch embeddings, named positional embedding, are added to them, as transformers do not inherently consider the order of patches. The embedded tokens are then passed through the transformer encoder, composed by normalization layers, parallel multi-head attention operations, and multilayer perceptron. A visual representation of the ViT is depicted in Fig.2.

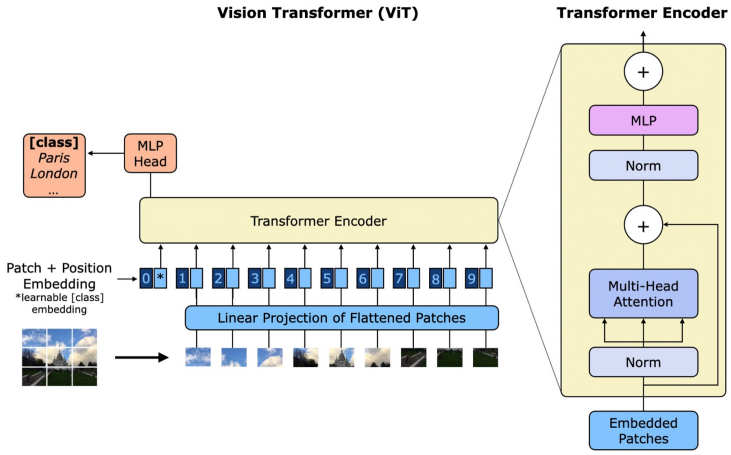

Fig. 2 Representation of the global Vision Transformer encoder architecture.

The self-attention mechanism in ViT allows each token to attend to other tokens, capturing the dependencies and relationships between the individual segmentations of the image. This attention mechanism enables the model to focus on important visual features and learn contextual representations, leading to effective image understanding and classification.

The implemented model uses the Python programming language and processes the image dataset. It fine-tunes a pre-trained ViT on ImageNet-21k at a resolution of 224x224 pixels using the HuggingFace Hub Transformer [22][23]. Images are presented as a sequence of fixed-size patches with dimensions of 16x16. The input images are normalized across the RGB channel with a mean of (0.5, 0.5, 0.5) and a standard deviation of (0.5, 0.5, 0.5). All the proposed models are trained with a batch size of 32, a learning rate of $2 \cdot 10^{-5}$, a warmup ratio of 0.1, and a weight decay of 0.1. ViT is trained for 40 epochs and an early stopping technique is employed to prevent overfitting. The training process is monitored on a separate dataset, the validation set, and is halted when the performance on the validation set does not increase based on a defined metric (F1 score) after 10 iterations.

4.1 Optimized Threshold

For evaluating the performance of classification of our models we have looked at the following metrics:

- Accuracy: it determines the proportion of the total correctly predicted data to all instances, giving a global overview of the classification process.
- Positive Predictive Value (PPV): it calculates the ratio of *event* data that are exactly classified to the sum of data that are predicted as *event*.
- Negative Predictive Value (NPV): it measures the ratio of right predicted *no event* data out of the total number of samples predicted as *no event*.
- Sensitivity (or Recall): as the true positive rate, it represents the ability of a model to correctly identify *event* data, focusing on a single class.
- Specificity: it calculates the proportion of *no event* data that are classified correctly by the model.
- F1-score: it provides a valuable metric for evaluating model performance through the computation of the harmonic mean PPV and sensitivity.
- Area under the curve (AUC): it is widely adopted in binary classification; it estimates the area under the ROC, providing important information about the ability of the model to discriminate between positive (*event*) and negative (*no event*) data.

Although all the experiments have been trained on a balanced dataset, the clinical perspective prioritizes accurate *event* predictions. In order to obtain the best specificity and recall metrics, we employ the ROC curve to evaluate prediction scores on the validation set, looking for an optimized threshold for classification processes. Let's briefly report the definitions of false positive rate (FPR) and true positive rate (TPR) in binary classification, using the notation of the confusion matrix (where TP represents true positives,TN indicates true negatives, FP stands for false positives and FN denotes false negatives). The false positive rate represents the proportion of negative samples that are incorrectly predicted as positive:

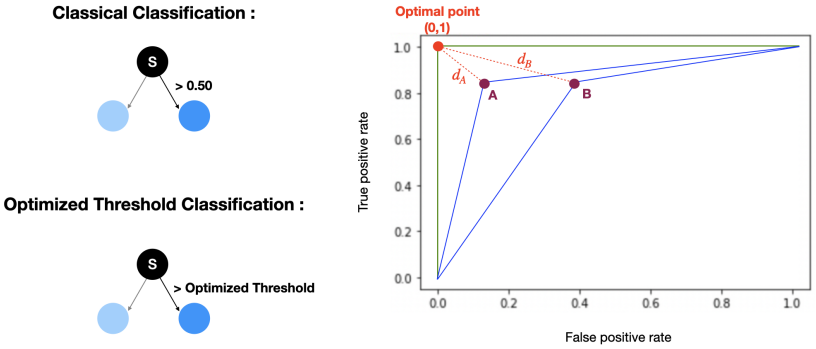

Fig. 3 Scheme of the classical classification process compared with the proposed one regulated by the research of an optimized threshold (left) and ROC curves with different thresholds and relatives distances from the optimal point (right) .

$$FPR = \frac{FP}{FP + TN} \tag{1}$$

On the other hand, the true positive rate, also known as recall or sensitivity, represents the proportion of positive samples that are accurately predicted by the model:

$$TPR = \frac{TP}{TP + FN} \tag{2}$$

The ROC curve is a graphical representation of the relation between the true positive rate and the false positive rate for various thresholds. Typically, a sample is predicted to belong to the positive class if its probability (softmax score) exceeds 0.5. However, this threshold can be chosen anywhere between 0 and 1. Then, we want to compare the distance between points on the ROC curve and the ideal point (0,1) for various thresholds and select the threshold that minimizes the distance (see Fig.3).

5 Results and Discussion

This section reports the average perfomance of the experimental results obtained from the test set using 12 loaded models acquired in the training process searching for the best F1-score performed in the validation process, coupled with the classification scheme controlled by an optimal threshold. The F1-score metric was chosen as it is more severe in penalizing incorrect predictions for *event* ECGs, while still considering the optimal classification of the *no event* class. The high negative predictive value (NPV) and sensitivity (see Table 1) of the models further enhance their effectiveness as valuable tests for screening individuals at high risk of developing fatal arrhythmic events. In fact, sensitivity measures the model capacity to correctly detect patients who are at risk.

Table 1 Mean and standard deviation (std) of the diagnostic metrics.

Metrics	**Mean**	**Std**
Accuracy	0.74	0.03
Positive Predictive Value (PPV)	0.49	0.03
Negative Predictive Value (NPV)	**0.95**	0.03
Sensitivity	**0.90**	0.08
Specificity	0.69	0.05
F1-score	0.64	0.03
AUC	0.80	0.03

In comparison to recent studies focusing on predicting fatal arrhythmic events in Brugada patients using extracted ECG features with various machine learning techniques [18], the proposed approach employing ViT gives similar results, indicating a promising starting point and preventing from a need for direct measurement of ECG features, which can simplify the diagnostic process without sacrificing performance. Moreover, our results can be compared with those obtained for predicting arrhythmic events in patients with short QT utilizing Vision Transformer [15]. In this context, the presented results are notably more encouraging, with an accuracy of 74% compared to the previously reported 63%.

These characteristics make AI-based ECG analysis a promising tool for risk stratification of patients with Brugada Syndrome, providing valuable support for clinical decision-making and potentially reducing the need for invasive surgical procedures and preventing sudden cardiac death. However, it is important to acknowledge that the optimal training of Vision Transformers requires a large amount of data, andthe limited number of BrS patients with documented ventricular tachycardia and SCD represents a hard challenge. Therefore, future studies should focus on collecting and curating more extensive datasets to ensure optimal training and robustness of the AI models in detecting and classifying arrhythmic events accurately.

Overall, the reported results indicate that ECG signals contain powerful information for risk stratification of Brugada patients. The utilization of AI-based ECG analysis holds significant potential in supporting clinical decision-making, mitigating the risk of SCD, and reducing the need for invasive surgical procedures.

6 Conclusion

In this study, we propose for the first time an AI-enhanced ECG analysis based on the Vision Transformer architecture, aiming to support the risk stratification of patients with Brugada Syndrome (BrS). The dataset utilized in this research was obtained from the Piedmont Brugada register, comprising 94 ECGs from patients diagnosed with serious arrhythmic events (such as VT and SCD), as well as 184 ECGs from patients without an arrhythmic event registered. Given the data imbalance, a singular Holter was used to extract additional 30 event ECGs, which were added to create

a test set. To determine the best model during training, we employed the F1-score because of its properties in weighing correct predictions. This metric was used during the validation process, ensuring that the best model was selected.

In addition to the Vision Transformer architecture, another technique employed in this study was the search for an optimized threshold for the classification process. This technique proved to be efficient in making necessary corrections to ensure consistent predictions, obtaining promising results (accuracy of 74%, NPV of 95%, and sensitivity of 90%) . In conclusion, our research demonstrates the potential of AI-enhanced ECG analysis, based on a Vision Transformer architecture, as a valuable tool for risk stratification of Brugada Syndrome patients. The interesting results may suggest that significant information could be contained in the ECG signals and a deeper study of the transformer attention map might unmask hidden patterns useful as clinical support in decision-making.

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