JACC: CLINICAL ELECTROPHYSIOLOGY
VOL. 9, NO. 8, 2023
© 2023 PUBLISHED BY ELSEVIER ON BEHALF OF THE
AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION

EDITORIAL COMMENT

Deep Learning for Premature Ventricular Contraction-Cardiomyopathy

Are We Digging Deep Enough?*

Gurukripa N. Kowlgi, MBBS, MS,[a] Zachi I. Attia, PhD,[a] Samuel J. Asirvatham, MD[a,b,c,d]

Premature ventricular contractions (PVCs) are remarkably pervasive, featuring in up to 75% of patients subjected to Holter monitors.[1] The abundance of PVCs might serve as a harbinger of the severity of left ventricular (LV) dysfunction.[2] The comprehension of premature ventricular contraction-mediated cardiomyopathy (PVC-CM) remains nascent because not all patients with frequent PVCs ultimately develop PVC-CM. Several factors—such as the total PVC burden, epicardial focus, short coupling interval between normal and PVC beats, LV dyssynchrony, atrioventricular dissociation, and post-extrasystolic potentiation—have been speculated to foretell the evolution of PVC-CM.[3-5] Yet, a consensus regarding risk stratification remains elusive. The management of asymptomatic patients burdened with high PVC count remains nebulous, replete with potential clinical implications, ranging from pharmacological intervention and catheter ablation to monitoring, all with an underpinning risk of progressive heart failure.[6]

The advent of artificial intelligence (AI) has catalyzed a paradigm shift in the practice of electrophysiology.[7] AI methodologies, such as machine learning and deep learning, have been integrated in a variety of applications, including arrhythmia detection, anomaly categorization, risk stratification, and prognostication of diseases.[8] These AI frameworks employ extensive data sets of electrocardiography (ECG) recordings to decipher patterns and features indicative of distinct cardiac conditions, thus enabling an automated and precise diagnosis. AI algorithms have shown the potential to eclipse human diagnostic capabilities. Deep learning models have been contrived to detect contractile dysfunction using a 12-lead ECG, but it remains uncertain whether these models are equally adept in ECGs with PVCs.[9] This issue necessitates further exploration because of its immense potential in the detection and management of PVC-CM.

In this issue of *JACC: Clinical Electrophysiology*, Lampert et al[10] report the findings of their elegantly conducted study based on a deep learning model that takes 12-lead ECG inputs to predict cardiomyopathy in patients with PVCs noted on ECGs. The training of this predictive model took place in a solitary center and was applied to 4 additional facilities for the purpose of external validation. Left ventricular ejection fraction (LVEF) values were obtained from echocardiograms within 6 months after the ECGs. Patients with abnormal LVEF prior to the index ECG were omitted. ECGs from 13,553 patients from a single center were used for training the model, and data from 688 patients were used for external validation. The primary outcome was the diagnosis of LVEF ≤40% within 6 months of the index ECG. Lampert et al[10] report that their model predicted the primary outcome with an area under the receiver-operating characteristic curve of 0.79. Gradient class-activation-map assessment was used to analyze the explainability of the model, and it highlighted the sinus rhythm QRS complex as opposed to the PVC beat. Lampert et al[10] concluded that the model could

*Editorials published in *JACC: Clinical Electrophysiology* reflect the views of the authors and do not necessarily represent the views of *JACC: Clinical Electrophysiology* or the American College of Cardiology.

From the [a]Division of Cardiovascular Diseases, Department of Medicine, Mayo Clinic, Rochester, Minnesota, USA; [b]Department of Pediatrics and Adolescent Medicine, Mayo Clinic, Rochester, Minnesota, USA; [c]Department of Biomedical Engineering, Mayo Clinic, Rochester, Minnesota, USA; and the [d]Department of Clinical Anatomy, Mayo Clinic, Rochester, Minnesota, USA.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

ISSN 2405-500X/$36.00
https://doi.org/10.1016/j.jacep.2023.07.003

accurately predict cardiomyopathy in patients with PVCs irrespective of their PVC burden. In the subsequent text, we will attempt to provide some perspectives about the thought-provoking aspects of this important research.

CAN WE CLAIM CERTAINTY IN DETECTING PVC-CM?

For the asymptomatic patient with 1 or more PVCs detected on a 12-lead ECG, the potential spectrum traverses from entirely benign idiopathic PVCs to those with the propensity to induce cardiomyopathy. The cost-effectiveness and accessibility of the 12-lead ECG render it a compelling modality for the screening of PVC-induced cardiomyopathy. Prior models that reported excellent LVEF predictive capability from a 12-lead ECG did not exclude patients with PVCs.[9] Hence, the necessity of a distinct model for ECGs with PVCs invites debate. Broadly, it is agreed that models crafted for a specific populace should be trained on the same, in this context, patients exhibiting PVCs to detect PVC-CM. But do we truly detect PVC-CM?

Lampert et al[10] elegantly showed how the sinus QRS complex appears to have more relevant information than the PVC beat itself. So, it is plausible that we are developing models that perform well in detecting subclinical CM, but we would require prospective enrollment and follow-up to be convinced that we are indeed specifically picking up PVC-CM. In the current study, a small number of patients (n = 15) had follow-up LVEF data after ablation, and 60% had LVEF recovery. Lampert et al[10] report that the rest had unsuccessful ablations; however, larger samples are required to solidify this argument. An avenue of an ongoing investigation is to apply the model to the same patients on ECGs with and without PVCs to see whether the prediction varies. Studies are underway to assess patients who undergo PVC ablation and who have LVEF recovery, and they should question how long it takes for the AI-ECG low LVEF prediction to normalize.

SHOULD THE MODEL INPUT BE MATRICES OR IMAGES?

The most popular deep learning models for tasks involving images use 2-dimensional (2D) or 3D convolutional neural networks to perform tasks such as classification or segmentation. ECGs are thought of as 2D images, because there is an amplitude axis (y-axis) plotted against time (x-axis). Thus, training a 2D convolutional neural network model for ECG analysis makes intuitive sense. However, with time-series data, we can economize computational resources by inputting the ECG data as matrices and training a 1D convolutional neural network without any decline in performance because all the information that exists in the 2D images, already exists in the 1D signals. For ECGs, one way to do this is by taking each sample as an input (number of samples = sampling frequency × time).[9] Such a technique allows us to ration the computational resources elsewhere and preferably train larger numbers to build more robust models. Lampert et al[10] did start out with ECG waveform data but later plotted them as images. Though this conversion facilitates human comprehension, it is an extraneous step that inadvertently confines the AI to human-like processing. Liberating the AI from such human-oriented constraints could potentially lead to more optimal outcomes. The conversion introduces an unnecessary restriction in the form of image resolution and generates an excess of superfluous white pixels surrounding the ECG tracing. Consequently, it can be questioned whether this is worth the additional computational currency.

IS THIS DEEP LEARNING MODEL PRIMED FOR WIDESPREAD USE?

As we enter an era of AI-enhanced medicine, we are inundated with a plethora of machine-learning models that promise to transform our practice of medicine. We advocate for the rigorous examination of each model in the following key domains:

- Clinical utility and safety: The present model has immense potential to have clinical utility with the promise of identifying patients with PVCs at risk of developing CM. Thus, it can affect early intervention and improve outcomes positively. There are many challenges in developing such models while keeping patient confidentiality paramount. Despite the limitations, Lampert et al[10] report a respectable area under the receiver-operating characteristic curve of 0.79, with an area under the precision-recall curve of 0.50, which is good for a model with low event rates. The external data set outperforming the training set is quite interesting, and further exploration would be needed to exclude significant variance that may limit model generalizability. In the era of big data, we can agree that larger samples enabled by data sharing may be the best way to improve the model performance and may be critical before we can implement models into clinical practice.

JACC: CLINICAL ELECTROPHYSIOLOGY VOL. 9, NO. 8, 2023
AUGUST 2023:1452–1454

- Health equity and bias: The efforts of Lampert et al[10] to include a multiethnic patient cohort are laudable; however, over one-half of the patients had an unknown race. Future models can build on these efforts, and perhaps with bigger samples, subanalyses can exclude patients of unknown race to get an accurate idea of ethnic comparisons.
- Transparency: Lampert et al[10] attempted an explainability analysis of the model with gradient class-activation-map assessment and reported an intriguing finding of the model leveraging the sinus QRS beat to detect cardiomyopathy. This insinuates that it may be prudent for these authors to evaluate the proficiency of the trained model in forecasting future cardiomyopathy using ECGs devoid of any PVCs. This is because their presupposition that the pathology is precipitated by PVCs is not corroborated by the activation maps. The PVCs perhaps led to some subclinical structural changes, elusive to human interpretation but picked up by the model. This concept is not foreign because it is akin to how we use sinus beats to measure LVEF as opposed to PVC beats on an echocardiogram. That is to say, the subclinical CM has already occurred, we are simply unable to perceive it. We naturally crave to comprehend how a machine functions, but in reality, we will never achieve that because, if we could decipher it, computers would never outperform us. Our visual and cerebral capabilities disallow us from feature identification performed by the model. So, whereas this is a gratifying intellectual exercise, as models increase in complexity, we should overcome this natural inclination and accept a model as long as it performs well.

In summary, Lampert et al[10] have made a mark on a clinical conundrum that plagues many cardiologists. With further model refinement, data sharing, and prospective multicenter studies, we can hope to have a future where high-risk patients with PVCs can be identified and treated early.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Samuel J. Asirvatham, Mayo Clinic College of Medicine, 200 First Street SW, Rochester, Minnesota 55905, USA. E-mail: asirvatham.samuel@mayo.edu.

REFERENCES

1. Panizo JG, Barra S, Mellor G, Heck P, Agarwal S. Premature ventricular complex-induced cardiomyopathy. *Arrhythmia Electrophysiol Rev*. 2018;7(2):128–134.

2. Bogun F, Crawford T, Reich S, et al. Radiofrequency ablation of frequent, idiopathic premature ventricular complexes: Comparison with a control group without intervention. *Heart Rhythm*. 2007;4(7):863–867.

3. Kowlgi GN, Tan AY, Kaszala K, et al. Left ventricular dyssynchrony as marker of early dysfunction in premature ventricular contraction-induced cardiomyopathy. *Front Cardiovasc Med*. 2022;9:978341.

4. Kowlgi GN, Ramirez RJ, Kaszala K, et al. Post-extrasystolic potentiation as a predictor of premature ventricular contraction-cardiomyopathy in an animal model. *Europace*. 2020;22:813–820.

5. Torrado J, Kowlgi GN, Ramirez RJ, et al. Eccentric hypertrophy in an animal model of mid- and long-term premature ventricular contraction-induced cardiomyopathy. *Heart Rhythm O2*. 2021;2(1):80–88.

6. Tseng A, Kowlgi GN, DeSimone CV. Management of premature ventricular complexes in the outpatient setting. *Mayo Clin Proc*. 2023;98(7):1042–1053.

7. Kowlgi GN, Ezzeddine FM, Kapa S. Artificial intelligence applications to improve risk prediction tools in electrophysiology. *Curr Cardiovasc Risk Rep*. 2020;14:13. https://link.springer.com/article/10.1007/s12170-020-00649-1

8. Siontis KC, Noseworthy PA, Attia ZI, Friedman PA. Artificial intelligence-enhanced electrocardiography in cardiovascular disease management. *Nat Rev Cardiol*. 2021;18(7):465–478.

9. Attia ZI, Kapa S, Lopez-Jimenez F, et al. Screening for cardiac contractile dysfunction using an artificial intelligence–enabled electrocardiogram. *Nat Med*. 2019;25(1):70–74.

10. Lampert J, Vaid A, Whang W, et al. A novel 12-lead ECG-based deep learning algorithm to predict cardiomyopathy in patients with premature ventricular complexes. *J Am Coll Cardiol EP*. 2023;9(8):1437–1451.

KEY WORDS artificial intelligence, cardiomyopathy, deep learning, electrocardiogram, premature ventricular contractions