Artificial Intelligence to Predict Outcomes in Peripheral Artery Disease

AI applications are a promising solution for PAD that may translate into earlier detection, customized risk assessment, and improved outcomes.

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Peripheral artery disease (PAD) frequently goes undiagnosed due to inconsistent screening, low patient and provider awareness, and high rate of asymptomatic or atypical presentations, until it may be too late to salvage the extremity. When diagnosed, patients with PAD often receive less aggressive therapy than those with coronary or cerebrovascular disease, compounding the risk of serious complications such as chronic limb-threatening ischemia, amputation, and cardiovascular mortality, which are significant causes of both morbidity and cost globally.

One of the major challenges with PAD is the nonlinear relationship between various longitudinally presenting factors and the ultimate outcome. A patient may be diagnosed with diabetes a decade prior to undergoing a below-knee amputation, and there are myriad factors that contribute to the ultimate amputation outcome. It is known that 80% of amputations in the United States are completely preventable; hence, having the ability to predict outcomes in PAD and intervene early to prevent adverse outcomes is paramount. Traditional predictive methods fall short, primarily because they rely on a points system that attempts to classify this highly heterogeneous group of patients into clean boxes with prediction scores. However, the intricate interplay among clinical demographics (diabetes, hypertension, chronic kidney disease), laboratory markers, imaging findings, hemodynamic parameters, procedural details, and biomarkers creates a complex, nonlinear clinical puzzle that is associated with ultimate outcome. In this multifaceted context, conventional linear models and risk scores simply cannot capture the synergistic and opposing relationships that influence PAD outcomes.

Artificial intelligence (AI) and machine learning (ML) offer a powerful solution by automatically modeling high-dimensional, nonlinear interactions and synthesizing disparate data—from electronic health records (EHRs) and imaging to Doppler waveform analyses—into accurate prognostic tools. By discerning subtle patterns amid noise, AI systems can predict clinical outcomes, stratify risk, and inform therapeutic decisions in real time. In PAD management, this translates into earlier detection, customized risk assessment, and ultimately improved limb and life preservation.

EXISTING RESEARCH ON AI IN PAD OUTCOME PREDICTION

Flores and colleagues at Stanford developed a deep learning algorithm trained on EHR data from over 3,000 PAD patients and 16,000 controls.[1] Their automated system identified undiagnosed PAD cases and prompted physicians through a dashboard, earning clinician support for integration into daily workflows.

Elsewhere, natural language processing (NLP) applications and computer vision tools, such as those analyzing Doppler waveform and CTA images, have automated both diagnosis and phenotyping of PAD. A 2023 review highlighted the emergence of image-based AI tools that could transform diagnosis, presurgical planning, and workflow, while also calling for rigorous validation in diverse cohorts.[2]

Quantitative imaging studies have shown promise in objectively measuring disease burden. Using a deep neural network, researchers segmented arterial systems in femoral endarterectomy CTA scans and quantified calcification with approximately 83% accuracy and a mean absolute percentage error of 9.5%.[3] These

KEY CHALLENGES TO ADDRESS BEFORE WIDESPREAD ADOPTION OF AI APPLICATIONS FOR PAD

- Improve data quality and generalizability
- Externally validate models through prospective testing in real-world settings and randomized controlled trials comparing AI-derived clinical decisions versus standard care
- Earn physician trust and ensure transparency by integrating AI features directly into EHR workflows
- Confirm adherence to strict ethical and regulatory standards to account for bias and ensure patient privacy
- Ensure cost-effectiveness of AI-driven interventions through prospective analyses

measurements, when validated, could become vital biomarkers for disease severity and progression. These studies focused on predicting risk but still relied on physician intervention to perform treatment.

Our team at the Massachusetts General Hospital used AI to decipher thrombosis prediction using thromboelastography with platelet mapping (TEG-PM). In a single-center, prospective study of 308 PAD patients undergoing lower extremity revascularization, elevated platelet aggregation and reduced inhibition on TEG-PM were significantly associated with subacute thrombosis over 1 year.[4] Our team combined routine clinical data with TEG-PM and ML models (logistic regression, extreme gradient boosting, and decision trees) to predict arterial thrombotic events within 1 year postrevascularization. Among 308 patients, 18.3% experienced arterial thrombotic events; the logistic regression model integrating both clinical and TEG-PM data achieved an area under the receiving operating curve (AUC) of 0.76, with 70% accuracy, 68% sensitivity, and 71% specificity. Interestingly, the performance of the TEG-PM–augmented model (AUC, 0.76) significantly surpassed that of the logistic model relying on clinical data alone (AUC, 0.51). Although these findings were a nice first step that underscores how AI can integrate advanced physiological measurements to enhance individualized risk assessment, with a low number of patients (N = 308), the ability of AI to truly be transformative is quite limited. AI relies heavily on large data sets to not only decipher nonlinear relationships but also test hypotheses. A small number of patients can lead to bias and incorrect correlations; therefore, it is imperative that the entire vascular community buy into the use of AI to improve PAD outcomes and pledge to contribute data toward this goal to obtain enough data points to be effective.

Complementary AI approaches are also being explored. Convolutional neural networks trained on Doppler waveform analysis have accurately classified phasicity patterns and predicted adverse limb events, and support vector machine models have shown early promise in graft thrombosis prediction.[5,6] Meanwhile, a model using six biomarkers demonstrated an AUC of 0.84 in predicting 2-year PAD outcomes in prospectively followed cohorts.[7] Although these are incredible advances, the final frontier will be using AI not only for prediction but also to provide treatment algorithms that lead to successful outcomes based on large volumes of data. The holy grail would be predicting patient outcomes, identifying mitigating factors, and providing treatment pathways to achieve risk reduction that can change in real time if the patient changes their lifestyle or develops new comorbidities, keeping the relative risk of an event below a designated threshold.

CHARTING THE FUTURE: WHAT COMES NEXT IN PAD AI RESEARCH

Even as AI applications in PAD continue to mature, several key challenges must be addressed before these tools can be widely adopted (Sidebar).

First, data quality and generalizability must be improved. Most models, including my own, are derived from single-center, homogeneous cohorts and thus may not translate well to diverse patient populations. Establishing multicenter PAD registries and adopting federated learning, whereby models are trained across decentralized data sets without sharing sensitive patient information, can enhance diversity and mitigate bias.

Second, external validation is critical. Models need prospective testing in real-world settings such as vascular clinics, catheterization labs, and community practices. Ideally, randomized controlled trials should compare AI-augmented clinical decisions against standard care, with endpoints including limb salvage, cardiovascular events, mortality, and cost-effectiveness.

Third, trust and transparency are essential. Clinicians are less likely to embrace "black box" AI. Integrating explainable AI features (eg, feature importance scores, transparent decision trees) and embedding them directly into EHR workflows will help clinicians interpret risk scores and guide patient discussions.

Further advancements are expected via multimodal AI models. Combining EHR data, TEG-PM, Doppler waveforms, imaging, and even real-time metrics from wearables creates holistic risk profiles capable of dynamic monitoring and early warning detection.

Ethical considerations and regulatory rigor are non-negotiable. Adhering to standards like TRIPOD+AI, CONSORT-AI, and DECIDE-AI is necessary for transparent and reproducible validation. Algorithmic bias must be evaluated across sex, race, age, and comorbidity groups, and patient privacy must be strictly maintained.

Ongoing technologic innovations will enhance performance further. Deep learning models applied to CTA images may automatically segment vessels and quantify plaque or calcification. Transformer-based algorithms and NLP can extract valuable insights from clinical notes. Reinforcement learning models may soon personalize treatment strategies, learning from patient responses and evolving risk profiles over time.

Lastly, economic evaluations remain essential. Prospective analyses should quantify whether AI-driven interventions yield net cost savings by preventing limb loss, reducing hospitalizations, and optimizing resource utilization. Ironically, this is a great job for AI!

CONCLUSION

PAD represents a complex, multifactorial condition in need of sophisticated prediction tools. AI and ML are particularly well-suited to this domain, offering advanced capabilities to model nonlinear interactions among heterogeneous data sources. Current studies—ranging from EHR-based PAD identification and Doppler-based AI tools to TEG-PM–informed ML models—underscore the transformative potential of these technologies.

To realize the full promise of AI in PAD, future efforts must emphasize large, diverse data sets; rigorous external validation; explainability; seamless clinical integration; ethical compliance; and economic viability. With these pillars in place, AI has the potential to transform PAD care—enabling earlier detection and proactive management and, ultimately, saving legs and lives. ■

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