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REVIEW

The use of artificial intelligence in the diagnosis of peripheral arterial disease: a systematic review

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ABSTRACT

INTRODUCTION: Peripheral artery disease (PAD) affects more than 200 million people worldwide. Despite this, doctors often fail to detect it due to inconsistencies in screening criteria, inadequate patients, and a high prevalence of quiet or unusual symptoms. It is believed that the use of artificial intelligence (AI) will overcome these problems. This systematic review aims to summarize various previous studies that have investigated the use of artificial intelligence in managing PAD.

EVIDENCE ACQUISITION: This is a systematic review using high-quality articles from the PubMed, Science Direct, and ProQuest databases published between 2011-2023. The method of selection and analysis of articles followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).

EVIDENCE SYNTHESIS: A total of six research articles were included in the analysis. Four studies documented its use to diagnose PAD based on clinical characteristics, with two of these studies revealing AI's capacity to predict prognosis and give automated risk stratification for cardiovascular diseases. One research also indicated that it was used to classify PAD more precisely and more effectively. There were three studies that described the use of AI in radiological modalities such as Doppler ultrasonography, Angiography, and Multispectral Imaging.

CONCLUSIONS: The use of AI based on clinical features and radiological examination AI based on clinical characteristics and radiological test findings can be utilized to manage PAD, particularly in the diagnostic and prognosis stratification processes.

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KEY WORDS: Peripheral arterial disease; Artificial intelligence; Machine learning; Doppler ultrasonography.

Introduction

Noncommunicable diseases (NCDs) have emerged as major sources of morbidity and death in both developed and developing countries. The disease burden associated with NCDs is increasing globally, with cardiovascular diseases (CVDs) being the primary cause of death and morbidity. As a result, the prevalence of peripheral artery disease (PAD) has been steadily increasing.[1] PAD is a progressive atherosclerotic disease of the lower legs that is used to diagnose generalized atherosclerosis.[2]

Claudication, cramping discomfort in the calves, thighs, or buttocks that is typically induced by walking and subsides with rest, is the most prevalent sign of PAD. Atypical pain on exercise and ischemic discomfort at rest may also be present. The last stages of the disease may result in tissue loss and amputation. PAD may be asymptomatic for some time, however symptomatic PAD is linked with substantial limits in physical function, particularly walking and a variety of everyday activities.[3] Even when the Ankle-Brachial Index (ABI) is more than 0.9, most individuals remain asymptomatic. Asymptomatic peripheral artery disease (APAD) in combination with established risk factors (hypertension, diabetes mellitus, and smoking) significantly increases the risk of cardiovascular disease (CVD). Patients with suspected underlying illness should have further noninvasive diagnostics performed.[4]

PAD has been linked to increased morbidity and mortality from cardiovascular disease (CVD), myocardial infarction (MI), stroke, and major adverse cardiovascular events (MACE). those with PAD have the same risk of having a future stroke or MI as those with coronary artery disease.[5] Individuals with early-stage PAD may not or commonly under-report claudication symptoms (pain in the lower limbs), and despite the substantial in-hospital expenditures associated with advanced stage PAD, the illness frequently goes unrecognized and untreated.[6]

The high number of misdiagnosed PAD patients is unfortunate because preventative medicines like statins and antithrombotic medications can save both life and limb. A significant investment has been made in recent years to find effective therapies for PAD, including multiple randomised clinical studies of both medicinal and revascularization techniques. At the same time, healthcare is at a tipping point, with vast volumes of data being generated from sources such as electronic health records (EHRs), medical imaging, wearables, and large-scale genetic sequencing. The large number of data provides chances to revolutionize how vascular patients are cared for.[7]

Since the original Compendium's release, several medical specialties have attempted to utilize "Big Data" and sophisticated analytics,[8] but real-world integration of artificially intelligent systems and medicine is still in its infancy. When applied to PAD, advanced analytics have the potential to discover latent illness, enhance disease and risk phenotyping, and help treatment decisions by considering a wide range of demographic, biological, and clinical data. Artificial intelligence-powered vascular imaging systems will also aid in diagnostic, prognostic, and surgical scenarios. Given that PAD treatment is frequently dispersed over several sites and specializations, AI can help with integrating care data points, supporting the holistic, multidisciplinary care that is crucial to optimizing management and results.[9] This study investigates the contributions of artificial intelligence and machine learning to PAD treatment and considers what combining AI and PAD care may entail to emphasize the importance of developing AI algorithms for PAD, particularly to assist saving individuals from dying.

Evidence acquisition

Study design and study selection

This study was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA) guidelines. We systematically searched for all relevant articles in the following online databases: PubMed, Science Direct, and ProQuest databases published between 2011-2023. The key terms used for the search were "artificial intelligence," "peripheral arterial disease," and various variations and derivatives of the word. Keywords were combined using Boolean searches and the search was made using keywords, Boolean operators, and MeSH descriptor depending on the guidelines in each database.

After the initial search, author assessed the eligibility of each publication. The inclusion criteria of selected study were as follows: 1) studies in adults; 2) explains in detail the protocol used for the machine learning. We excluded the following: 1) articles irrelevant to the topic; 2) duplicate publications; and 3) trials of a cross-over study design.

Data extraction, quality assessment, data synthesis, and analysis

Author evaluated the quality assessment of all eligible articles. Data from all the studies were extracted, analyzed, and compared qualitatively.

Evidence synthesis

Five hundred and one non-duplicate publications identified from the databases, 493 publications were excluded from this study because screening of titles and abstracts showed that there was no relevance of the results to the problems raised in this review. Then eight publications were included in our qualitative synthesis after critical review and finally there were six publications that were worthy of being analyzed in depth (Figure 1, Table I).[8, 10-14]

The purpose of this systematic review was to identify and assess high-quality studies demonstrating the usefulness of artificial intelligence in managing PAD. A total of three studies reported the use of artificial intelligence in analyzing radiological examination results to diagnose PAD. A study by McBane *et al.* uses the results of Doppler ultrasound examinations to be analyzed by artificial intelligence. The study reported that the accuracy of using artificial intelligence in analyzing the results of Doppler

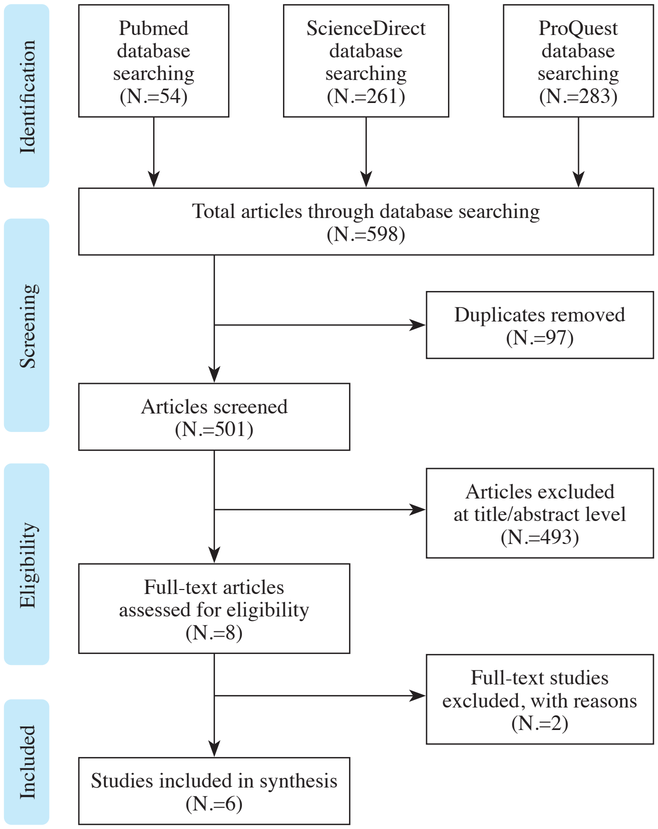

Figure 1.—Flow diagram showing the selection of articles for review.

ultrasound examinations to diagnose PAD was included in the high category with a sensitivity value of 83% and a specificity of 88%. The results of the area under the curve (AUC) analysis also showed a high value, which is 0.94 (0.92-0.96).[10] Another study conducted by Squiers *et al.*[11] used another modality, namely multispectral imaging. The study found that the use of artificial intelligence in analyzing multispectral imaging results has an accuracy of 91% sensitivity and 86% specificity for prediction of PAD at non-healing amputation sites (area under curve 0.89).[11]

A study by Weissler *et al.*[12] analyzed other radiological modalities, which are arteriography to angioplasty. Using natural language processing analysis techniques, this study analyzed the finding of the phrase "angiography" or "angioplasty" in the medical records of patients with confirmed PAD and non-PAD. The results of the artificial intelligence analysis in this study found that these two phrases (or their derivatives/variations) were significantly more common in patients with confirmed PAD (P<0.001).[12]

A total of four studies reported the use of artificial intelligence based on clinical findings to diagnose PAD. Study conducted by Gao *et al.*[14] reported that artificial intelligence can be used to analyze 28 clinical features to diagnose PAD. Its use is reported to have better sensitivity and specificity than the results of logistic regression analysis and the results of ABI measurements alone. Then of the 28 features, seven of them were re-analyzed by artificial in-

TABLE I.—*Characteristics of articles for review.*[8, 10-14]

Study	Deep learning method used	Main findings
McBane *et al.*[10]	Inception Time	The predictive model with highest performance identified PAD with an AUC 0.94 (CI = 0.92–0.96), sensitivity 0.83, specificity 0.88, accuracy 0.85, and positive predictive value (PPV) 0.90
Ross *et al.*[13]	Elastic Net, penalized regression model, and Random Forest	Machine-learned models outperformed stepwise logistic regression models both for the identification of patients with PAD (AUC 0.87 *versus* 0.76, respectively, P=0.03), and predicting future mortality (AUC 0.76 *versus* 0.65, respectively, P=0.10)
Squiers *et al.*[11]	Very Deep Convolutional Networks for Large-Scale Image Recognition modified with a Feature-wise Linear Modulation technique	Machine learning algorithm had 91% sensitivity and 86% specificity for prediction of non-healing amputation sites (area under curve 0.89). Machine learning algorithm combining multispectral wound imaging with patient clinical risk factors may improve prediction of amputation wound healing and therefore decrease the need for re-operation and incidence of delayed healing
Weissler *et al.*[12]	Label-Embedding Attentive Model (LEAM) and a Least Absolute Shrinkage and Selection Operator (LASSO)	The median (standard deviation) of the area under the ROC curve for the NLP model was 0.888 (0.009). The median (standard deviation) of the area under the PR curve was 0.909 (0.008) for the structured data-based approach
Ross *et al.*[8]	Penalized linear regression and random forest algorithms	Utilizing almost 1000 variables, our best predictive model accurately determined which PAD patients would go on to develop MACCE with an area under the curve (AUC) of 0.81 (95% CI, 0.80-0.83)
Gao *et al.*[14]	Logistic regression and a random forest (RF) model	Thirteen of the 28 features differed significantly between PAD and non-PAD participants. The respective sensitivities and specificities of logistic regression, RF, and ABI were as follows: logistic regression (81.5%, 83.8%), RF (89.3%, 91.6%) and ABI (85.1%, 84.5%). In the prospective study, the newly designed RF model based on the most significant seven features exhibited an acceptable performance rate for the diagnosis of PAD with 100.0% sensitivity and 90.3% specificity

telligence and found greater accuracy, namely 100% sensitivity and 90.3% specificity. These seven features are the results of measurements of ABI, creatinine, fasting blood glucose, age, heart disease, diabetes, and hypertension.

A study by Weissler *et al.*[12] identified that the characteristics of gender, race (predominantly in the Caucasian race), history of PAD more than twice, history of revascularization procedures, and history of treatment at a specialist were clinical characteristics that were significantly associated with PAD based on artificial intelligence analysis.[12] As previously mentioned, this study uses natural language processing analysis techniques. This shows that when artificial intelligence is trained to be able to identify phrases related to these various clinical characteristics, the diagnosis of PAD can be predicted accurately and more quickly.

A study conducted by Ross *et al.* reported that various risk factors and clinical conditions can be used to predict the diagnosis of PAD through analysis by artificial intelligence. Of the several risk factors and clinical conditions analyzed, it is known that cumulative tobacco pack years, weakness in leg, and claudication are the three variables with the greatest diagnostic value. Overall analysis of risk factors and clinical conditions using artificial intelligence has high accuracy for diagnosing PAD, with an AUC of 0.87.[13]

Study conducted by Ross *et al.* also reported that several clinical conditions can be used to predict the diagnosis of PAD through artificial intelligence. Characteristics that can be used for analysis by artificial intelligence include age, sex, race, diagnosis code (hypertension, coronary artery disease, type II diabetes, hyperlipidemia, atrial fibrillation), use of certain drugs (saline, tylenol, glucose, potassium, ondansetron), and certain laboratory results (serum potassium, erythrocyte mean corpuscular hemoglobin concentration, serum carbon dioxide).[8]

Among the four studies, two of them, namely Ross *et al.* and Ross *et al.*, reported that various risk factors and clinical conditions can be used to predict the occurrence of major adverse cardiac and cerebrovascular events (AUC) 0.81; 95% CI: 0.80-0.83) to future mortality (AUC 0.76).[8, 13]

It is important to note that the deep learning methods used in the study analyzed in this systematic review vary widely. The study by McBane *et al.* uses InceptionTime, the study by Squiers *et al.*[11] uses Very Deep Convolutional Networks for Large-Scale Image Recognition modified with a Feature-wise Linear Modulation technique, the study by Weissler *et al.*[12] using Label-Embedding Attentive Model (LEAM) and a Least Absolute Shrinkage and Selection Operator (LASSO), as well as the studies by Ross *et al.*[8] and Gao *et al.*[14] using regression and random forest models. This shows that although the analysis techniques used by artificial intelligence vary, their benefits for diagnosing PAD show similarities.

Conclusions

The use of AI based on clinical features and radiological examination AI based on clinical characteristics and radiological test findings can be utilized to manage PAD, particularly in the diagnostic and prognosis stratification processes.

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Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions
Sri P. Negoro: conception and design, drafting of the article and collection and assembly of data. Yan E. Sembiring: critical revision of the article for important intellectual content and final approval of the article. Latifah A. Zati: provision of study materials or patients. Jeffrey J. Dillon: statistical expertise and critical revision of the article for important intellectual content. I G. Putra: conception and design. All authors read and approved the final version of the manuscript.

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