Korean Circ J. 2023 Nov;53(11):772-774
https://doi.org/10.4070/kcj.2023.0231
pISSN 1738-5520·eISSN 1738-5555

kcj
Korean Circulation Journal

Editorial

Artificial Intelligence-enhanced Electrocardiogram for Atrial Fibrillation in Embolic Stroke With Undetermined Source: Heroic Detective or Overfitting Alarm?

Yong-Soo Baek, MD, PhD[1,2]

[1]Division of Cardiology, Department of Internal Medicine, Inha University College of Medicine and Inha University Hospital, Incheon, Korea
[2]School of Computer Science, University of Birmingham, Birmingham, United Kingdom

▸ See the article “Identifying Atrial Fibrillation With Sinus Rhythm Electrocardiogram in Embolic Stroke of Undetermined Source: A Validation Study With Insertable Cardiac Monitors” in volume 53 on page 758.

Received: Oct 18, 2023
Accepted: Oct 20, 2023
Published online: Oct 23, 2023

Correspondence to
Yong-Soo Baek, MD, PhD
Division of Cardiology, Department of Internal Medicine, Inha University College of Medicine and Inha University Hospital, 27, Inhang-ro, Jung-gu, Incheon 22332, Korea.
Email: existsoo@inha.ac.kr

ORCID iDs
Yong-Soo Baek
https://orcid.org/0000-0002-6086-0446

Funding
The author received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest
The author has no financial conflicts of interest.

Historically, atrial fibrillation (AF) has been linked as a culprit for strokes, supporting Virchow’s classical pathophysiology and highlighting blood clot formation in the left atrium. However, this association has been examined more extensively in relation to embolic strokes of undetermined source (ESUS), which has shown to be a multifaceted and miscellaneous condition with various possible thromboembolic causes.1) Recent studies reported these risks by noting a temporal discrepancy in some patients who first detected AF after diagnosing stroke. Hypertension, intrinsic atrial substrate and CHA2DS2-VASc score may play important roles in this interaction. Additionally, atrial shape, function, duration, and severity of AF burden add complexity. Interestingly, atrial cardiomyopathy, although a clear definition has not yet been established, could contribute to thromboembolism even in the absence of AF.2) Given these complexities, it is critical to recognize that identifying AF as the real villain in the stroke story may be an oversimplification; It cannot be ruled out that it is an innocent bystander in many situations.

In this issue of the *Korean Circulation Journal*, Jeon et al.3) presented the efficacy of a deep learning algorithm (DLA) in detecting AF using sinus rhythm 12-lead electrocardiogram (ECG). From a database of over 44,000 ECGs, the DLA achieved a diagnostic accuracy of 0.811, an area under the receiver operating characteristic of 0.827, and an F1 score of 0.572. Significantly, the logistic regression analysis revealed an impressive odds ratio of 11.63 (95% confidence interval, 3.979–41.51) for AF detection in 221 ESUS patients who underwent insertable cardiac monitor (ICM), underscoring the DLA’s potential to outperformed conventional models.

Although the results seem promising, it is worth noting the limitations in generalizing the positive outcomes to patients with ESUS. For instance, the NAVIGATE ESUS study suggested that although rivaroxaban diminished recurrent stroke risk, it brought about a heightened bleeding risk compared to aspirin.4) Similarly, the RE-SPECT ESUS study found a non-statistically significant reduction in recurrent stroke with dabigatran compared to aspirin but noted more non-major bleeding incidents. These studies emphasize the careful

Data Sharing Statement

The data generated in this study is available from the corresponding author upon reasonable request.

consideration required before applying ESUS treatment practices based on AF findings by artificial intelligence-enhanced ECG (AI-ECG). [5] If the AI-ECG that can detect whether AF is the main cause or culprit of a stroke in patients is developed, it will herald a paradigm shift in ESUS clinical management. To achieve this, it may be necessary to develop more sophisticated AI specifically designed for stroke patients.

In patients with stroke attributed to large- or small-vessel disease, the STROKE-AF trial demonstrated that long-term monitoring using ICMs were superior to usual care in detecting AF over a 12-month period.[6] The AF detection rate was 12.1% in the ICM group versus 1.8% in the control group. This trial was not focused on elucidating the cause of the index stroke, but rather than on identifying patients who may be at risk for future AF-related stroke. While discerning AF in ESUS does not unequivocally establish a therapeutic target, the significance of this research lies in its validation of AF using an ICM for definitive long-term monitoring. While a variety of wearable devices, such as smartwatches, have emerged, the often-asymptomatic nature of AF underscores the importance of continuous, long-term monitoring.

There are 2 pioneering studies for AI-ECG to identify AF during normal sinus rhythm (NSR). In a 2019 study, Attia et al.[7] used CNN to train an AI-ECG algorithm on a self-test dataset of NSR from Mayo Clinic. The algorithm accurately identified AF patients 79%, even when presented with NSR. Accuracy increased to 83% when ECGs taken one month before diagnosis of AF were included, suggesting that electrical and structural remodeling were occurring even before diagnosis.[7] Korean researchers also demonstrated that a new deep neural network could identify paroxysmal AF during NSR from standard 12-lead ECGs. By enhancing the optimal interval of AF and improving accuracy through data labeling by expert, they succeeded in doubling the F1 score of 0.73 compared to the previous study.[8] Recent research has demonstrated a threefold increase in AF detection using AI-ECG compared to conventional methods for high-risk patients. While arrhythmia diagnosis has been well-researched, its role in direct patient care remains under-explored.[9] To address this, a comprehensive multi-center study is ongoing to investigate the relationship between AI-ECG findings and associated clinical outcomes.

There are common challenges that we must address in AI-ECG. First, the algorithms used in AI are generally known as "black boxes" regarding the way they reach conclusions. This can be recognized as a key barrier to the adoption of AI systems because it is difficult to understand why the algorithm has reached a specific conclusion, especially in the medical field, where medical staffs must understand the reasoning behind recommendations to promote trust and encourage patients. However, there have been attempts to explain this, such as the Class Activation Map (CAM), Grad-CAM, the SHapley Additive exPlanations (SHAP) method, and Dense Neural Networks by global weights importance, which are referred to as explainable AI.[10] The attempt "ShapeExplainer" from Jeon et al.[3] to explain deep learning algorithms is a praiseworthy attempt. However, further research is needed to determine whether this is truly an AI that "explains" the cause, or simply a marker. Second, since most studies have been retrospective and performed on limited datasets, large-scale prospective studies or verification and certification experiments in other medical environments are needed, and the problem of imbalanced datasets and a limited number of patients must be addressed. Third, although the performance of deep learning algorithms is excellent, overcoming false positives and negatives to identify optimal treatments and predict outcomes is still an important issue. In addition, overfitting must be carefully considered according to the characteristics of diseases. Therefore, research that includes long-term

https://doi.org/10.4070/kcj.2023.0231

follow-up may be necessary. Fourth, it is essential to use an accurately labeled dataset that has been labeled by experts when designing and developing AI algorithms. This is crucial because some contaminated data can lead to AI performance and data bias.

Currently, AI-ECG can detect even subtle differences in cases where a cardiologist or ECG machine interpretation has classified it as "normal" for some diseases. As early diagnosis and management are crucial for cardiovascular diseases, this AI method is highly suitable for large-scale ECG screening and is expected to be utilized in clinical settings in the future. There are significant advantages to using AI-ECG, such as risk prediction and integration with traditional clinical variables, personalized treatment planning, and cost-effectiveness through real-time on-site analysis of inexpensive ECG. Therefore, it is expected that in the near future, this will serve as a game-changer and a heroic detective, bringing innovative changes to the diagnosis and management of cardiovascular diseases.

REFERENCES

1. Ntaios G. Embolic stroke of undetermined source: JACC review topic of the week. *J Am Coll Cardiol* 2020;75:333-40.
   PUBMED | **CROSSREF**
2. Freedman B, Kamel H, Van Gelder IC, Schnabel RB. Atrial fibrillation: villain or bystander in vascular brain injury. *Eur Heart J Suppl* 2020;22:M51-9.
   PUBMED | **CROSSREF**
3. Jeon KH, Jang JH, Kang S, et al. Identifying atrial fibrillation with sinus rhythm electrocardiogram in embolic stroke of undetermined source: a validation study with insertable cardiac monitors. *Korean Circ J* 2023;53:758-71.
   CROSSREF
4. Hart RG, Sharma M, Mundl H, et al. Rivaroxaban for stroke prevention after embolic stroke of undetermined source. *N Engl J Med* 2018;378:2191-201.
   PUBMED | **CROSSREF**
5. Diener HC, Sacco RL, Easton JD, et al. Dabigatran for prevention of stroke after embolic stroke of undetermined source. *N Engl J Med* 2019;380:1906-17.
   PUBMED | **CROSSREF**
6. Schwamm LH, Kamel H, Granger CB, et al. Predictors of atrial fibrillation in patients with stroke attributed to large- or small-vessel disease: a prespecified secondary analysis of the STROKE AF randomized clinical trial. *JAMA Neurol* 2023;80:99-103.
   PUBMED | **CROSSREF**
7. Attia ZI, Noseworthy PA, Lopez-Jimenez F, et al. An artificial intelligence-enabled ECG algorithm for the identification of patients with atrial fibrillation during sinus rhythm: a retrospective analysis of outcome prediction. *Lancet* 2019;394:861-7.
   PUBMED | **CROSSREF**
8. Baek YS, Lee SC, Choi W, Kim DH. A new deep learning algorithm of 12-lead electrocardiogram for identifying atrial fibrillation during sinus rhythm. *Sci Rep* 2021;11:12818.
   PUBMED | **CROSSREF**
9. Noseworthy PA, Attia ZI, Behnken EM, et al. Artificial intelligence-guided screening for atrial fibrillation using electrocardiogram during sinus rhythm: a prospective non-randomised interventional trial. *Lancet* 2022;400:1206-12.
   PUBMED | **CROSSREF**
10. Nakamura T, Aiba T, Shimizu W, Furukawa T, Sasano T. Prediction of the presence of ventricular fibrillation from a Brugada electrocardiogram using artificial intelligence. *Circ J* 2023;87:1007-14.
   PUBMED | **CROSSREF**

https://doi.org/10.4070/kcj.2023.0231