Applications of Artificial Intelligence in Peripheral Neuropathy: A Systematic Review

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Abstract

Background:
Peripheral neuropathy (PN) is a common complication of metabolic and systemic diseases, particularly diabetes mellitus, resulting in sensory loss, pain, and motor impairment. Conventional diagnostic tools often detect PN only after irreversible nerve injury. Artificial intelligence (AI), especially machine learning (ML), has emerged as a promising tool for early diagnosis and risk prediction by integrating clinical, imaging, and genetic data.
Methods:
Following PRISMA 2020 guidelines, PubMed, EMBASE, IEEE Xplore, and Scopus were systematically searched up to September 2025. Studies applying ML or deep learning algorithms to PN were included, while reviews, grey literature, and studies lacking methodological details or performance metrics were excluded.
Result:
Our study included participants with diabetic, chemotherapy-induced, or pain-related neuropathies. Deep learning models, such as multilayer perceptrons and neural networks, achieved diagnostic accuracies of 87–93%, while classical algorithms including random forest, XGBoost, and SVM reported AUCs of 0.80–0.93. Radiomics-based SVMs using ultrasound showed external validation AUCs of 0.70–0.90. Key predictors included HbA1c, diabetes duration, lipid profile, and BMI.
Conclusions:
Machine learning demonstrates strong potential for improving the prediction, diagnosis, and phenotypic classification of PN. However, heterogeneity in datasets and limited external validation restrict clinical translation. Future work should focus on standardized data, multicenter validation, and interpretable AI models to facilitate integration into clinical practice.

Introduction

Peripheral neuropathy (PN) represents a common and debilitating complication of metabolic, infectious, toxic, and hereditary disorders, characterized by sensory loss, pain, and motor impairment.[1,2] Globally, it affects an estimated 2–3% of the general population, with prevalence rising to over 50% among individuals with long-standing diabetes mellitus.[3,4] Diabetic peripheral neuropathy (DPN) remains the most prevalent form, contributing to substantial morbidity including foot ulceration, amputation, and reduced quality of life.[4–6] Early identification and risk stratification are critical, yet clinical assessment and electrophysiological testing remain resource-intensive and often detect the condition only after irreversible nerve damage has occurred.[6]

Advances in artificial intelligence (AI), particularly machine learning (ML), offer promising tools for improving the diagnosis, prediction, and management of PN.[7] ML algorithms can analyze high-dimensional clinical, electrophysiological, genetic, and imaging data to uncover subtle patterns beyond human perception. In neurology, ML has demonstrated value in disease classification, imaging interpretation, and biomarker discovery, while in diabetic complications it has shown potential in predicting nephropathy, retinopathy, and cardiovascular risk.[8] However, despite increasing research attention, the translation of ML-based approaches to PN into routine clinical practice remains limited, underscoring the need for a comprehensive synthesis of the existing evidence.

Therefore, the present study aims to systematically identify and summarize original, peer-reviewed research articles that have applied machine learning techniques to the assessment, diagnosis, or prediction of peripheral neuropathy, excluding all types of review articles and grey literature. This review seeks to clarify the current applications, methodologies, and clinical implications of ML in peripheral neuropathy, providing a foundation for future translational and clinical research.

Material And Methods

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.[9]

A comprehensive search was performed across PubMed, EMBASE, IEEE Xplore, and Scopus databases from their inception until 29 September 2025. The search strategy combined Medical Subject Headings (MeSH) and free-text terms related to machine learning, deep learning, and peripheral neuropathy, including variations such as “diabetic neuropathy,” “chemotherapy-induced neuropathy,” and “artificial intelligence.” Reference lists of included articles were also screened to identify additional eligible studies. All identified records were imported into a reference manager, and duplicates were removed before screening.

Inclusion criteria were: (1) original peer-reviewed studies; (2) application of machine learning or deep learning algorithms directly related to peripheral neuropathy; and (3) availability of sufficient methodological details and performance metrics. Exclusion criteria included: (1) review articles (systematic, scoping, umbrella, narrative); (2) conference abstracts, theses, or other grey literature; (3) studies unrelated to peripheral neuropathy; and (4) articles without primary data or machine learning implementation.

All authors independently and blindly screened titles and abstracts for relevance, followed by full-text assessment of potentially eligible articles. Any discrepancies during screening were resolved through discussion and consensus. The same independent, blinded approach was used for data extraction, which captured information on study title, authors, publication year,

country, population characteristics, sample size, type of peripheral neuropathy, machine learning technique used, comparator method, input data type, and model performance (accuracy, AUC, sensitivity, specificity).

The risk of bias for each included study was assessed using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool, focusing on domains such as patient selection, index test, reference standard, and flow/timing.

For each study, performance metrics such as accuracy, sensitivity, specificity, precision, recall, F1 score, and area under the receiver operating characteristic curve (AUC) were extracted and compared narratively. When multiple models were presented within a single study, the best-performing algorithm as reported by the authors was noted. Model performance was contextualized relative to traditional statistical or clinician-based comparators to highlight incremental improvements achieved by machine learning or deep learning approaches. All extracted numerical results were tabulated, and trends were analyzed according to model type, input modality (clinical, imaging, or genetic data), and neuropathy subtype. Statistical pooling was deemed inappropriate due to differences in outcome definitions and validation methods across studies.

Result

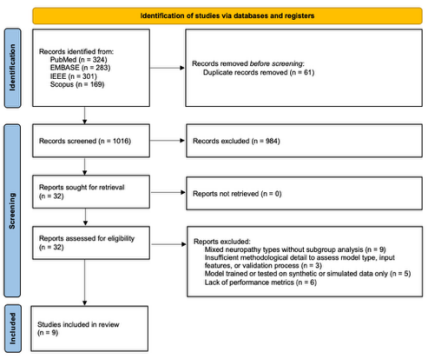

Figure 1. PRISMA flow with details on how many studies were excluded in each selection process.

The flow diagram shows that a total of 1,077 records were identified from four databases: PubMed (324), EMBASE (283), IEEE (301), and Scopus (169). After removing 61 duplicate records before screening, 1,016 records remained. Of these, 984 were excluded after screening, leaving 32 reports sought for retrieval, all of which were successfully retrieved. These 32 reports were assessed for eligibility, and 23 were excluded for various reasons: mixed neuropathy types without subgroup analysis (9), insufficient methodological detail to assess model type, input features, or validation process (3), models trained or tested on synthetic or simulated data only (5), and lack of performance metrics (6). Ultimately, 9 studies were included in the final review. Detailed numbers during each selection process are described in figure 1.[7,10–17]

A total of nine original studies (table 1) involving machine learning applications in peripheral neuropathy were included. Collectively, these studies encompassed over 5,000 participants across diverse clinical contexts, including DPN, chemotherapy-induced peripheral neuropathy (CIPN), and neuropathic pain phenotyping. The mean age of participants ranged from the mid-40s to late-60s, reflecting the typical demographic at risk for neuropathic complications. Most studies reported a predominance of male participants (approximately 55–65%), consistent with the higher prevalence of diabetes and neuropathic complications in men. The majority of studies were conducted in hospital-based settings in Asia (China, Japan), followed by Europe and multicenter collaborations, indicating a geographically diverse representation.

Machine learning and deep learning models demonstrated strong potential for improving the prediction, diagnosis, and classification of peripheral neuropathy. Deep learning architectures, particularly multilayer perceptron (MLP) and artificial neural network (ANN) models, achieved

the highest diagnostic accuracies, up to 87.5–93.1% for predicting neuropathic foot ulcers and early-onset diabetic peripheral neuropathy, respectively. Classical ML algorithms such as XGBoost, random forest, and support vector machines (SVMs) also showed robust performance, with reported AUCs ranging from 0.80 to 0.93 in predicting neuropathy risk or classifying disease severity. Studies applying radiomics-based SVMs using ultrasound images achieved external validation AUCs of 0.70–0.90, highlighting their potential for noninvasive diagnosis. Genetic and pharmacogenomic studies using SVM and neural networks reached accuracies near 94% for predicting vincristine-induced neuropathy, while ensemble models like stochastic gradient boosting effectively identified key metabolic predictors (e.g., HbA1c, diabetes duration, uric acid).

Comorbidities such as long-standing diabetes mellitus, hypertension, and dyslipidemia were frequently reported, aligning with known metabolic risk factors for neuropathy. In diabetic cohorts, mean diabetes duration ranged from 8 to 15 years, and average HbA1c levels were typically above 7.5%, suggesting poor glycemic control in many study populations. Studies investigating genetic and pharmacologic neuropathies included smaller cohorts (n = 50–150) with younger age distributions.

Table 1. Summary of Included Studies on Machine Learning Applications in Peripheral Neuropathy

Authors	ML Technique(s) Used	Application Area	Dataset Source/Type	Key Findings
Sun *et al.* 2025	Stochastic Gradient Boosting, Random Forest, XGBoost, SVM, Neural Network	Prediction of DPN in type 2 diabetes	1,544 diabetic patients; clinical data (China)	Gradient boosting achieved best performance (AUC 0.933 training, 0.811 testing); top predictors: diabetes duration, HbA1c, uric acid.
Wu *et al.* 2024	Logistic Regression, Random Forest, XGBoost	Diagnosis of DPN and LEAD	479 diabetics; hospital-based cohort (China)	XGBoost best for DPN detection (recall 83.7%); identified shared and distinct risk factors for DPN and LEAD.
Shi *et al.* 2025	Random Forest, Decision Tree, Logistic Regression, KNN, XGBoost, MLP	Prediction of neuropathic foot ulcer	400 DPN patients (China–Japan Friendship Hospital)	MLP model highest accuracy (AUC 0.901); key predictors: triglycerides, HDL, diabetes duration, age.
Jiang *et al.* 2025	Support Vector Machine (SVM)	Diagnostic classification of DPN via ultrasound	516 feet from 262 diabetic patients (two institutions)	Co-plane SVM model outperformed single-plane models (AUC 0.88 internal, 0.70 external).
Yamada *et al.* 2022	Random Forest, SVM, Naive Bayes, Neural Network	Genetic prediction of chemotherapy-induced PN	72 patients receiving vincristine (GWAS data)	SVM and NN models predicted neuropathy onset with 93.8% accuracy using two SNPs.
Xiao *et al.* 2021	Logistic Regression	Long-term risk prediction of DPN	90 type 2 diabetic patients; prospective follow-up (~5.5 years)	High BMI significantly increased DPN risk (OR 12.5); percussion entropy protective (OR 0.89).
Xiao *et al.* 2022	ANN, Logistic Regression, Fisher Discriminant Analysis	Early prediction of DPN	Physiological signal dataset (toe PPG)	ANN accuracy improved from 86.8% to 93.1% with data augmentation.
Kazemi *et al.* 2016	Multiclass Support Vector Machine	Classification of DPN severity	Cross-sectional diabetic cohort (Iran)	SVM achieved 76% accuracy in distinguishing DPN severity levels.
Baskozos *et al.* 2022	Random Forest, MARS, Naive Bayes	Classification of DPN pain phenotype	1,230 diabetic patients; multicohort data	Random Forest and MARS achieved best discrimination (AUPRC ~0.77); key predictors: QoL, HbA1c, BMI, mood scores.

Discussion

The present review demonstrates that ML, particularly DL architectures, has emerged as a powerful tool for improving the prediction and diagnosis of peripheral neuropathy. Traditional clinical and electrophysiological assessments often detect neuropathy only after significant axonal loss has occurred.[18,19] In contrast, ML models can integrate multiple clinical, biochemical, imaging, and electrophysiological parameters to recognize subclinical patterns of nerve injury.[19] This capability aligns with the pathophysiological understanding that peripheral neuropathy begins with small-fiber dysfunction and metabolic microvascular injury before structural degeneration becomes evident. The superior accuracy of neural network–based models (AUCs up to 0.93) reflects their strength in capturing complex nonlinear relationships inherent in metabolic and neurophysiological data.

When compared with previous literature, these findings are consistent with the growing application of AI across diabetic complications, where ensemble and deep learning methods outperform traditional regression approaches. Prior studies in diabetic retinopathy and nephropathy prediction have reported AUCs around 0.85–0.90 using similar architectures, suggesting that neuropathy prediction is approaching comparable accuracy.[20–22] The current synthesis expands on earlier work by demonstrating that ML-based approaches can also classify neuropathic pain phenotypes and integrate imaging and genomic data. Radiomics-based SVM models, for instance, represent an innovative step toward objective, noninvasive assessment of nerve integrity, complementing established physiological tests such as nerve conduction studies and corneal confocal microscopy.[23]

The success of these models likely reflects their ability to integrate the

multifactorial underpinnings of peripheral neuropathy into predictive frameworks. By identifying key modifiable features such as HbA1c, triglycerides, and BMI, ML algorithms provide clinically actionable insights that align with known mechanisms of neuronal injury and repair. Nevertheless, the heterogeneity in datasets, small sample sizes, and limited external validation underscore the need for larger, multicenter studies using standardized definitions of neuropathy. Future research should focus on integrating multimodal data, such as neuroimaging, electrophysiology, and metabolomics, within interpretable AI frameworks to facilitate clinical adoption.[24,25]

Study Limitations

This review has several limitations that should be acknowledged. First, there was substantial heterogeneity in study design, population characteristics, and machine learning methodologies, which limited direct quantitative comparison between studies. Most included research used retrospective, single-center datasets with relatively small sample sizes, increasing the risk of overfitting and limiting generalizability. Additionally, few studies performed external validation, and those that did often reported a decline in model accuracy when tested on independent datasets. Another limitation is the variability in neuropathy definitions and diagnostic criteria. Finally, publication bias and the exclusion of grey literature may have omitted relevant but unpublished findings, potentially overestimating model performance in the published literature.

Conclusion

Machine learning has demonstrated substantial promise in enhancing the early diagnosis, risk prediction, and phenotypic classification of peripheral neuropathy. Deep learning models, in particular, show the capacity to integrate diverse clinical, biochemical, imaging, and genetic data to uncover hidden patterns aligned with known pathophysiological mechanisms. By identifying key modifiable predictors such as glycemic control, lipid metabolism, and inflammatory markers, these models hold potential for guiding personalized preventive strategies and timely interventions. However, translation into clinical practice will require standardized data collection, larger multicenter validation studies, and improved model interpretability to ensure reproducibility and clinician trust. Overall, this review underscores the growing importance of machine learning as a complementary tool in the assessment and management of peripheral neuropathy, paving the way toward data-driven precision neurology.

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