


Machine Learning in Cardiology: A Potential Real-World Solution in Low- and Middle-Income Countries

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Abstract: Artificial intelligence (AI) and machine learning (ML) is a promising field of cardiovascular medicine. Many AI tools have been shown to be efficacious with a high level of accuracy. Yet, their use in real life is not well established. In the era of health technology and data science, it is crucial to consider how these tools could improve healthcare delivery. This is particularly important in countries with limited resources, such as low- and middle-income countries (LMICs). LMICs have many barriers in the care continuum of cardiovascular diseases (CVD), and big portion of these barriers come from scarcity of resources, mainly financial and human power constraints. AI/ML could potentially improve healthcare delivery if appropriately applied in these countries. Expectedly, the current literature lacks original articles about AI/ML originating from these countries. It is important to start early with a stepwise approach to understand the obstacles these countries face in order to develop AI/ML-based solutions. This could be detrimental to many patients' lives, in addition to other expected advantages in other sectors, including the economy sector. In this report, we aim to review what is known about AI/ML in cardiovascular medicine, and to discuss how it could benefit LMICs.

Keywords: artificial intelligence, machine learning, cardiology, low, middle, income, countries

Plain Language Summary

- AI/ML is a rapidly developing field that could improve healthcare delivery and disease outcome in many medical fields, and cardiology in particular.
- AI/ML could potentially improve healthcare delivery in LMICs if appropriately applied; however, this necessitates a thorough understanding of the obstacles that these countries face in the health-care sector.
- AI implementation in LMICs is not only the issue of finding the problem and developing an ML-based solution. It is a collective teamwork between physicians, AI/ML developers, policy makers, researchers, and educators to fully understand the issues and subsequently find practical solutions. All components are vital, and the absence of any of them could be detrimental to AI/ML implementation in LMICs.

Introduction

Artificial Intelligence (AI), specifically Machine Learning (ML), is expected to improve health-care operations and delivery.¹ In some countries, it is already revolutionizing the health-care sector. Economically, it is expected that AI can reduce United States (US) healthcare expenditure by 150 billion dollars by 2026.¹ Hence, it is speculated that ML could be of particular aid to low- and middle-income countries (LMICs) where human and financial resources are comparatively constrained.² Cardiology is of central importance in LMICs since cardiovascular disease (CVD) prevalence and death rates are the highest in these countries and cardiovascular care is costly and often complex.^{3,4}

Late diagnosis and presentation, co-morbidities including infections and malnutrition, fragmented referral system, lack of advanced diagnostic facilities, shortage of skilled teams, and inadequate financial support systems are among the leading causes of poor outcomes associated with cardiac diseases and their management in LMICs.^{5,6} AI technology can potentially bring considerable expertise close to where patients live by better focusing on population health, functioning as a clinical decision supporting tool for physicians, assisting in virtual health care for continuity of care, and triaging patients as a front-line server. Such a solution may help bridge the gaps in a patient's care continuum with CVD in LMICs. However, AI application in these countries will likely face some challenges on both, systemic (ie, less-developed health informatics ecosystems) and individual levels (ie, access to internet, smart devices). This report provides an overview of AI/ML, discusses what is known about ML in LMICs and explores how AI/ML can potentially improve cardiovascular medicine in LMICs.

AI Basics: The Process of Learning

To analyze complex input, one can breakdown inputs using pattern recognition in a step-by-step approach. [Figure 1S](#) shows a simple representation of an assumed algorithm for our brain. Within this theoretical framework, the learning process can be broken down into smaller parts of 1) feeding and 2) neural networks that interact in a dynamic way to reach a final decision. According to the American Psychological Association (APA) dictionary of psychology, learning is defined as “the acquisition of novel information, behaviors, or abilities after practice, observation, or other experiences, as evidenced by a change in behavior, knowledge, or brain function”.⁷

To understand ML, it is crucial to describe common terms used in the AI field.⁸ There are several types of ML, including deep learning, supervised learning (SL), unsupervised learning (UL), and reinforcement learning.⁹ DL is made of numerous algorithms arranged to give machines the ability to learn from a vast amount of data using multilayer neural networks. SL and UL refer to teaching machines with labeled versus unlabeled data, respectively. The former can aid in pattern recognition, whereas UL can be used to discover unnoticed patterns. Reinforcement learning, derived from the psychological term “reinforcement”, functions using a trial-and-error mode, wherein systems are reward-driven, so they keep going back and forth trying different steps to achieve the desired outcome. All these ways receive input, process the data, and generate a certain outcome ([Figure 1](#)).

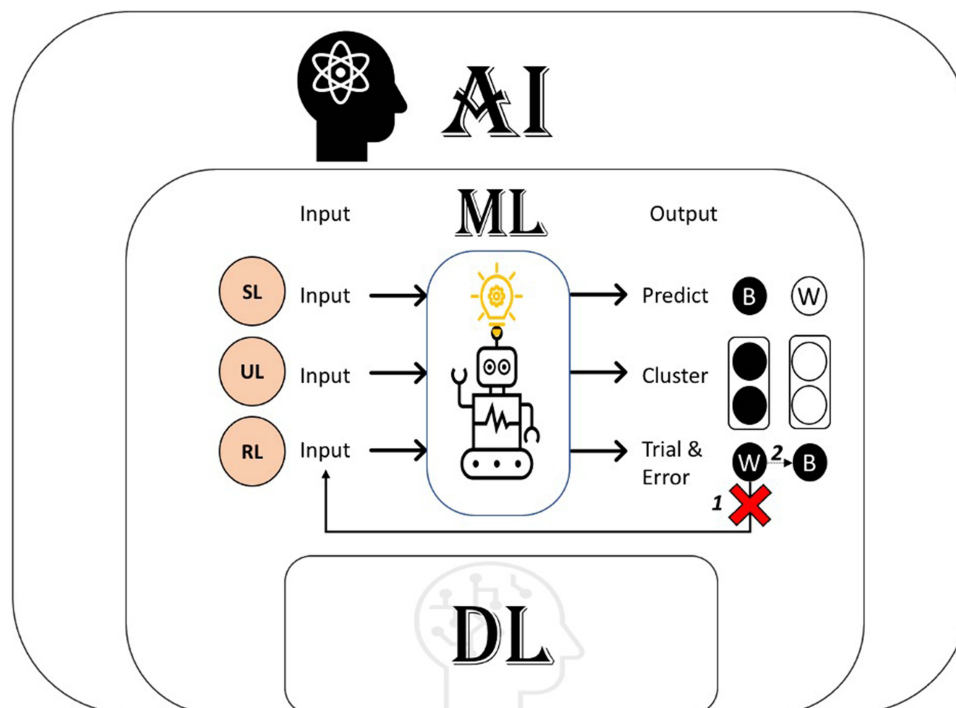


Figure 1 Artificial intelligence and machine learning. 1: First step there is a wrong prediction, which then allows the machine to predict the correct color of the circle in step 2. **Abbreviations:** AI, Artificial intelligence; ML, Machine learning; DL, Deep learning; SL, Supervised learning; UL, Unsupervised learning; RL, Reinforcement learning; B, Black; W, White.

AI/ML in Medicine

Although the efficacy of most of the AI software has been demonstrated in many research applications, their effectiveness in practice is yet to be as well established. The potential utility of AI has been demonstrated in pharmaceutical, medical (diagnosis, treatment, and follow-up), and analytical purposes.¹⁰ For instance, systems have been created that can recognize consolidation on chest x-rays with minimal human input. [Figure 2S](#) depicts a simplified diagram of a presumed AI algorithm for consolidation detection. Behzadi-Khormouji et al published an AI model that can detect consolidation on CXR with an accuracy of 94.7%.¹¹

Current literature has numerous articles, with promising results, that shed the light on AI applications in different fields of medicine ([Figure 3S](#)) including nephrology¹² (acute kidney injury and chronic kidney disease alert systems, wearable dialysis devices, kidney transplantation prognosis), neurology¹³ (epilepsy, stroke, dementia, movement disorders), dermatology¹⁴ (tumors, ulcers, inflammatory lesions, dermatopathology), endocrinology,¹⁵ surgery,¹⁶ obstetrics and gynecology¹⁷ (risk assessment of preterm labor, pregnancy complication, gynecological surgery) in addition to cardiology. AI was an important tool against the coronavirus during the pandemic, with different successful applications. During the COVID-19 pandemic, AI has been used as a warning system, diagnostic and prognostic tool, and in building robots that aid in food and medications delivery to quarantined patients,¹⁸ although with high risk of bias in majority of tools during the COVID-19 pandemic, perhaps due to short period between development to application because of the pandemic.¹⁹ Many AI-based software packages have already been approved by the US Food and Drug Administration (US-FDA), including diagnostic software for CVD.²⁰

Cardiology and ML in Low- and Middle-Income Countries: What is Already Known?

As per the World Development Indicators, 2016, countries can be categorized based on income.^{21,22} Around 90% of the worldwide CVD burden is present in the LMICs, yet surprisingly, they only have 10% of research and health-care resources required to deal with this issue.²³ The greatest percentage of deaths due to CVD worldwide is present in LMICs, which is estimated to be around 80%.²⁴ Due to this burden, it is believed that efforts to decrease CVD's impact would have the greatest global effect in these countries.²⁵ Interestingly, Rosengren et al showed that the risk factor profile for CVD is considered optimum in low-income countries among all income groups, except for high blood pressure, in which low-income countries rank first.²⁶ However, it is impractical to generalize this since many of the LMIC do not have population-based studies on CVD incidence, prevalence, and associated risk profiles.

Another challenge is the inappropriate number of physicians in different parts of the world. As of 2020, according to the WHO, there is one medical doctor for 3324 persons in Africa, 1239 Southeast Asia, 989 Eastern Mediterranean, 533 Western Pacific, 417 Americas, and 293 in Europe.²⁷ Most low-income countries are located in Africa and Southeast Asia, which can further support the linear relationship between their weak economies and numbers of physicians in these countries, since increased numbers of physicians is associated with overall better healthcare quality.²⁸ The lack of resources has been inversely proportional to major adverse cardiovascular events. By targeting patients with high CVD risk, a study assessed the association between major adverse cardiovascular events and the availability and affordability of three classes of medications that are essential and commonly used in cardiology (anti-hypertensive agents, antiplatelets, and statins). They included patients from low, lower-middle, upper-middle, and high-income countries. They were divided into three groups based on medications availability and affordability (group: 1 available and affordable; 2: available but not affordable; 3: not available). In comparison to group 1, major CVD events were higher in group 2 (hazard ratios [HR] 1.19, 95% CI 1.07 to 1.31) and group 3 (HR 1.25, 95% CI 1.08 to 1.50). Expectedly, low and lower-middle-income countries had the lowest percentages in group 1 and group 2; in other words, medications availability and affordability were directly proportional to the country's income (ie, low-income countries had the lowest percentages in both groups).²⁹ This example highlights the important relationship between limited resources of lower-income countries with CVD outcomes.

LMICs have a low expenditure on healthcare and its workforce, which is expected to be inversely linked to the number of deaths from CVD since the management requires both resources and well-trained personnel.³⁰ Delay of diagnosis and treatment is among the most important reasons which make CVD the top cause of death. While this delay is often related to the fact that heart diseases develop insidiously and present acutely, in LMICs, this might not be the only reason behind their high fatality, where resources are scarce compared to the other countries.

Potential Advantages of AI/ML in Cardiology

In cardiology, AI has been well studied and has various applications. AI can be applied at least to 5 domains of cardiology, including electrophysiology, imaging, heart failure, preventive, and interventional cardiology. Atrial fibrillation (AF) is an example that can be diagnosed with an ECG where AI/ML can be applied to aid in this. Algorithmically speaking, ECGs can be broken down to heart rate, regularity, waves (P-QRS-T), intervals, and segments. Figure 2 shows a suggested AI algorithm that can detect AF. Noteworthy, AI not only uses the classical ECG findings to diagnose AF but also can do that with subtle ECG changes that often go unnoticed by the naked eye. A recently developed AI model was able to detect AF using a single normal sinus rhythm (NSR) ECG with an accuracy of 79.4% (receiver operating characteristic [ROC] curve, area under the curve [AUC] = 0.87), which increased to an accuracy of 83.3% (AUC = 0.90) when multiple ECGs were used.³¹ Thus, one can speculate that shortly a low cost, widely available test such as ECGs can function as a great diagnostic tool for AF before it is clinically apparent, with high diagnostic abilities that are comparable to other tests such as B-type natriuretic peptide for heart failure (AUC 0.60–0.70)³² and the CHA2DS2-VASc Score³³ for stroke risk assessment (AUC 0.57–0.72).³¹ However, this would first need a rigorous validation in a particular geographic location before considering implementing clinically.

Data is extracted from ECGs; however, this type of data needs special means to detect the hidden patterns, since in our example, NSR was used for AF detection. These commonly appearing ECGs carried a particular AF “signature”, as described by Attia et al.³¹ This could also aid in decreasing the time to initiate treatment. In our example, time refers to

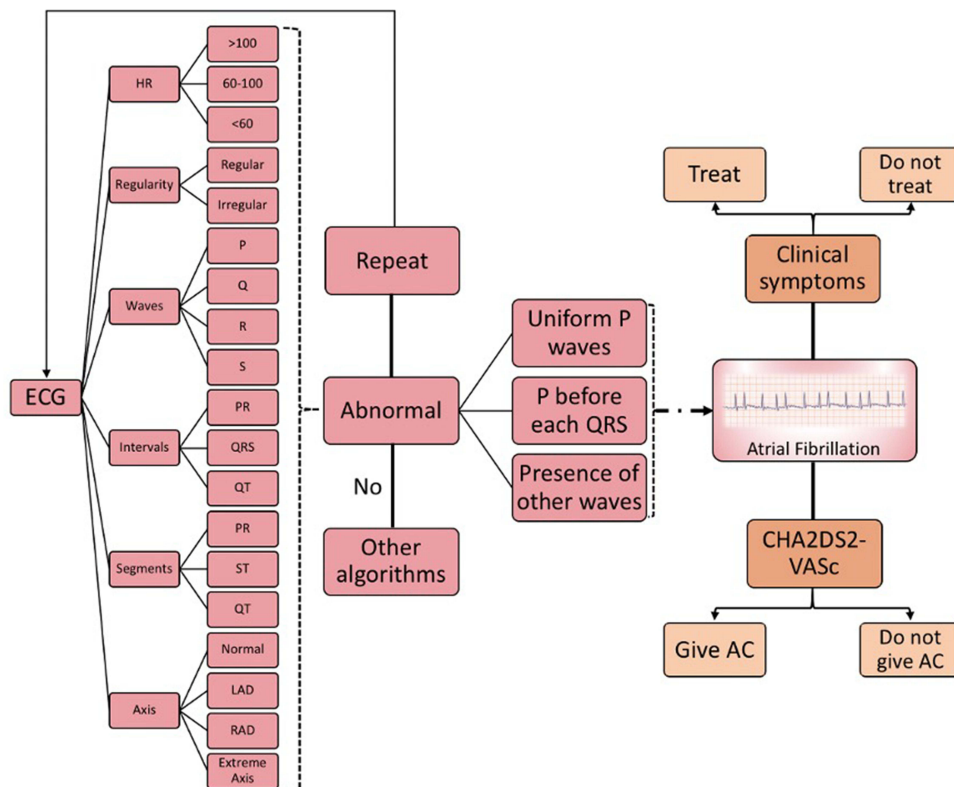


Figure 2 Simplified algorithm in the field of cardiology that can help in atrial fibrillation diagnosis and treatment. **Abbreviation:** AC, Anti-coagulation.

the fact that early detection of AF allows early initiation of therapy (if indicated) or stroke prevention measures, which may potentially reduce the risk of AF complications (ie cardiovascular, neurological), its associated significant socio-economic impact given the potential for long-term morbidity and even death. If well implemented in countries with limited resources, this AF AI algorithm could provide substantial clinical (eg, early AF detection) and economic (eg, less testing, less loss of productivity) benefits.³⁴ Nonetheless, it is essential to consider that detecting AF in NSR could lead to more downstream testing (eg, long-term monitors), and this could increase incidental ECG findings. More testing means higher demand for resources, which could be detrimental to LMICs.

To date, many randomized clinical trials (RCT) have been published about ML in Cardiology. To evaluate this, PubMed Search was done (June 6th, 2022) using the following search string: machine learning AND Cardiology, and by applying “clinical trials” filter. This search string generated 43 results, 37 studies of which are focused on cardiology and ML and are RCT. These RCT focused on all 5 different fields of cardiology and started to be published in 2017 onward. Gevaert et al have shown that clinical phenotypes are more helpful than left ventricular ejection fraction (LVEF) in predicting heart failure outcomes (n = 1693).³⁵ This was done through cluster analysis of UL, which detected 6 phenotypes that are LVEF-independent. Primary composite outcome (all-cause death or rehospitalization) at 6 months had an HR of 1.25 (95% CI 1.00–1.58 for AF) and 2.04 (95% CI 1.62–2.57 for chronic obstructive pulmonary disease) (log-rank $P < 0.001$), while HR at 12 months was 1.15 (95% CI 0.94–1.41 for AF) and 1.87 (95% CI 1.52–3.20 for chronic obstructive pulmonary disease) ($P < 0.002$). LVEF-based categorization did not show such separation (6 months [$P = 0.69$] and 12 months [$P = 0.30$]). This evidence may suggest that UL cluster analysis (a form of ML) may be a better prognostic tool than LVEF in outcome prediction. Another study³⁶ showed that ML through ML and cluster analysis was able to generate various echocardiographic phenotypes in asymptomatic community-based cohorts (n = 827), which were divided into 3 groups including mostly normal (MN), diastolic changes (D), and diastolic changes with structural remodeling (D/S). These results were externally validated, and they were associated with an adjusted HR of 1.87; (95% CI: 1.04 to 3.37) in the D phenotype, and an adjusted HR of 3.02 (95% CI: 1.71 to 5.34) in the D/S phenotype for both cardiovascular mortality and heart failure hospitalization. These RCT are examples of potential applications of ML in heart failure and heart imaging, but many others are available in other fields including electrophysiology,³⁷ interventional^{38,39} and preventive cardiology.^{40,41} That is one way to look at ML in cardiology. Another way to look at various aspects wherein ML could be applied in cardiovascular care, including improving diagnosis,^{31,42} risk prediction,^{43,44} disease monitoring,⁴⁵ access to care,⁴⁶ point-of-care testing,⁴⁷ and decision support tools.^{48–50}

The advancement we are witnessing in the medical field is also associated with a proportional increase in complexity. This not only makes it more challenging to reach a decision but also becomes a time- and money-consuming process if these algorithms are operated by humans, with a possible chance of missing important information altogether. Besides, with the increase in patient number that is being dealt with on daily basis, error rates can rise when using these algorithms, rendering patient care in jeopardy. These issues are most prominent in LMICs, where cardiovascular health is deteriorating. In the current era of smart machines,⁵¹ it is crucial to consider employing these tools in discovering a more precise and quicker way to analyze the vast data in various medical fields, especially in cardiology.

Discussion

We presented data on the role of AI/ML in CVD, but the essential question that arises is whether AI has already been deployed to improve the health-care sector in LMICs or will be soon. To have an idea about the current use of AI-cardiology in LMICs, we searched PubMed using the following search string: ((cardiology) AND (artificial intelligence) AND (countries)) AND ((low) OR (middle) OR (high) OR (poor) OR (developing)) on the March 15th, 2021. A total of 21 studies were found, most of which were related to AI-cardiology. However, only two articles focused on the issue of AI-cardiology use in resource-limited countries/LMICs. The first study was done in a tertiary care center in the UK and did not examine AI's outcomes on LMICs.⁵² The second study was a review that focused on AI's potential benefits and advice for resource-limited countries.⁵³ A bibliometric analysis published in 2021 on AI/ML-cardiology found out that research output on PubMed in this field is mainly achieved by developed countries, with the US, United Kingdom, and China ranking as the top three countries, respectively.⁵⁴ The insufficient number of articles arising from LMICs shows the gap between AI advancement and its applications in the countries that need it the most. This is not unexpected. The

relatively new development of AI-cardiology, the underdeveloped research structure in LMICs, and their poor economies, altogether may account for the delay in AI-cardiology application in these countries. Of note, this search string is not inclusive since some studies might describe an application of AI without using its terms explicitly.

AI/ML may come into play in such scenarios where it can help potentially improve work productivity,⁵⁵ by occupying vacancies, as an independent, functional entity. A recently published prospective study assessed cardiovascular events in patients ($n = 154,169$) from different countries (low, middle, and high-income) and their association with socioeconomic status (education and wealth) over a follow-up mean of 7.5 years. They found out that major cardiovascular events (deaths, strokes, infarction, and heart failure) and all-cause mortality are inversely proportional to the level of education, and this association was much more apparent in low-income countries among the three. Contrary to that, there was no clear association between individual wealth and these two outcomes between the three groups.²⁶ This might indicate that households with good financial status who are living in low-income countries are, nevertheless, impacted in a similar way to poor families, perhaps due to lack of good and reliable medical care, even if they are willing to spend on it. It is unlikely that implementing AI in healthcare in the LMICs will directly improve any outcomes based on economic benefits. It can help improve clinical efficacy, safety, effectiveness, and productivity in healthcare.

CVD, as a group, is of special importance, particularly in LMICs since it puts these countries in a vicious cycle. These countries face a substantial financial and disease burden of CVD,⁵⁶ and each of these two further exacerbates the other infinitely (Figure 3). AI can play a very effective and efficient role in CVD management in LMICs. By reducing the healthcare expenditure on CVD, it might be possible to achieve better medical and financial outcomes (eg, budget allocation, redistribution/acquisition of human resources).

The applications of AI-cardiology in LMICs can take many forms and shapes. In LMICs, detecting myocardial infarction using the standard criteria and prompt activation of the closest health-care center for possible intervention might be a valuable evolution to these countries. Having an AI tool that can detect AF in “normal” ECGs is interesting, but to the people in LMICs, early myocardial infarction detection and arranging for a possible intervention is, likely, far more valuable. Detection or diagnosis is an essential step in managing any disease, but not the only one that AI can potentially improve. Care continuum refers to health-care delivery that spans all phases of an illness, including recognition, diagnosis, prioritization, referral, transportation, treatment, and follow-up.^{57–59} In AI-Cardiology, it is essential to consider each one of these steps in the care continuum of any single disease to improve outcomes.

Another example in LMICs is the use of echocardiography, which technicians can operate. The data obtained from each echocardiogram for each patient can be overwhelming. But if the basic findings of each echocardiogram are employed in a way that alerts the responsible physician when an abnormality is detected, this can solve a part of the problem (ie, low ejection fraction is automatically reported to the assigned cardiologist). Many other examples can be

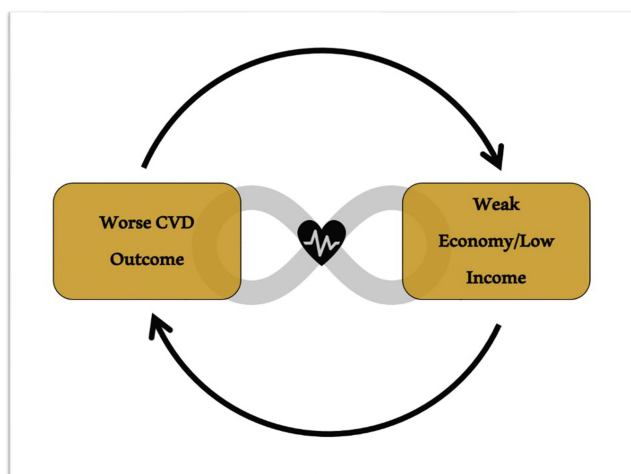


Figure 3 The “Positive Feedback Effect” of CVD in LMICs.
Abbreviation: CVD, Cardiovascular Disease.

thought of in LMIC-cardiology, which revolve around two main factors that are probably deficient in LMICs: adequate human power and resources. Another issue is that although many AI-cardiology tools have been proven to be efficacious, the effectiveness is yet to be established, especially in LMICs where many unforeseen factors might influence the functionality and applicability of these tools.

A promising example from the literature shows that AI could potentially be used in resource-limited countries. In a study that was done in Bangalore, India, mobile health (mHealth) clinics were compared to the standard-care clinics in patients with rheumatic and structural heart diseases. This study aimed to see which of these two clinics have shorter time-to-intervention and better clinical outcomes. mHealth clinics gathered data from pocket echocardiography, smartphones, 6-minute walk test, and BNP point-of-care testing. On the other hand, the standard-care clinics collected data from 12-lead ECG, imaging, and lab tests. Patients in both groups underwent transthoracic echocardiography. The mHealth group was found to have shorter time until intervention and better outcomes.⁶⁰ This randomized clinical trial highlights the important role that AI-cardiology could play when applied in resource-limited countries (ie, LMICs), but it is important to note that this was not a decision support system. Another paper highlighted the promising applications of AI-cardiology which were driven from electro-cardiographical-based studies. In this review, it was shown that AI-cardiology can be employed for diagnostic, prognostic, and therapeutic purposes, in addition to disease monitoring and risk stratification in a multitude group of CVDs including AF, heart failure, hyperkalemia, and hypertrophic cardiomyopathy.⁶¹ Of note, all of these applications were derived from ECG mainly, which may suggest that other fields of cardiology are fertile fields for AI. Although most of these applications are still being studied and will likely take time until they become ready for clinical use, they carry huge potentials if applied in LMICs. Moreover, while AI/ML development in high-income countries is mainly focused on improving diagnostic time and accuracy, it is crucial to employ this tool to target each step of the care continuum of CVDs diagnosis and treatment, including improving patient triage (ie, avoid unnecessary ER visits, while decrease time for true emergent cases), finding cheaper diagnostic tests, augmenting human power by establishing independent AI units that can be operated with minimal human input, and avoiding unnecessary care by creating AI prognostic tools. These interventions would be designed to streamline care rather than generate additional “new” patients to treat and would be valuable in LMICs.

AI-Cardiology in LMICs: Implementation and Ethical Consideration

Nowadays, many AI-cardiology softwares have been approved by the US-FDA. One of the main issues with echocardiography is that it is operator-dependent; thus, clinical decisions that are based on certain echocardiograms can be biased due to many limitations including a problem in image acquisition. Image acquisition of diagnostic quality requires special training, which is deficient in LMICs. One of the possible solutions is the recently and first US-FDA approved cardiac ultrasound software, Caption Guidance. Caption Guidance guides the users to capture echocardiograms in a quality that is comparable to trained echocardiographers.⁶² A recently published study assessed Caption Guidance on 240 patients by allowing 8 nurses with no prior training in echocardiography to acquire echocardiograms to assess different cardiac parameters. 90% of the cases the nurses were able to acquire images that were of diagnostic quality. No significant differences were detected when these images were compared to other images taken by expert sonographers.⁶³ The US-FDA has also approved the AI-ECG Platform for clinical use.⁶⁴ It is a fully automated, accurate (98.3%), rapid (3s), and economical tool that can help in ECG interpretation through AI neural networks.⁶⁵ Other examples of US-FDA AI tools in the field of cardiology include Arterys Cardio DL, EchoGo Core, AliveCor, BioFlux, eMurmer ID, and many more.⁶⁶ This highlights that AI is not only a promising idea that is being studied but also a reality with many approved options for clinical use. These tools, if appropriately implemented, could dramatically improve the health-care systems in LMICs, especially in remote areas where subspecialized cardiologists are few in numbers. The turn now is on policymaker in the LMICs to carefully study and assess the situation to start with AI/ML implementation in their health-care systems to be ready for clinical use.

Figure 4 depicts a suggested algorithm for the application of AI/ML in LMICs. High-risk cardiac patients in resource-limited areas can be monitored using wearable devices that work based on the Internet-of-Things, which include simple accessories (eg, a watch or a wristband). These devices are connected to a central AI unit, streaming data continuously about the status of the patients from different parameters. These units would analyze the signal using the embedded

Table I Future Directions to Help AI/ML Implementation in LMIC

1.	AI/ML applications in cardiology should be examined in terms of effectiveness in addition to efficacy, to better understand their impact once applied to daily clinical practice.
2.	Researchers should examine possible roadblocks affecting cardiovascular care in LMICs and how these could be solved by ML.
3.	In addition to improving the timing and accuracy of diagnostic tests, ML/AI tools developers should focus on developing cheaper alternatives to the already existing, yet expensive ones.
4.	Educators in LMICs should expose advanced learners (eg, masters, Ph.D., fellows) to basic concepts of AI/ML and especially in LMICs.
5.	Policymakers should raise awareness about ML use in medicine, while ensure that these are there to help healthcare providers, not replace them.

Abbreviations: AI, Artificial intelligence; ML, Machine learning; LMICs, Low- middle- income countries.

Abbreviations

AF, Atrial fibrillation; AI, Artificial Intelligence; AUC, Area under the curve; CVD, Cardiovascular disease; HR, Hazard ratios; LMICs, Low- and middle-income countries; LVEF, Left ventricular ejection fraction; ML, Machine learning; NSR, Normal sinus rhythm; RCT, Randomized clinical trials; ROC, Receiver operating characteristic; SL, Supervised learning; SLUL, Unsupervised learning; ULUS, United States; USUS-FDA, US Food and Drug Administration.

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