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Perspective

Role of AI-enabled ECG Analysis

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INTRODUCTION

Although the public is enamored with the role of artificial intelligence's large language models (e.g., CHAT GPT-4, Google's Gemini, Microsoft's Copilot, Claude and Perplexity), medical researchers are equally excited about the role machine learnings' convolutional neural networks (CNNs) are playing in screening and diagnosing diseases and conditions heretofore unknowable by current technology.

The ECG is the aggregate of the electrical activity of millions of individual cardiomyocytes recorded from the body's surface. In most conditions the underlying pathophysiologic process begins many years in advance of clinical presentations. Numerous distinct biological factors can subtly and nonlinearly impact cardio myocyte electrical function resulting in subclinical ECG alterations not evident on a normal 12-lead sinus rhythm ECG.

CNNs are modeled upon the human brain's network of neurons, with each AI neuron being a simple mathematical equation with parameters that are adjusting during network training. When these electrical neurons are connected in many layers, it is referred to as a Deep Learning (DL) network.

An ECG's time and voltage are easily digitized and have proved to be ideal inputs into a CNN. The CNN is trained with large ECG datasets (input) and the output is finding a specific condition (such as "hidden" atrial fibrillation, heart failure and other conditions). During the learning phase, parameters (sometimes called 'weights') are constantly being adjusted to minimize the 'errors', the difference between the desired output and the known outputs (*i.e.*, input being a 'normal ECG' and the desired output being a specific condition such as atrial fibrillation).

DESCRIPTION

AI-enabled ECGs

A group at the Mayo Clinic hypothesized that they may be able to detect the presence of intermittent AF from a normal sinus rhythm ECG. In a retrospective study, approximately one million ECGs from patients with no AF (controls) and patients with episodic AF (cases) were studied. The network was never shown ECGs with AF, but only normal sinus rhythm ECGs from patients with episodic AF and from controls. After training, the AI-ECG network accurately detected paroxysmal AF from an ECG recorded during normal sinus rhythm with an accuracy 79%-83% and an AUC 0.87.1

A large (908,000 ECGs from 6 US Veterans Affairs hospitals) VA study applied a deep-learning model to predict the presence of AF within 31 days of a sinus rhythm ECG. Their AUC was 0.93 with an accuracy of 0.87. Among individuals deemed high risk by their AI-ECG model, the number needed to screen to detect a positive case of AF was 2.47 individuals for a testing sensitivity of 25% and 11.5 individuals for testing sensitivity of 75%.

These and other articles have led to the conclusion that an AI-ECG applied to a normal sinus rhythm ECG may permit identification of individuals experiencing AF either previously or occurring in the future (*i.e.*, their current ECG shows sinus rhythm, but atrial fibrillation is present at other times). In patients at risk for AF, AI-ECG is strongly predictive of concurrent AF within 30 days of a normal sinus rhythm ECG with a high degree of accuracy, suggesting that an ECG (current or stored) may be a surrogate for prolonged rhythm monitoring.

AI-ECG screening for left ventricular systolic dysfunction

Sangha et al. used 385,601 normal sinus rhythm ECGs with paired low EF <40% (HFrEF) echocardiograms in both in-hospital and outpatient settings. Their AI-ECG model yielded AUCs of 0.88-0.94 in testing in several large medical centers in the US. An AI-ECG suggestive of LV systolic dysfunction portended >17-fold higher odds of LV systolic dysfunction on subsequent transthoracic echocardiogram. A positive AI-ECG in individuals with an LV ejection fraction 40% by echocardiogram at the time of initial assessment was associated with a 3.9-fold increased risk of developing incident LV systolic dysfunction in the future (median follow-up was 3.2 years).

Another study from the Mayo Clinic trained a CNN on paired 12-lead ECG and echocardiogram ejection fractions from almost

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45,000 patients with validation testing on an independent set of almost 53,000 patients. Their network model yielded an AUC of 0.93 with sensitivity and specificity of 86% and an accuracy of 86%. Again, in patients without ventricular dysfunction but with a positive AI screen (*i.e*., 'false positives'), there was a 4-fold risk of development of future ventricular dysfunction compared to persons with a negative screen over a median follow-up of 3.4 years.

A study from South Korea used a deep-learning model to detect Heart Failure with preserved Ejection Fraction (HFpEF). Their model yielded an AUC of 0.87. Again, in individuals without HFpEF on initial echocardiography, patients whose deep learning model indicated a higher risk proved, in fact, to have a significantly higher chance of developing HFpEF in the future than those in the low-risk group (34% *vs.* 8%, $p<0.001$).

These and other articles support the argument that an AI-ECG algorithm applied to a standard 12-lead (or single-lead) ECG enables occult stages of both HFrEF and HFpEF and the ability to predict future risk for developing LVD.

Screening for aortic stenosis

Cohen-Shelly combined 258,607 patients with paired ECG and TEE studies to screen for aortic stenosis. Their model's AUC was 0.85. In their testing group, 3.7% of patients were labelled as AI-ECG-positive AS with sensitivity 78%, specificity 74% and accuracy 74% for predicting echo-positive AS. Because of the low prevalence (4%) of AS in the population studied, the positive predictive value was low at 10.5% but the negative predictive value was high at 98.9%, allowing the authors to conclude that AI-ECG can be used to exclude asymptomatic moderate-severe AS.

CONCLUSION

In a study using 3060 expertly diagnosed patients from a hypertrophic cardiomyopathic clinic and comparing their findings with a control group of patients who had both ECG and echocardiographic data, their model yielded an AUC of 0.96 with sensitivity 87%, specificity 90%, positive predictive value 31% and negative predictive value of 99% when the optimal probability threshold was 11%. When higher HCM probability thresholds were applied, the performance characteristic changed to favor specificity and to reduce the false-positive rate. For example, with a probability threshold of 75% (instead of 11%), specificity was 99% and false-positive rate was 1%. The authors concluded that ECG-based detection of HCM by an AI algorithm can be achieved with high diagnostic performance, particularly in younger persons. Negative predictive values remained high regardless of thresholds selected for probability.