Applications of artificial intelligence for patients with peripheral artery disease

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ABSTRACT

Objective: Applications of artificial intelligence (AI) have been reported in several cardiovascular diseases but its interest in patients with peripheral artery disease (PAD) has been so far less reported. The aim of this review was to summarize current knowledge on applications of AI in patients with PAD, to discuss current limits, and highlight perspectives in the field.

Methods: We performed a narrative review based on studies reporting applications of AI in patients with PAD. The MEDLINE database was independently searched by two authors using a combination of keywords to identify studies published between January 1995 and December 2021. Three main fields of AI were investigated including natural language processing (NLP), computer vision and machine learning (ML).

Results: NLP and ML brought new tools to improve the screening, the diagnosis and classification of the severity of PAD. ML was also used to develop predictive models to better assess the prognosis of patients and develop real-time prediction models to support clinical decision-making. Studies related to computer vision mainly aimed at creating automatic detection and characterization of arterial lesions based on Doppler ultrasound examination or computed tomography angiography. Such tools could help to improve screening programs, enhance diagnosis, facilitate presurgical planning, and improve clinical workflow.

Conclusions: AI offers various applications to support and likely improve the management of patients with PAD. Further research efforts are needed to validate such applications and investigate their accuracy and safety in large multinational cohorts before their implementation in daily clinical practice. (J Vasc Surg 2023;77:650-8.)

Keywords: Artificial intelligence; Machine learning; Deep learning; Big data; Neural network; Natural language processing; Peripheral artery disease

Peripheral artery disease (PAD) affects more than 230 million people worldwide.[1,2] The disease is associated with high rates of morbidity and mortality.[3-7] The diagnosis relies on the combination of clinical examination, measurement of ankle-brachial index, functional assessment (treadmill test), and identification of arterial lesions on imaging.[8] Several imaging techniques can be used including duplex ultrasound (US) examination, digital subtraction angiography, computed tomography angiography (CTA) and magnetic resonance angiography.[8]

Despite the elevated risks of cardiovascular mortality and amputation, PAD remains underdiagnosed and underestimated.[5,9-12] It is often diagnosed at an advanced stage of the disease owing to low patient awareness and high prevalence of asymptomatic disease or atypical symptoms.[5,9,13] In addition, several studies have suggested that these patients may be undertreated, especially considering best medical treatment, pointing to the need to improve the use of evidence-based recommended therapies in patients with PAD.[14-17]

Artificial intelligence (AI) is a broad topic that regroups several fields including natural language processing (NLP), which corresponds with applications of AI for written or oral language, and vision, with applications for

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images or videos analysis.[18] Machine Learning (ML) is considered as a subfield of AI where algorithms are used to give the ability to the system to learn[18,19] (see the Supplemental the glossary for definitions of technical terms). AI-derived techniques such as ML have brought new insights in cardiovascular diseases and have demonstrated their interest to improve image segmentation, identify patterns from patients data and develop predictive scores.[20-23] Although AI applications have been well-described in cardiac or aortic diseases,[21,24-28] their use in patients with PAD has been less often reported.[29] The aim of this review was to summarize the main applications of AI in patients with PAD, discuss current limitations, and highlight future directions.

AI IN RESEARCH AND PRACTICE

NLP

Medical notes and electronic health records (EHRs) provide a wide source of medical data. They include data in a structured format (ie, laboratory test results) or unstructured free-text narratives (ie, medical notes, images, video, or audio).[30] EHRs have been used extensively in epidemiological research because they are a source for rapid and automated identification of large cohorts of patients.[31] However, the validity of the information derived from EHRs depends on the quality, availability of the data, accuracy (internal validity), appropriate selection criteria, interpretability and representativeness (external validity) of the EHR to general target population.[31] The *International Classification of Diseases* (ICD) provides terminology and classification that is considered as health data standard by the World Health Organization.[32] Although the classification helped to standardize coding and billing system, several studies have highlighted that the use of ICD classification alone is sometimes incomplete to identify patients' diagnosis and phenotypes, especially in PAD.[33,34] Additional codes defined by national systems are, therefore, often used to complete the characterization of the disease and its treatment.

Identification of patients with PAD. NLP techniques have received increasing attention to enhance analysis of biomedical texts[35] and several studies aimed to use it to improve identification of PAD based on medical records (Table I). Using a dataset of 1569 patients (including 806 patients with PAD and 763 controls), Afzal et al[36] developed a NLP system for automatic ascertainment of PAD cases from clinical narrative notes. The NLP algorithm was knowledge driven and had two main components, including text processing and patient classification.[36] The performances of the NLP were compared with two previously developed models based on ICD-9 diagnostic codes and demonstrated better accuracy.[36] The NLP algorithm developed by Afzal et al offers the advantage to be applied on clinical notes including progress notes collected during the hospitalization course or during outpatient contacts. The algorithm used keywords and rules independent from billing codes, improved the accuracy to identify PAD, and offered the perspective to potentially implement it on other EHR systems. The authors further improved the NLP method by developing and validating sub-phenotyping algorithms to identify critical limb-threatening ischemia (CLTI) from clinical notes.[37] Compared with algorithms based on ICD-9 billing codes, the NLP algorithm showed a higher positive predictive value and specificity to identify CLTI. Such tools offer perspectives to improve the automatic identification of PAD and CLTI from clinical notes and brings potential to further link it to clinical decision support tools.[37] Savova et al[38] also developed NLP algorithms to identify PAD cases from radiology notes (including lower extremity angiograms or US examination) and demonstrated an overall agreement of 0.93 between the system and the gold standard created manually and consisting of 223 positive, 19 negative, 63 probable, and 150 unknown cases. Finally, using a cohort of 6861 patients, another study aimed to leverage NLP to identify more accurately patients with PAD in EHRs compared with a structured data-based approach.[39] The median of the area under the curve (AUC) was significantly higher with the NLP system compared with the structured-based approach (0.888 vs 0.801; $P < .0001$).

Perspectives and limits. Altogether, NLP offers perspectives of applications in clinical research, by improving large-scale PAD search and in clinical practice to facilitate PAD identification and targeted interventions. In addition, several studies have highlighted the interest of AI algorithms to automate the literature screening procedures.[40-42] AI could be of use to provide a quick and precise overview of current and relevant literature. It can also reveal hidden connections between findings and data, bringing new perspectives and hypotheses. It offers the potential to decrease workflow and it would be worth investigating its applications to enhance literature search and evidence-based decisions for patients with PAD. Although these preliminary results are promising, several challenges remain before such technologies can be implemented in both research and daily clinical practice. First, all the methods developed would require external validation in multiple clinical centers to assess the generalizability of the results. Moreover, because there is increasing evidence for substantial differences between countries and reimbursement systems, a multinational validation seems appropriate. The interpretability of the algorithms remains difficult to assess. Multidisciplinary collaboration between clinicians, computer scientists, and biostatisticians should be promoted in all the stages of creation and validation of the NLP algorithms to enhance the development of

Table I. Summary of the main studies investigating the use of Natural Language Processing (*NLP*) for patients with peripheral artery disease

Aim	Study design	Results	References
Develop a NLP system for automated ascertainment of PAD cases from clinical narrative notes	Dataset of 1569 PAD patients: 806 PAD and 763 controls. Comparison of the performance of the NLP algorithm to previously validated algorithms based on relevant ICD-9 diagnostic codes (simple model) and a combination of ICD-9 codes with procedural codes (full model).	The NLP algorithm demonstrated higher accuracy, higher PPV, higher specificity compared with the simple and full model.	Afzal et al[36] 2017
Extend a previously validated NLP algorithm for PAD identification to develop a subphenotyping NLP algorithm for identification of CLI cases from clinical notes.	Dataset of 792 PAD patients: 295 CLI and 497 controls (without CLI), 270 336 clinical notes. Comparison of the performance of the CLI-NLP algorithm with CLI-related ICD-9 billing codes.	The CLI-NLP algorithm had higher PPV and higher specificity compared with the CLI-related ICD-9 billing codes.	Afzal et al[37] 2018
Apply, extend and evaluate an open source clinical NLP system for the task of phenotype extraction from radiology notes for identifying PAD cases	Extension of an open source clinical NLP system (Mayo's Clinical Text Analysis and Knowledge Extraction System) for the discovery of PAD cases from radiology reports. Comparison to manually created gold standard including 223 positive, 19 negative, 63 probable and 150 unknown cases.	The overall accuracy agreement between the system and the gold standard was 0.93.	Savova et al[38] 2010
Leverage NLP to more accurately identify patients with PAD in an EHR compared with structured data-based approach	Dataset of 6861 patients: 3746 patients with PAD and 3115 without PAD Comparison with an administrative data-based LASSO approach using DeLong test	The median of the AUC for the NLP was significantly higher compared with the LASSO-based approach.	Weissler et al[39] 2020

ABI, Ankle-brachial index; *CLI*, critical limb ischemia; *EHR*, electronic health record; *ICD*, *International Classification of Diseases*; *LASSO*, least absolute shrinkage and selection operator; *NPV*, negative predictive value; *PAD*, peripheral artery disease; *PPV*, positive predictive value.

efficient systems that meet the expectations and needs in medical practice.[43]

ML

Identification and diagnosis of patients with PAD. Several studies developed ML algorithms to identify PAD (Table II). In a cohort of 1755 patients admitted for elective angiography, Ross et al[44] used supervised ML algorithms based on diverse data including clinical, demographic, imaging and genomic information to identify patients with PAD. The ML models showed better performance than logistic regression models to identify PAD, with an AUC of 0.87 versus 0.76 ($P = .03$).[44] In another cohort of 354 patients, McCarthy et al[46] aimed at combining biomarkers with clinical risk factors to identify obstructive PAD using ML. ML identified the variable predictive of obstructive PAD and the final score included one clinical variable (history of arterial hypertension) and six biomarkers (midkine, kidney injury molecule-1, IL-23, follicle-stimulating hormone, angiopoietin-1, and eotaxin-1). The AUC for identification of obstructive PAD was 0.84 and higher scores were associated with increased severity of angiographic stenosis.[46] Finally, ML was also used to investigate the relationship between functional limitation and PAD symptoms.[47] In this study involving 703 patients, functional limitation was evaluated by a 6-minute walk distance and symptoms using a quality-of-life questionnaire. Interestingly, this study highlighted a nonlinear relationship between these two variables.[47] Their results suggested that ML could bring new tools to help optimizing diagnostic strategy to early detect PAD, especially in asymptomatic patients.[47]

Evaluation of the prognosis of patients with PAD. In addition, to enhance the detection and the diagnosis of PAD, improving the evaluation of the outcomes and the prognosis of patients is a major concern. A few predictive models have previously been built toward this aim,[4,51,52] but they presented some limitations because they were built on selected groups of patients with PAD. Automatic extraction of medical data from EHRs may help to extend the numbers of patients included to build accurate patient specific risk prediction models.[53] Some have already been deployed to estimate cardiovascular risks.[54-56] In a retrospective analysis of 87,293 patients with PAD, Kreutzburg et al[7] developed a prognostic score to predict the risk of amputation using Cox

Table II. Summary of the main studies investigating the use of machine learning (*ML*) for patients with peripheral artery disease (*PAD*)

Aim	Study design	Results	References
Develop ML algorithms for the identification of PAD and the prognostication of mortality risk	Dataset from 1755 patients who presented for elective coronary angiography. Development of multiple supervised ML algorithms form diverse clinical, demographic, imaging and genomic data. Comparison of the ML model to standard stepwise linear regression models.	ML models outperformed stepwise logistic regression models both for the identification of patients with PAD and predicting future mortality.	Ross et al[44] 2016
Develop a novel predictive model using ML methods on EHR data to identify which PAD patients are most likely to develop MACCE	Dataset of 7686 patients included in learning the predictive models. Development of predictive models using structured (coded) and unstructured (text) data.	The best predictive model used almost 1000 variables and accurately determined which PAD patients would go on to develop MACCE with an AUC of 0.81.	Ross et al[45] 2019
Combine biomarkers and clinical risk factors to increase the accuracy of predicting clinically significant PAD using ML	Dataset of 354 patients referred for diagnostic peripheral and/or coronary angiography, 132 patients with PAD. Development of ML predictive models using more than 50 clinical variables and 109 biomarkers.	The final ML score consisted of 1 clinical variable (history of hypertension) and 6 biomarkers and had a cross-validated AUC of 0.84.	McCarthy et al[46] 2018
Explore the relationship of functional limitation and PAD symptoms	Dataset of 703 patients from an administrative database. Development of ML analysis to plot functional tests against PAD severity.	ML allowed exploration of nonlinear relationship between functional limitation and symptom severity.	Qutrio Baloch et al[47] 2020
Develop a personalized prediction model that utilizes patient characteristics prior to CLI diagnosis to predict 1-year all-cause hospitalizations and total annual health care costs	Database of 3189 patients. Use of a novel Bayesian ML platform to build models to identify predictors of all-cause hospitalizations and total annual all-cause health care costs.	The main predictors of all-cause hospitalizations were skin and subcutaneous tissue infections, cellulitis, abscess, use of nonselective beta-blockers, other aftercare, and osteoarthritis. The leading predictors for total all-cause costs included region of residence and comorbid health conditions.	Berger et al[48] 2020
Develop an assessment tool of the femoral PAD diagnosis and treatment using a RBFNN	Dataset of 186 patient records with 16 characteristic features associated with a binary treatment decision (being medical or surgical treatment). Development of a RBFNN to assess PAD diagnosis and treatment.	RBFNN demonstrated its potential interest as an effective assessment tool for femoral PAD treatment.	Yurtkuran et al[49] 2013
Examine factors associated with 90-day hospital readmission after vascular procedures using big data and ML system.	Dataset of 246 405 patients, of whom 30.3% were readmitted within 90 days. Development of predictive model of 90-day hospital readmission for patients undergoing elective carotid endarterectomy, aortofemoral bypass/aortic aneurysm repair, and femoral-distal arterial bypass.	Shrinkage discriminant analysis was the best performing model to predict 90-day readmission. Main variables for the best predictive model included length of stay in the hospital, comorbidity scores, endarterectomy procedure, and elective admission type.	Amato et al[50] 2020

ANN, Artificial neural networks; *AUC*, area under the curve; *MACCE*, major adverse cardiac and cerebrovascular events; *NPV*, negative predictive value; *PPV*, positive predictive value; *RBFNN*; radial basis function neural network; *ROC*, area under the receiver operating characteristic curve.

regression model. Arruda-Olson et al[57] further aimed to automatically extract data from EHRs and develop a real-time and individualized risk prediction model. The model allowed to stratify patients' mortality by subgroups, bringing perspectives to implement the tool to support clinical decision-making.[57] ML techniques allow the analysis of data in a hypothesis-free manner and their use to predict future mortality of patients with PAD have been reported in other studies.[44] Ross et al[45] further developed another model to predict major adverse cardiovascular and cerebrovascular events using ML on EHRs, showing the interest of the technique to predict mortality as well as complications.

Other prediction models have been developed to better assess the risk of clinical complications related to PAD (Table II). As an example, a prediction system for chronic leg ulcer was created from a cohort of 80 patients with PAD based on fuzzy logic.[58] The algorithm provided a reliable score for the risk of ulcer and could be of use for classification of PAD.[58] Another study developed a personalized prediction model based on baseline patients' characteristics prior to CLTI diagnosis to predict 1-year all-cause hospitalization.[48] The model identified main predictors of all-cause hospitalizations and could potentially be a useful tool to identify at risk patients and target them for early prevention and intervention to deliver cost-effective medical services.[48]

Evidence-based decision and decision-making. The therapeutic options for patients with PAD depend on several factors including anatomic locations and severity of lesions, symptoms, functional tests, comorbidities, and risks related to surgery and anesthesia.[6,59] Despite current guidelines, the choice of the most appropriate therapeutic option can be difficult to evaluate and a multidisciplinary approach can be useful for the management of patients.[8,49] AI could bring new tools to support evidence-based decision and guide clinicians in decision-making. Some investigators aimed to develop a clinical decision support system for classifying the treatment options regarding femoral PAD.[49] Using a radial basis function neural network, they showed that such AI algorithm could be useful to enhance evidence-based decision.[49] Finally, Amato et al[50] aimed to develop ML models to predict 90-day hospital readmission in patients who underwent vascular repair including elective carotid endarterectomy, aortofemoral bypass, aortic aneurysm repair, or femoral-distal arterial bypass. Their study identified main variables impacting on 90-day hospital readmission and included length of stay in the hospital, comorbidity scores, endarterectomy procedure, and elective admission type.[50] This model may help to better stratify patients to prevent or anticipate unplanned readmission.[50] Although these methods would require validation in larger cohorts of patients, the results are encouraging to develop new tools to enhance precision medicine in patients with PAD.

Limits and perspectives. ML brings new tools to better detect, classify PAD and predict the outcomes of patients to anticipate and optimize cares. Nevertheless, there are current limitations. Despite encouraging results, the sensitivity and/or the specificity of the models developed are not perfect and would have to be taken in consideration before using them in practice. The models were developed on datasets that have been collected for a specific aim and their accuracy depends on the quality, accuracy, availability, and representativeness of the data used. Beyond this sample and exclusion bias, further challenges have to be considered appropriately, for example, using different technical solutions for training and validation may lead to measurement bias while insufficient methods may introduce algorithmic bias. External cross-validation from data with multiple institutions and different countries would help to evaluate the robustness of the systems developed. Finally, ML functions as a black box and the accountability of the factors implemented in the predictive models can sometimes be difficult to explain. Traditional epidemiologic approaches may help to identify causal links and ML could be a complementary tool to investigate and take into consideration the nonlinear relationships between variables. Despite the many advantages of ML for both research projects and clinical care, it must be emphasized that these technologies also introduce new challenges. An important aspect of ML that gets increasing attention is related to the individual privacy of patients.[60] It seems reasonable and for certain projects even inevitable to involve experienced information scientists to secure data privacy-compliant ML.[60]

Vision

Doppler US examination. Imaging plays a central role in the management of patients with PAD.[3,8] US imaging provides extensive information on arterial anatomy and hemodynamics and has the advantage of being low cost, noninvasive, and easily available. Doppler US examination can be used for the screening of PAD, for preoperative planning as well as the postoperative follow-up of PAD. However, with two-dimensional US examination, it is difficult to visualize the lower limb vascular tree within an acceptable time frame and the measurements of atherosclerotic lesions can be associated with interobserver variations.[61] Several three-dimensional US systems have thus been developed for vascular imaging,[62] and Janvier et al[61] aimed to enhance it by creating a three-dimensional US imaging robotic system to control and standardize the acquisition process by scanning arterial lower limb segments. The accuracy of the robotic system to locate and quantify lower limb vessel stenoses was evaluated in a phantom model as well as in vivo on a volunteer and showed encouraging results to facilitate identification and evaluation of stenotic lesions.[63-65]

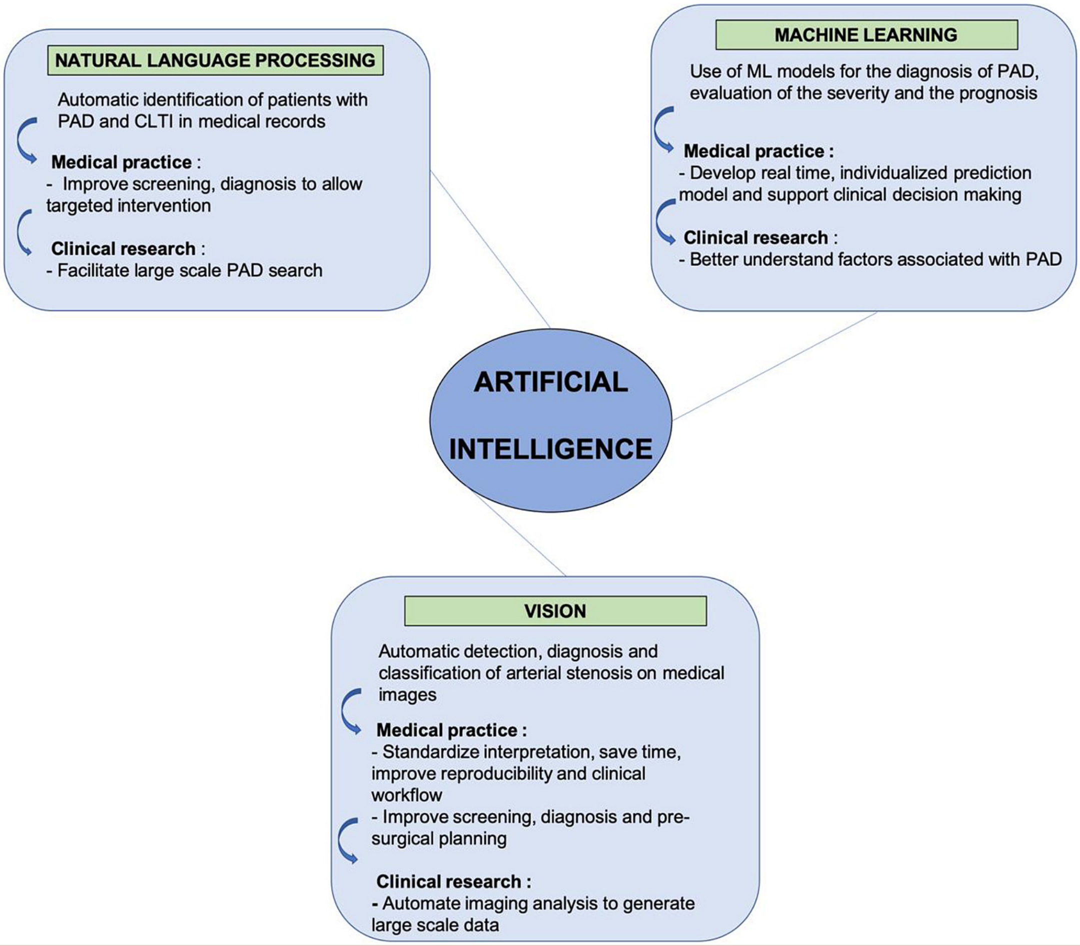

Fig. Main applications of artificial intelligence (AI) for patients with PAD. *CLTI*, Critical limb-threatening ischemia; *ML*, machine learning; *PAD*, peripheral artery disease.

The interpretation of US examination for PAD also requires to analyze and interpret pressures and waveforms. The use of artificial neural networks (ANN) to classify photoelectric plethysmography (PPG) waveforms was early investigated by Allen and Murray.[66] They successfully trained an ANN to distinguish PPG pulses from normal and diseased lower limb arteries.[66] The performance of the algorithm was tested in 200 patients and showed a sensitivity of 92% and a specificity of 63%, with a diagnostic accuracy for PAD of 80%.[67] ANN demonstrated better performances to classify arterial pulse waveforms as compared with classification techniques based on linear discriminant classifier or k-nearest neighbor classifier.[68] AI techniques could be used to recognize and differentiate the signals and waveforms to identify, classify, and evaluate the severity of atherosclerotic lesions. Using a virtual patient database of 28,868 patients, Jones et al[69] developed ML algorithms to identify vascular diseases including carotid artery stenosis, subclavian artery stenosis, abdominal aortic aneurysm and PAD. The sensitivity and specificity for PAD were greater than 90%. Kim et al[70] also developed deep learning (DL) models to diagnose PAD based on the analysis of PPG and showed the accuracy of the method in 2000 virtual patients. From 5761 US examination studies on PAD in which blood pressure and waveform data were available, Luo et al[71] developed a DL model to classify aortoiliac, femoropopliteal, and trifurcation disease. The DL algorithm showed an accuracy of 97% for predicting normal cases, 88.2% accuracy for aortoiliac disease, 90.1% for femoropopliteal disease, and 90.5% for trifurcation disease.[71] The study demonstrated the ability of the ML models to differentiate normal from diseased arterial systems and classify the extent of vascular disease.[71] Such application could help to facilitate US interpretation, save time and reduce variability. Finally, the proof of concept of the use of DL to identify PAD based on PPG signals in real-world medical practice was then demonstrated in a cohort of 214 participants, where the overall test sensitivity was 86.6% and the specificity 90.2%.[72] Such a tool could be of interest to automate and facilitate PAD diagnosis using affordable and noninvasive US technique. In time, it could be used potentially to enhance screening programs and improve the detection of patients with PAD.

CTA. CTA is another imaging technique that can be used to identify arterial lesions, plan the treatment and determine the feasibility and modality of invasive treatments.[3,8] Accurate detection and classification of lesions is necessary to determine the optimal revascularization strategy.[73] The interpretation and analysis of CTA is time consuming, tedious, requires expertise of the operator, and can be associated with variations among studies.[74-76] Automated vessel identification in patients with PAD is challenging owing to the heterogeneity of the presentation of the disease, the discontinuity of vascular flow channels owing to stenoses, presence of atherosclerotic calcifications, or presence of preexisting stents that can cause artefacts.[77] DL could provide a feasible solution to automatically detect and classify lower extremity arterial plaque. In a cohort of 265 patients who underwent lower extremity CTA, Dai et al[78] trained a convolutional neural network to classify the lower extremity artery segments according to the degree of stenosis. The model demonstrated good performance, with an accuracy of 91.5% in classifying above-knee artery and 90.9% in classifying below-knee artery.[78] Such an application could be used potentially as an auxiliary tool to locate the arterial plaque, improve the detection of PAD, help to better classify lesions, and optimize the workflow and screening of the disease. ML algorithms require a large volume of data to be trained and scientific research in this field is limited by the fact that obtaining labeled data to serve as ground truth is difficult and require manual segmentation by human experts, which can be tedious and extremely time consuming.[77] To cope with this current limit, Mistelbauer et al[77] proposed a novel semiautomatic vessel tracking approach for peripheral arteries to enhance the creation of annotated training data by human experts by limiting manual interactions and decreasing processing time. Their method enabled expert physicians to identify all relevant lower extremity arteries, with an average sensitivity of 92.9%, an average specificity and overall accuracy of 99.9%.[77] Such an approach requires less user interaction, offering perspectives for clinical practice, but also for clinical research by facilitating the generation of labeled ground truth data that could then be further used for ML. Although AI offers interesting perspectives to automate imaging analysis and detection of arterial stenosis, further research is required to investigate the generalizability of the applications developed. External validation in multicenter studies is required and would be of interest to further explore the accuracy of the algorithms in subpopulation known to develop specific patterns of arterial lesions, such as diabetic patients or patients with severe chronic kidney disease.[79-81]

CONCLUSIONS

AI offers a wide range of perspectives to support and likely improve the management of patients with PAD (Fig). Although PAD is an underestimated condition, NLP and ML bring new tools that may help to better identify and diagnose the disease, classify complex phenotypes, and develop predictive models to evaluate the outcomes and prognosis of patients. Imaging analysis through automatic detection and characterization of arterial lesions could also help to improve screening programs and offers new tools for clinicians to improve workflow and better plan the surgical intervention. In addition, PAD is often undertreated.[14-17] AI may bring new tools to diagnose the disease at early stage and may help to develop precision medicine and propose a personalized therapeutic approach by taking into account the severity of PAD balanced with patients' risks. Although perspectives of applications are very wide, AI medical devices or software are not yet validated for use in daily clinical practice for patients with PAD. This factor underlines the real need to pursue research efforts in this field and should encourage multidisciplinary collaboration between engineers and health professionals to enhance validation and implementation of AI devices in medical practice.

AUTHOR CONTRIBUTIONS

Conception and design: FL, CAB, AC, RL, MC, CA, CDL, JR
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SUPPLEMENTARY DATA (online only).

Glossary of technical terms

Artificial Neural Network (ANN). ANN are DL algorithms inspired by biological nervous system in which neurons transmit signals to another one. They are composed of node layers, containing an input layer, one or more hidden layers, and an output layer. Each node, or artificial neuron, connects to another and has an associated weight and threshold which weaken or enhance the signal during the learning process. Neural networks rely on training data to learn and improve their accuracy over time. The black box often refers to hidden layers because it is not known how the neural network derived a specific result.

Black box. The decision-making process of a ML model is often referred to as a black box. Although the users and researchers know the inputs and the outputs, the process and what is going on inside hidden layers are not straightforwardly interpretable to humans.

Convolutional neural network (CNN). A CNN is class of ANN biologically inspired from the connectivity patterns and organization of neurons in the visual cortex of human brain. CNN is composed of multilayer networks with mathematical models that make them very efficient and often used for image analysis including processing, detection, segmentation or visual recognition.

Cox regression model. A statistical method used for investigating the effect of several variables upon the time for a specific event to happen. It builds a predictive model for time-to-event data.

Deep learning (DL). A type of ML method that allows the model to be fed and learn from a large quantity of data. DL regroups various algorithms among which neural networks are most commonly used for medical applications.

Fuzzy logic. An approach to compute the degree of truth in a way that mimics the decision-making process in humans. Human decision-making often includes a wide range of possibilities between yes or no to a specific question or problem to solve. Fuzzy logic is designed to solve problems by considering all available information and making the best possible decision given the input.

k-Nearest neighbor classifier. A nonparametric supervised ML method used for classification.

Linear discriminant classifier. A statistical method used to find a linear combination of features that characterizes or separates two or several classes of objects or events. It is used for classification.

Logistic regression model. A statistical method used to predict the probability of a certain class or event to happen.

Machine learning (ML). ML corresponds with algorithms that have the ability to learn and automatically improve their performance through experience and use of data. ML algorithms are built from training data to feed the model and to learn how to solve the problem for which it is designed. Several techniques can be used to train the models including supervised, unsupervised or reinforcement learning.

Radial basis function neural network (RBFNN). A type of ANN that is commonly used for function approximation problems. They are typically composed of three layers: an input layer, a hidden layer (with radial basis function as activation function) and an output layer.