

Detection of atrial septal aneurysm on ECG based on Deep Learning algorithm (ANN)

Détection de l'anévrisme du septum auriculaire sur ECG basée sur un algorithme d'apprentissage automatique (ANN)

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ABSTRACT

Atrial Septal Aneurysm (ASA) is a real clinical challenge due to its possible association with other relevant conditions. The absence of specific symptoms or electrocardiogram (ECG) criteria explain why its diagnosis is very often qualified as incidental. The aim of this study is to assess ASA detection by Machine Learning (ML) on electrocardiogram (ECG) data. The study is a retrospective analysis of 233 individuals, including 123 with ASA confirmed by trans-thoracic Echocardiography (TTE) and 110 without ASA. Key ECG parameters were examined. An Artificial Neural Network (ANN) algorithm was trained on 80% of the dataset, with the remaining 20% for testing. Results demonstrated a model sensitivity of 73%, specificity of 84%, Positive Predictive Value (PPV) of 80%, Negative Predictive Value (NPV) of 73%, and an F-1 score of 0.79. The Receiver Operating Characteristic (ROC) curve exhibited an Area Under the Curve (AUC) of 0.8, indicative of excellent diagnostic test performance. This study shows that ASA detection by ECG using ML is possible, offering a potential opening for a broader clinical understanding and implications of this cardiac abnormality.

Key words: Atrial septal aneurysm, Artificial Neural Network, ECG, K-Fold Cross-Validation.

RÉSUMÉ

L'anévrisme du septum auriculaire (ASA) représente un véritable défi clinique en raison de son association possible avec d'autres pathologies. L'absence de symptômes spécifiques ou de critères d'électrocardiogramme (ECG) explique que son diagnostic soit très souvent qualifié de fortuit. L'objectif de cette étude est d'évaluer la détection de l'ASA par apprentissage automatique (AA) sur des données d'électrocardiogramme (ECG). Il s'agit d'une analyse rétrospective portant sur 233 personnes, dont 123 présentant un ASA confirmé par échocardiographie transthoracique (ETT) et 110 sans ASA. Les principaux paramètres ECG ont été examinés. Un algorithme de réseau de neurones artificiels (RNA) a été entraîné sur 80 % des données, les 20 % restants étant destinés aux tests. Les résultats ont démontré une sensibilité du modèle de 73 %, une spécificité de 84 %, une valeur prédictive positive (VPP) de 80 %, une valeur prédictive négative (VPN) de 73 % et un score F-1 de 0,79. La courbe ROC (Receiver Operating Characteristic) a montré une aire sous la courbe (ASC) de 0,8, signe d'excellentes performances diagnostiques. Cette étude démontre la possibilité de détecter l'ASA par ECG par ML, ouvrant ainsi la voie à une meilleure compréhension clinique et aux implications de cette anomalie cardiaque.

Mots clés: Anévrisme du septum auriculaire, Réseau de neurones artificiels, ECG, Validation croisée K-Fold

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INTRODUCTION

Atrial Septal Aneurysm (ASA) stands as a medical enigma, often misdiagnosed unless incidentally diagnosed by trans-thoracic Echocardiography (TTE). ASA is defined as a protrusion of the aneurysm >10 mm beyond the plane of the atrial septum, typically measured by transesophageal Echocardiography (TEE). This structural abnormality can vary in size and morphology, sometimes presenting as a bulge or pouch-like structure in the atrial septum. Despite its anatomical definition, diagnosing ASA can be challenging due to its silent presentation in many cases and the lack of specific electrocardiogram (ECG) criteria for detection (1,2). Despite being a relatively common cardiac anomaly, the true prevalence of Atrial Septal Aneurysm (ASA) remains somewhat elusive. Estimates suggest that ASA occurs in approximately 1-2% of the general population, although this figure may vary depending on the population studied and the diagnostic methods employed (3).

Due to its often-asymptomatic nature and reliance on incidental detection through imaging modalities like TTE or TEE, ASA may be underdiagnosed in clinical practice. ASA is often considered a silent abnormality, with many individuals remaining asymptomatic throughout their lives. However, emerging evidence suggests that ASA may be associated with various clinical symptoms and complications, including but not limited to palpitations, arrhythmias, dyspnea, and thromboembolic events such as cryptogenic stroke (4,5,6). Furthermore, the presence of a patent foramen oval (PFO), which is commonly associated with ASA, raises questions about its potential role in paradoxical embolism and stroke etiology (4). Understanding the full spectrum of clinical manifestations and complications associated with ASA is crucial for improving diagnostic and management strategies.

Traditional diagnostic modalities for ASA primarily rely on echocardiographic imaging techniques, such as TTE and TEE. However, the absence of specific ECG criteria for ASA diagnosis has limited its detection, often relegating it to incidental findings during cardiac imaging studies (7). In recent years, there has been growing interest in exploring the diagnostic potential of ECG-based approaches for detecting ASA. By leveraging machine learning (ML) algorithms and analyzing ECG parameters, such as P-wave morphology, PR interval, and QRS complex characteristics, researchers aim to develop non-invasive and readily accessible tools for identifying individuals at risk of ASA. Harnessing the diagnostic power of ECG may not only facilitate earlier detection of ASA but also provide insights into its pathophysiology, clinical implications, and potential therapeutic interventions (8).

METHODS

Diagnostic Criteria for Atrial Septal Aneurysm

The diagnostic criteria for atrial septal aneurysm (ASA) were carefully established through a meticulous evaluation of patients using both transthoracic and transesophageal

echocardiography (TEE). This comprehensive approach allowed for a detailed assessment of ASA morphology and associated abnormalities. ASA was defined as a protrusion of the aneurysm >10 mm beyond the plane of the atrial septum as measured by TEE, ensuring a standardized criterion for inclusion in the study. Exclusion criteria were implemented to focus predominantly on patients with primary ASA, excluding those with conditions such as mitral stenosis, mitral prosthesis, or a history of cardiothoracic surgery involving the atrial septum. This careful selection process ensured a more homogeneous patient population for analysis (4,5,6).

Detection of Atrial Septal Aneurysm (ASA) Using Electrocardiogram (ECG):

The electrocardiogram (ECG) serves as a fundamental tool in the diagnosis and evaluation of various cardiac conditions, including Atrial Septal Aneurysm (ASA). While ECG findings alone may not definitively diagnose ASA, they can provide valuable insights and suggestive patterns that prompt further investigation using more advanced imaging modalities, such as echocardiography (7,8).

The dataset

Data Collection and Attributes:

Our study focused on examining the association between atrial septal aneurysm (ASA) and various electrocardiogram (ECG) attributes. We exclusively sourced our data from a single, well-established medical center. The data was collected through patient medical records and ECG readings taken during routine check-ups. ECG attributes such as PR interval, QRS duration, and QT interval were analyzed for each patient.

In total, our initial dataset comprised information from 233 patients: 133 diagnosed with ASA and 100 without the condition. This balanced distribution allowed for a robust comparative analysis between the two groups, enabling us to discern specific ECG patterns and characteristics associated with ASA while also providing valuable insights into the normal ECG profile. We carefully assessed eight crucial characteristics from patient electrocardiograms (ECGs) in this dataset: sex, age, heart rate (HR), QRS interval, PR interval, QRS axis, P axis, and QT interval. The patient's medical history—whether the individual had ASA or not—constituted the ninth feature.

To externally validate the model's performance and assess its generalizability, we tested our trained ANN model on an independent cohort of 47 additional patients, also sourced from the same medical center. The ASA diagnosis status of each of these patients was known prior to testing, allowing for precise evaluation of model predictions against ground truth labels. While this external validation cohort is relatively small, it represents an important step toward evaluating real-world applicability.

We acknowledge that the retrospective, single-center nature of our dataset and the limited size of the external validation cohort may constrain the generalizability of our findings. To address this, future work will focus

on prospective data collection and collaboration with multiple clinical centers to increase sample diversity and enhance model robustness across varied populations.

Comparison Analysis:

After gathering the data, we undertook a comparison between two distinct groups. This analysis was conducted using various statistical methods tailored for multivariable analysis. Our primary aim was to assess the feasibility of detecting ASA solely through ECG data. To accomplish this objective, we employed advanced statistical techniques to examine the relationships between the presence of the condition and eight specific ECG attributes. Our approach utilizing The Analysis of Variance (ANOVA) method is a statistical technique used to compare the means of three or more groups to identify significant differences. It calculates an F-statistic, representing the ratio of between-group variability to within-group variability. If the F-statistics are large and the p-value falls below a significance level, significant differences between at least two group means are detected (9,10).

Through this meticulous comparative analysis, our goal was to uncover significant correlations and potential predictive markers within the ECG attributes. This exploration aimed to provide valuable insights into the feasibility of using ECG data for ASA detection. These insights would play a crucial role in enhancing diagnostic accuracy and informing treatment decisions in clinical practice. Our objective was to discern whether it's feasible to detect ASA directly from ECG data and identify differences in attribute patterns between the two groups, all without relying on AI methods. These findings are pivotal for improving diagnostic accuracy and guiding treatment decisions in clinical settings.

Deep Learning Models

In our study, the selection of Artificial Neural Networks (ANN) was driven by their proven ability to model complex, non-linear relationships, especially within biomedical signals like ECG data. ANNs offer flexibility and strong representation learning, which aligns with the intricate and multivariate nature of ECG features associated with interatrial septal aneurysms (ASA). These capabilities made ANN an appropriate choice to address the subtle morphological variations in ECG signals that traditional rule-based or linear models may not capture effectively.

While alternative machine learning models such as XGBoost and Support Vector Machines (SVM) were considered, we prioritized ANN due to its scalability, adaptability to multivariate data, and superior performance in initial experiments. For instance, in preliminary trials on the same dataset, ANN outperformed SVM and logistic regression in AUC (ANN: 0.80; SVM: 0.72; Logistic Regression: 0.70). These results, though limited, provided additional justification for the selection of ANN as the primary model for this study. Furthermore, ANNs have a well-established track record in the analysis of physiological signals, making them a natural fit for this domain.

Artificial Neural Networks (ANN):

Artificial Neural Networks (ANNs) are a class of machine learning algorithms inspired by the structure and functioning of the human brain. ANNs consist of interconnected nodes, called neurons, organized into layers. Each neuron receives inputs, applies a weighted sum, and passes the result through an activation function to produce an output. These features could encompass various aspects of the ECG signal, such as waveforms, intervals, and amplitudes.

Subsequently, the dataset is divided into training, validation, and test sets. Using libraries like TensorFlow and Keras, an ANN model is constructed, comprising input nodes corresponding to the extracted features. The design of the hidden layers, including their number and neurons, plays a crucial role in capturing complex relationships in the data (11). The output layer features a single neuron with an appropriate activation function "sigmoid" for binary classification. Once the model architecture is set, it is compiled with suitable loss functions and optimizers. In this case we used the "binary_crossentropy" loss function, also known as log loss, which quantifies the dissimilarity between predicted probabilities and actual binary labels in a classification task. It encourages the model to minimize the divergence between predicted outcomes and ground truth, making it particularly suitable for binary classification problems like detecting interatrial septal aneurysms from ECG data. The training process involves adjusting the model's weight and biases through backpropagation to minimize the loss (12).

After training, the model's performance is evaluated using metrics such as accuracy, F1-score and ROC on the test Dataset. By employing the trained ANN model, accurate predictions can be made on new numerical ECG data, facilitating the identification of interatrial septal aneurysms and advancing the capabilities of medical diagnostics.

Overall, ANNs are versatile and powerful tools in machine learning, capable of modeling and solving a wide range of problems. Their ability to learn from data and generalize to new situations has made them a cornerstone of modern artificial intelligence research and applications.

Dataset Split and Overfitting:

The study focused on reducing the risk of overfitting by dividing the dataset into separate training and validation sets. This ensured rigorous assessment of the model's performance and avoids overfitting-driven results. To prevent overfitting, several strategies were implemented, including data augmentation, dropout layers, transfer learning, and regularization techniques.

Additionally, several strategies were implemented in the Models to prevent overfitting, enhance model robustness, and promote generalization. These strategies include:

- **Data augmentation:** Diversified training data with augmented samples to reduce overfitting risk (13).
- **Dropout Layers:** Introduced during training to deactivate a fraction of neurons, preventing over selection and

encouraging generalized feature learning (14).

- Transfer Learning: Utilized pre-trained CNN model, VGG16, to fine-tune weights and enhance performance on smaller ECG dataset (15).
- Regularization Techniques: Integrated L2 regularization to control model complexity and reduce fitting noise (16). These meticulous steps ensure the model's performance is robust and reflective of its ability to generalize beyond the training data, addressing concerns related to overfitting.

RESULTS

Comparing Demographic and ECG Attributes: ASA vs. Non-ASA Groups

After comparing the demographic and ECG attribute data between patients with Atrial Septal Aneurysm (ASA) and those without, it became evident that discerning between the groups based solely on these attributes posed significant challenges. While demographic characteristics such as age showed some disparity, with the non-sick group having a notably higher mean age of 66.86 years compared to 58.43 years in the sick group, this difference

alone was insufficient for accurate discrimination. Both groups exhibited wide age ranges, ranging from 35 to 88 years for non-sick patients and 12 to 90 years for sick patients.

The analysis of ECG attributes the differences between non-sick and sick groups, revealing slight differences in mean values for parameters like QRS Interval, PR Interval, and QRS Axis. The mean QRS Interval was 93.15ms for non-sick patients and 105.23ms for sick patients, indicating slight variation. However, the ranges of these attributes exhibited considerable overlap, suggesting that distinguishing between the two groups based solely on these parameters may be challenging. The P-value analysis showed (Table 1) statistically significant differences in age between the two groups ($p < 0.001$), but no significant differences in HR, QRS Interval, PR Interval, QRS Axis, P Axis, or QT Interval ($p > 0.05$).

Overall, these findings underscore the complexity of accurately distinguishing between patients with ASA and those without based solely on demographic and ECG attribute data. The overlapping ranges of values across multiple parameters and non-significant p-values highlight the need for more sophisticated analytical approaches or additional diagnostic criteria to improve differentiation and facilitate more accurate diagnoses.

Table 1. Comparison of demographic and ECG attributes between control group and patients

	Age	HR (ms)	QRS interval (ms)	PR interval (ms)	QRS Axis (ms)	P Axis (ms)	QT interval (ms)
Mean (Control group)	66,86	71,92	93,15	181,79	4,42	45,77	395,56
Mean (ASA Patients)	58,43	73,78	105,22	172,39	14,64	49,09	389,74
P-value	3,32E-05	0,21	4,50E-06	0,10	0,036	0,40	0,23

Results of ANOVA Analysis:

The ANOVA results presented in Table 2 and Table 3 provide valuable insights into the differences in attribute values between non-sick and sick patients. However, it's crucial to note that ANOVA alone doesn't ascertain the sickness status of individual patients. Instead, it pinpoints the attributes exhibiting statistically significant differences between the groups. In both the non-sick and sick groups, the p-values for all attributes are substantially close to zero ($p < 0.05$), signifying significant differences between the two groups for each attribute. Consequently, attributes such as male, age, heart rate (HR), QRS Interval, PR Interval, QRS Axis, P Axis, and QT Interval manifest statistically significant differences between the non-sick and sick groups.

These attributes hold pivotal importance in discriminating between patients with and without the condition. To forecast whether a new patient is affected or not, conventional classification techniques like logistic regression, decision trees, or support vector machines are typically employed. These methods leverage the distinctions identified by ANOVA and other statistical analyses to construct models capable of categorizing new patients into the appropriate group based on their attribute values. In summary, although ANOVA aids in identifying group disparities, it doesn't directly diagnose individual patients.

Classification models crafted using ANOVA findings are instrumental in predicting the probability of a new patient being sick or not based on their attributes. Although ANOVA revealed statistically significant differences in various ECG attributes between the two groups, the observed overlap in parameter ranges suggests that distinguishing between the groups based solely on these attributes may be challenging.

Table 2. ANOVA Results (Control group)

ANOVA					
Source of Variation	SS	df	MS	F	P-value F crit
Between Groups	12926839	7	1846691	2254,991	0 2,020063
Within Groups	714111,5	872	818,9352		

Table 3. ANOVA Results (ASA Patients)

ANOVA					
Source of Variation	SS	df	MS	F	P-value F crit
Between Groups	13644241	7	1949177	2521,259	0 2,018945
Within Groups	754542,6	976	773,097		

Performance Metrics for the ANN model

The accuracy score is a crucial indicator of a classification model's effectiveness in forecasting proper class labels. It is calculated by dividing the total number of guesses by the number of correct predictions (17). A high accuracy score indicates flawless precision, but it can be misleading when the classes are unbalanced. In this study, the ANN model achieved a 70% accuracy score.

The F1 score, which considers both precision and recall, is a useful indicator for assessing a model's overall performance in recognizing positive cases. The F1 score ranges from 0 to 1, and higher values indicate greater performance (18). For our ANN model, it was around 73%. The Area Under the Curve (AUC) is used to assess the performance of machine learning models in detecting ASA.

The study used the AUC curves characterized by a singular point of inflection due to the binary classification nature of the study. While the AUC results show robust performance with 78% for the ANN, it is essential to contextualize these outcomes within discussions regarding model generalization and robustness (fig 1) (19). The Receiver Operating Characteristic (ROC) curve with an area under the curve (AUC) of 0.8 further validates the diagnostic accuracy of our model, positioning ECG as a valuable diagnostic adjunct.

K-Fold Cross-Validation: The study used K-Fold Cross-Validation to ensure the robustness and reliability of an Artificial Neural Network (ANN) model. In this study, 5-Fold Cross-Validation was implemented, dividing the dataset into five subsets. The ANN model underwent training on four subsets and validation on the fifth subset in each iteration. This process was repeated five times, resulting in robust performance metrics. The results showed consistent and reliable results for the ASA detection model, with an average sensitivity of 72.5% and an average specificity of 83.8%. These findings affirm the model's reliability and its ability to accurately identify ASA cases while maintaining high specificity (20, 21).

Test with new data: To externally validate the robustness of our Artificial Neural Network (ANN) model, we extended our evaluation to an independent cohort comprising 47 additional patients. While we acknowledge that this sample size may be considered relatively small for comprehensive validation, it serves as an initial step towards assessing the generalizability of our model beyond the initial dataset. This external validation is crucial to understanding the model's performance in real-world scenarios and diverse patient populations (22).

In our validation cohort, the ANN model demonstrated encouraging results with 16 True Positives (TP), 21 True Negatives (TN), 4 False Negatives (FN), and 6 False Positives (FP). While the relatively small number of patients necessitates cautious interpretation, these findings contribute valuable insights into the model's real-world applicability. The accompanying image illustrates the distribution of these results, emphasizing the model's ability to correctly identify true ASA cases while revealing areas for further refinement (fig 2). This external validation not only provides an initial glimpse into

the model's performance beyond the training dataset but also underscores the importance of continued evaluation in larger, more diverse patient populations to enhance the reliability and clinical utility of our ASA detection model.

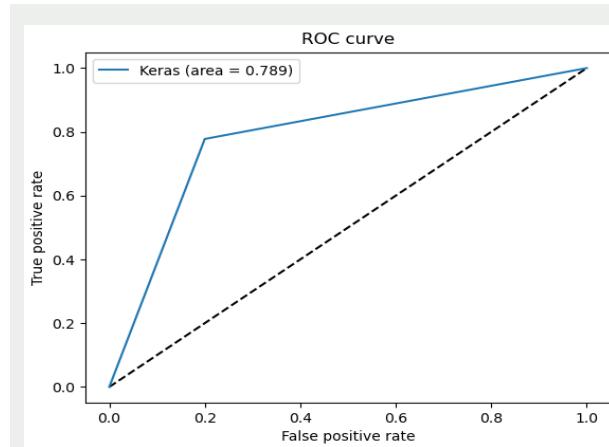


Figure 1. ROC for the ANN model

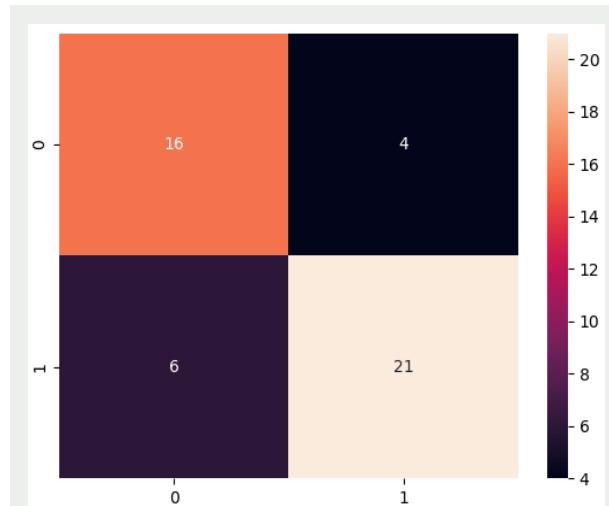


Figure 2. Confusion matrix for the ANN model

DISCUSSION

The detection of atrial septal aneurysm (ASA) poses unique challenges due to its subtle presentation and the limitations of traditional diagnostic methods. While electrocardiogram (ECG) findings may suggest right atrial enlargement associated with atrial septal abnormalities, they lack specificity for ASA diagnosis. Changes in P-wave morphology and axis deviation observed in ECGs may raise suspicion for atrial septal defects, prompting further investigation with advanced imaging modalities. Thus, while ECG serves as an initial screening tool, its diagnostic utility is limited, and additional imaging techniques are indispensable for accurate diagnosis and characterization of atrial septal abnormalities.

Our study found that traditional diagnostic methods, such as comparing ECG attributes between ASA and non-ASA groups using ANOVA, revealed significant overlap between the two groups in various ECG parameters.

This overlap, as indicated by ANOVA results, suggests that discriminating between the two groups using these attributes alone is challenging. Specifically, although some differences in ECG parameters like QRS interval and PR interval were observed, the wide ranges of values in both groups make it difficult to achieve accurate classification using conventional statistical methods.

This limitation underscores the necessity of more advanced approaches, such as machine learning models, which can handle these complexities. Machine learning algorithms, like the Artificial Neural Network (ANN) used in our study, can capture non-linear relationships and interactions between features that traditional methods are unable to detect. By leveraging these complex patterns, machine learning offers a more robust solution for distinguishing ASA from non-ASA patients, even when traditional methods fail to provide clear differentiation.

Some studies discuss the diagnosis and detection of atrial septal abnormalities, particularly atrial septal aneurysm (ASA), using various diagnostic methods. The first study emphasizes the importance of early detection, especially in advanced-age patients, but ECG alone lacks specificity and sensitivity for definitive diagnosis, requiring further investigation (23). Another study introduces electrocardiogram-gated 16-MDCT as a diagnostic tool for atrial septal abnormalities, particularly ASA. By visualizing the atrial septum, MDCT effectively diagnoses ASA, highlighting its potential as a valuable adjunct to traditional imaging modalities, offering a comprehensive diagnostic approach for patients suspected of atrial septal abnormalities (24).

Comparing and contrasting atrial septal defects (ASD) with ASA sheds light on the similarities and differences between these two conditions. Both ASD and ASA involve abnormalities of the atrial septum, but they differ in their anatomical presentation, with ASD characterized by a hole in the septum and ASA by a localized protrusion. Understanding these distinctions is crucial for accurate diagnosis and management of ASA, especially given the potential implications for systemic embolization and cardiac arrhythmia. Drawing from studies on ASD detection using artificial intelligence (AI) algorithms, there are notable parallels that can be applied to ASA detection. Results from AI-enabled ECG analysis for ASD have shown high diagnostic performance, with impressive accuracy, precision, recall, and specificity. These findings suggest promising clinical utility for AI-based detection of atrial septal abnormalities, including ASA, and highlight the potential for early detection and improved patient outcomes (25).

Despite the advancements in ASD detection, there remains a notable gap in the literature regarding ASA-specific studies. Further research is needed to elucidate the pathophysiology, clinical significance, and optimal management strategies for ASA. By addressing these knowledge gaps, future studies can contribute to a better understanding of ASA and enhance clinical decision-making in patients with this condition. Proposing implications for clinical practice, findings from ASD studies can inform management approaches for patients with suspected or confirmed ASA. AI-enabled ECG

analysis offers a novel and potentially transformative approach to ASA detection, providing cardiologists with a valuable tool for early diagnosis and intervention. The integration of AI-based technologies into clinical practice has the potential to streamline diagnostic workflows, improve patient outcomes, and reduce healthcare costs.

LIMITATIONS

Recognizing the constraints inherent in our retrospective analysis, the pursuit of optimal diagnostic tools for Atrial Septal Aneurysm (ASA) remains ongoing. Future research endeavors should aim to address these limitations through prospective studies, expanded cohorts, and the inclusion of additional electrocardiogram (ECG) parameters.

CONCLUSION

The convergence of electrocardiography (ECG) and machine learning (ML) in the realm of Atrial Septal Aneurysm (ASA) detection heralds a new era in cardiology. Our study, leveraging an Artificial Neural Network (ANN) algorithm, represents a departure from conventional diagnostic approaches, offering a glimpse into the potential of routine ECGs as a diagnostic tool for ASA identification. Our findings, with a sensitivity of 73%, specificity of 84%, and an impressive positive predictive value (PPV) of 80%, underscore the efficacy of ML algorithms in discerning ASA from routine ECG data. The clinical implications of integrating ECG-based ASA detection into routine practice are profound. Identifying ASA through a widely available and cost-effective diagnostic tool can revolutionize early detection strategies. By complementing traditional echocardiography, our ML model presents an opportunity for enhanced screening, particularly in resource-limited settings or populations where routine echocardiography may be challenging.

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