Artificial Intelligence in Diagnosis and Management of Nail Disorders: A Narrative Review

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Abstract

Background: Artificial intelligence (AI) is revolutionizing healthcare by enabling systems to perform tasks traditionally requiring human intelligence. In healthcare, AI encompasses various subfields, including machine learning, deep learning, natural language processing, and expert systems. In the specific domain of onychology, AI presents a promising avenue for diagnosing nail disorders, analyzing intricate patterns, and improving diagnostic accuracy. This review provides a comprehensive overview of the current applications of AI in onychology, focusing on its role in diagnosing onychomycosis, subungual melanoma, nail psoriasis, nail fold capillaroscopy, and nail involvement in systemic diseases. **Materials and Methods:** A literature review on AI in nail disorders was conducted via PubMed and Google Scholar, yielding relevant studies. AI algorithms, particularly deep convolutional neural networks (CNNs), have demonstrated high sensitivity and specificity in interpreting nail images, aiding differential diagnosis as well as enhancing the efficiency of diagnostic processes in a busy clinical setting. In studies evaluating onychomycosis, AI has shown the ability to distinguish between normal nails, fungal infections, and other differentials, including nail psoriasis, with a high accuracy. AI systems have proven effective in identifying subungual melanoma. For nail psoriasis, AI has been used to automate the scoring of disease severity, reducing the time and effort required. AI applications in nail fold capillaroscopy have aided the analysis of diagnosis and prognosis of connective tissue diseases. AI applications have also been extended to recognize nail manifestations of systemic diseases, by analyzing changes in nail morphology and coloration. AI also facilitates the management of nail disorders by offering tools for personalized treatment planning, remote care, treatment monitoring, and patient education. **Conclusion:** Despite these advancements, challenges such as data scarcity, image heterogeneity, interpretability issues, regulatory compliance, and poor workflow integration hinder the seamless adoption of AI in onychology practice. Ongoing research and collaboration between AI developers and nail experts is crucial to realize the full potential of AI in improving patient outcomes in onychology.

Keywords: *Nail diseases, nail psoriasis, nailfold capillaroscopy, onychology, onychomycosis*

Introduction

Artificial intelligence (AI) refers to a field of computer science dedicated to the creation of systems that can perform tasks that usually require human intelligence.[1,2] AI in healthcare includes the utilization of computational algorithms and models to perform cognitive functions conventionally performed by humans. Under this broad definition, there is a range of algorithms designed to analyze complex medical data (patient records, medical images, genomic sequences, etc.) to extract meaningful patterns, make predictions, and assist healthcare practitioners in clinical decision-making.[2] Various subfields of AI in healthcare include (but are not limited to) the following:

- Machine learning (ML), which enables AI systems to learn from large datasets without being explicitly programmed.
- Deep learning (DL), inspired by the human brain neural networks, excels in tasks involving intricate data representations and hierarchical feature learning.
- Natural language processing (NLP), which enables AI systems to understand and extract information from medical texts or literature, facilitating information retrieval, summarization, and automated medical coding.

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- Expert systems, which integrate domain-specific knowledge and logical reasoning to provide diagnostic assistance, treatment recommendations, and personalized healthcare interventions based on established medical guidelines.

Overall, AI-enabled healthcare has demonstrated capabilities in disease diagnosis, prognostication, treatment planning, and patient monitoring with an aim to address complex healthcare challenges and improve patient outcomes.[2] It encompasses multiple methodologies to tackle specific healthcare challenges, as summarized in Supplementary Table 1.[2,3] The basic workflow of an AI system is shown in Figure 1.

AI in Onychology

AI seems to be a promising avenue in the management of nail disorders due to its capacity to analyze intricate patterns and variations in nail morphology and pathology. The modus operandi of AI systems seems to be particularly suitable to onychology for various reasons [Table 1], explaining the rapid increase in AI applications in this field.[4] Multiple reports of AI algorithms trained to recognize subtle differences in nail characteristics or specific nail abnormalities are fast emerging. Capturing biometrics is a standard, refined, and prevalent practice. Images of nails can be easily captured in a similar way. AI-based image analysis has demonstrated high proficiency, sensitivity, and specificity in interpreting nail images, including those captured through onychoscopy or microscopy. It has also been used to facilitate the automation of diagnostic processes to increase speed.[5] By analyzing large datasets of nail images and associated clinical data, AI systems have the potential to uncover novel correlations with underlying health conditions, facilitating early detection and personalized treatment strategies. AI-powered decision support systems could assist dermatologists in formulating differential diagnoses, treatment planning, monitoring, and providing prognostic insights.[1-8] This review aims to track this rapidly emerging trend of AI in onychology and summarize future directions.

Methodology

For the purpose of this review, a PubMed and Google Scholar database search was conducted to identify published literature in English language (till April 2024) on the use of AI in nail disorder, using the keywords (Artificial intelligence [Title/Abstract]) AND nail [Title/Abstract]). The search included case reports, clinical studies, trials of all types, comparative studies, guidelines (including pragmatic), reviews (including systematic), and meta-analyses, with a filter applied as studies involving human subjects. It yielded 16 and 287 search results, respectively. Titles and abstracts of articles were reviewed, and full texts of pertinent articles were obtained. Relevant cross-references were retrieved and examined in detail. The data are presented in a narrative fashion to highlight learnings relevant to dermatologists.

AI Terminology

AI in medicine is rapidly evolving, and so is the AI lexicon with key definable terms. These include fundamental AI concepts and advanced architectures [Supplementary Table 2 and Figures 2 and 3].[1-8] The multistep process involved in the development of AI systems is the key to understanding and evaluating studies reporting the performance of AI models. The performance of AI models is often reported in terms of the Youden index, a tool that evaluates both sensitivity and specificity. While sensitivity refers to the model's ability to correctly identify true positives; specificity reflects its capacity to correctly identify true negatives. Both these aspects are important in healthcare to prevent unnecessary investigations, while at the same time, picking up even a small number of cases. The Youden index is calculated by subtracting specificity from sensitivity and adding 1, giving a single value (range: −1 to +1). Values closer to +1 represent a good performance with a balanced trade-off between sensitivity and specificity, while values closer to 0 indicate a less desirable balance, where the model might excel in one aspect but struggle in the other. Negative values suggest an inverted relationship, where the model performs better at identifying negatives than positives.

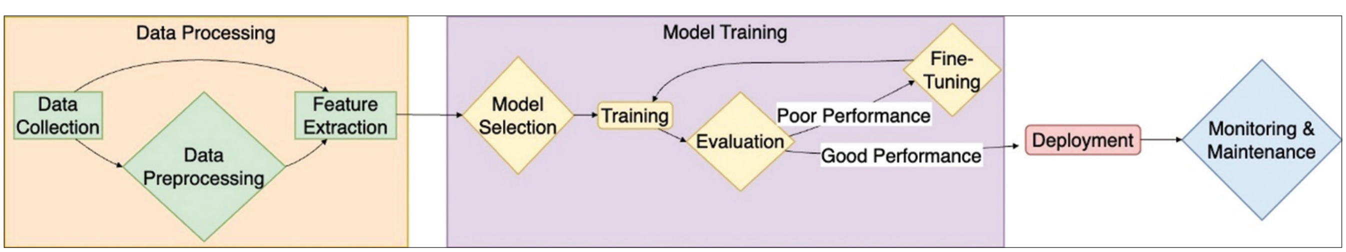

Figure 1: The workflow starts with data collection from various sources. The data goes through data preprocessing to clean and prepare it for further processing. If the data has issues, it is looped back to data collection for improvement. Feature extraction identifies relevant attributes from the preprocessed data. Based on the problem, a suitable model (e.g. machine learning) is chosen. The model undergoes training using the prepared data, learning patterns and adjusting parameters. The trained model is then evaluated on a separate dataset to assess performance using metrics such as accuracy. If the evaluation shows poor performance, the model undergoes fine-tuning by adjusting hyperparameters or architecture. This loop continues until satisfactory performance is achieved. Finally, the optimized model is deployed in real-world applications, making predictions or decisions based on new data. Monitoring ensures the deployed AI system continues to perform well and is updated with new data which involves retraining or addressing any operational issues

Table 1: Strengths of artificial intelligence applications in the field of onychology

AI Functions	Utility in onychology
Pattern Recognition	Diagnosis of nail disorders relies heavily on pattern recognition. This is a strength of AI algorithms, which excel in identifying subtle variations and anomalies in morphology, aiding accurate diagnosis.
Efficiency in Repetitive Tasks	AI can efficiently perform repetitive tasks on all 20 nails, which is labor-intensive and time-consuming for clinicians. This streamlines the examination process, ensuring a comprehensive assessment of each nail with consistency and precision.
Time Efficiency	AI significantly reduces the time taken to score the same features in all nails. With the automation of repetitive tasks, AI expedites the diagnostic process, allowing clinicians to focus on interpretation and decision-making rather than manual data collection.
Minimal Racial Differences	Nail features of various diseases exhibit minimal racial differences, making AI-based analysis universally applicable across diverse population groups. AI algorithms can accurately recognize and interpret nail abnormalities irrespective of racial variations, enhancing diagnostic consistency and reliability.
Accessibility for Examination and Imaging	Nails are easily accessible for examination by AI, as compared to other body parts, which may require special methods for image acquisition. Thus, AI can be integrated for nail examination required in various healthcare settings, including clinics, hospitals, and telemedicine platforms. This accessibility ensures timely diagnosis and management, especially in remote or underserved areas. Capturing of biometric data is a routine practice in many AI-based applications. The same procedure can be easily modified to capture nail images.
Confidentiality in Images	There are minimal to absent privacy issues with nail images. This means acquiring big data may not be a problem; thus, AI models can be more easily trained. Confidentiality concerns associated with other medical images, where patient identifiers need to be masked, do not apply here to the same degree. With appropriate privacy measures in place, AI can facilitate the aggregation of large datasets for analysis, enabling comprehensive research and clinical insights without compromising confidentiality.
Screening of Histopathology Specimens	AI enables efficient screening of large numbers of histopathology specimens, a task that traditionally requires significant time and expertise from pathologists. AI algorithms can analyze histological features of nail biopsies, aiding in the accurate diagnosis of underlying nail pathology and guiding treatment decisions.
Standardization of Crucial Steps	AI offers a standardized approach to crucial steps in nail examination and imaging. Specialized AI models can automatically scan and select images of the hand, extract images of nails, and correct distortions, if any. Sophisticated algorithms can differentiate nail images from "non-nail" images using two-layered feedforward neural networks, ensuring accuracy and reliability in data collection.
Performance Superiority to Dermatologists	AI-based systems have demonstrated performance ratings superior to dermatologists in evaluated aspects. They have shown higher accuracy, consistency, and speed in identifying nail disorders compared to human experts.

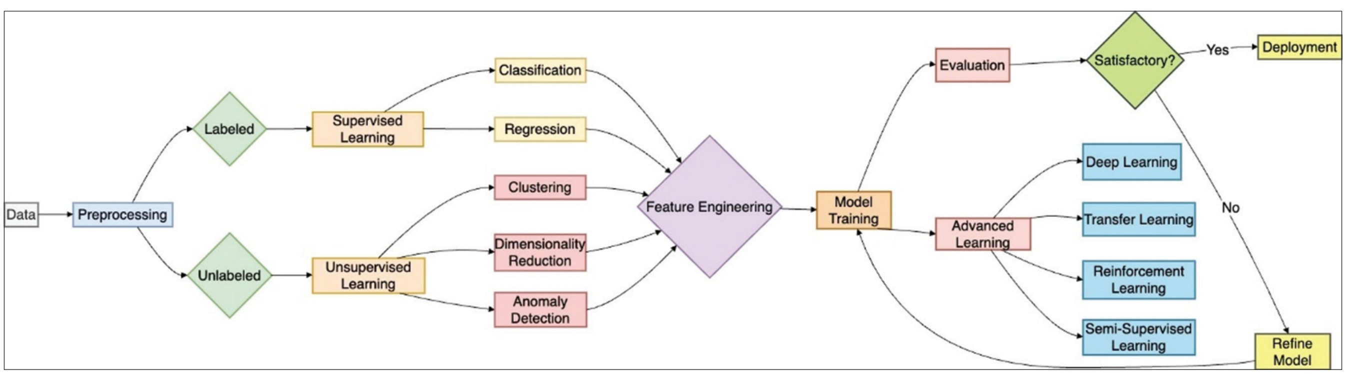

Figure 2: Different types of machine learning and their relationships. The data undergoes preprocessing to clean and prepare it for analysis. The preprocessed data can be labeled (with known outcomes) or unlabeled (without known outcomes). Labeled data feeds into supervised learning, which further branches into classification for predicting categories (e.g. disease diagnosis) and regression for predicting continuous values (e.g. blood pressure). Unlabeled data are used for unsupervised learning, which includes clustering (grouping similar data points, e.g. customer segmentation), dimensionality reduction (simplifying data by reducing features), and anomaly detection (identifying unusual data points). Feature engineering (optional) can be applied after data selection to improve model performance. Advanced learning techniques within the model training stage include deep learning (utilizing complex neural network architectures for tasks such as image or language recognition), and transfer learning (reusing pretrained models on similar problems, saving training time and resources). Reinforcement learning involves an agent interacting with an environment and learning through rewards or penalties, while semi-supervised learning utilizes a combination of labeled and unlabeled data, particularly useful when labeled data is scarce

AI in Diagnosis of Nail Disorders

The literature search revealed that AI models have been predominantly used in diagnostic onychology. The evaluated fields include the following:

Computer-aided nail diagnosis

The diverse nature of nail diseases presents challenges for accurate diagnosis as many nail diseases exhibit similar features. Computer-aided diagnostic systems

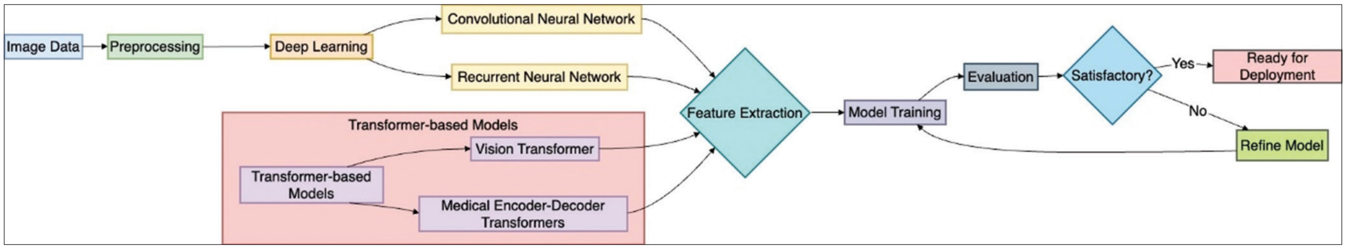

Figure 3: Flowchart depicting commonly used neural networks for medical image processing and their interrelationships. The image data undergoes preprocessing for cleaning and preparation. Preprocessed data feeds into deep learning (DL), which branches into specific network types: convolutional neural network (CNN), which is ideal for image analysis tasks such as classification or object detection; and recurrent neural network (RNN), which is suitable for processing sequential data, potentially useful for analyzing time-series data associated with medical images. Both CNNs and RNNs (or any chosen DL model) perform feature extraction, identifying relevant characteristics from the processed image data. Extracted features are used for model training, where the neural network learns to map input data to desired outcomes. Transformer-based models are a separate branch within DL, particularly suited for natural language processing (NLP) tasks. However, their potential adaptation for medical image processing includes Vision Transformer (ViT), which utilizes transformer architecture for image classification tasks and Medical Encoder-Decoder Transformers, which can be applied to tasks such as image segmentation or medical image captioning. Deep learning (DL) acts as an umbrella term encompassing various neural network architectures such as CNNs, RNNs, and Transformer-based models. CNNs are the dominant choice for medical image analysis due to their ability to capture spatial relationships within images, while RNNs are used for tasks involving time-series data associated with medical images. Transformer-based models are a rapidly evolving field, showing promise in adapting to medical image processing tasks beyond traditional NLP applications

based on transfer learning (TL) have been shown to be useful in identifying multiple-lesion nail diseases.[9] In a study by Coşar Soğukkuyu *et al*.,[10] AI image analysis was performed using a TL-based Visual Geometry Group Network (VGGNet), a deep convolutional neural network (CNN) architecture developed by the Visual Geometry Group at the University of Oxford. Models were tested for early diagnosis of nail diseases. A total of 723 images (Beau's lines: 39.5%, melanonychia: 34.2%, clubbing: 26.3%) were used to train the model (468 images) and then test it (255 images). The system showed a promising accuracy (VGG-16: 94% accuracy, VGG-19: 93% accuracy). In another study, Hadiyoso *et al*.[11] utilized the VGG-16 NN architecture with an Adam optimizer (an algorithm used for optimizing the training of deep learning models) for classifying nail disease images using Kaggle open dataset. Training data consisted of 333 simulated images, and test data involved images of koilonychia (20), Beau's lines (26), and leukonychia (21). Python programming was employed for simulation, yielding a maximum classification accuracy of 96% after 10 epochs. Nijhawan *et al*.[12] introduced an innovative DL framework aimed at identifying 11 distinct nail disorders (onychomycosis, subungual hematoma, Beau's lines, yellow nail syndrome, psoriasis, hyperpigmentation, koilonychia, paronychia, pincer nails, leukonychia, and onychorrhexis). It could effectively discern these with an accuracy of 84.58%. It utilized a hybrid approach incorporating CNNs, facilitating feature extraction. Abdulhadi *et al*.[13] investigated differentiation between four specific nail conditions: healthy nails, nail hyperpigmentation, nail clubbing, and nail fungus. Representative images were subjected to classification using five pretrained TL models of deep CNN: AlexNet, VGG-16, GoogleNet, ResNet50, and DenseNet201. Assessed performance metrics included accuracy, recall, specificity, precision, F-score, and processing time. Overall accuracy of 92.5%, 87.5%, and 93.98% was seen for models based on AlexNet, VGG-16, and GoogleNet, respectively, while those employing ResNet50 and DenseNet201 achieved accuracies of 96.39%.

Onychomycosis

Onychomycosis is a disorder seemingly best suited for AI-based diagnosis as it is a common condition across populations, but it shows minimal racial differences. Traditional diagnostic methods (direct microscopy, fungal culture, and histopathology) have limitations in terms of time, invasiveness, and sensitivity. Non-invasive, real-time techniques such as onychoscopy and deep CNNs are thus being evaluated.[14] AI algorithms have been developed to distinguish between normal nails, onychomycosis, and other disorders such as nail psoriasis and traumatic onychodystrophy.

The history of AI in onychomycosis goes back to 2006 when Boon *et al*.[15] demonstrated the efficacy of a NN scanning system for computer-assisted microscopy as histopathology is frequently used for screening but is time-consuming. Sensitivity is also a concern if fungal load is low. In this study, 117 suspected onychomycosis nail specimens were screened by two independent pathologists and a NN. Both humans and the NN reported 50 positive and 47 negative specimens, respectively; however, in the remaining 20 specimens, the NN failed to pick up fungi present in the sections. It also recorded artifacts that were mistaken for fungal spores. Nevertheless, it reduced the number of cases requiring manual screening, thus increasing efficiency. In a more recent work, Jansen *et al*.[16] explored a U-Net-based segmentation approach (a type of CNN) for detecting fungal elements on digitized histologic sections of human nails. This model was trained on a dataset of 664 corresponding hematoxylin and eosin (H and E) and periodic acid Schiff (PAS) stained whole-slide images. It demonstrated a sensitivity (90.5%) comparable to dermatopathologists (89.2%). The positive and negative predictive values were 88% and 87%, respectively, showing a potential to aid pathologists in screening.

In 2018, Han *et al*.[17] used a region-based CNN (R-CNN) to generate training datasets of 49,567 images, used to further fine-tune two CNN algorithms, namely ResNet-152 and VGG-19, to classify nails as onychomycosis or another diagnosis. The first dataset (A1, n = 49,567) was used to generate standardized clinical images by a hand and foot image selecting CNN, followed by a nail part-extracting R-CNN, and then a fine image CNN. The second dataset (A2, n = 3,741) had clinically diagnosed onychomycosis images. After training on A1 and A2, the diagnostic capability of ResNet-152 and VGG-19 was validated against four datasets of mycologically confirmed onychomycosis of different ethnicities (B1 = 100, B2 = 194, C = 125, and D = 939 images). It was found that algorithms trained with A1 were more accurate in diagnosing onychomycosis than A2. Overall, the two-layered feedforward NN computing the combined output of ResNet-152 and VGG-19 achieved test sensitivity, specificity, and area under the curve (AUC) values of (96.0/94.7/0.98), (82.7/96.7/0.95), (92.3/79.3/0.93), and (87.7/69.3/0.82) for the B1, B2, C, and D datasets, respectively. This performance was better than most of the 42 dermatologists screening the same images. The Youden index was significantly higher than that for dermatologists ($P = 0.01$).

Onychoscopy has shown promise in improving diagnostic accuracy in various types of onychomycosis. Zhu *et al*.[18] reported a high specificity (>82%) for AI in identifying characteristic onychoscopic patterns. These DL-based models exhibited test accuracy, specificity, and sensitivity exceeding 87.5%, 93.0%, and 78.5%, respectively. Kim *et al*.[19] evaluated AI algorithm as a standalone method for diagnosing onychomycosis in dystrophic toenails based on photographs and by onychoscopy, as compared to diagnosis by five experienced, board-certified dermatologists. Clinical photographs of 90 patients were taken by research assistants, and diagnosis was determined either by direct microscopy or fungal culture. The sensitivity and specificity of the algorithm (70.2% and 72.7%, respectively) and dermatologists (73.0% and 49.7%, respectively) were comparable. The Youden index of the algorithm (0.429) was comparable to that of dermatologists ($P = 0.667$).

Direct microscopic examination of potassium hydroxide (KOH) mounts is a rapid and low-cost method for diagnosis of onychomycosis. Yilmaz *et al*.[20] compared fungal detection in full-field photographs by a deep NN structure versus dermatologists. AI was found to be statistically superior to dermatologists in terms of accuracy and specificity but not sensitivity ($P < 0.0001$, $P < 0.005$ and $P > 0.05$, respectively). Gao *et al*.[21] designed and evaluated the application of an automated microscope for fungal detection in 292 skin (236), nail (50), and hair (6) samples with an image processing model based on ResNet-50. The automated microscope showed a sensitivity for fungal detection of 99.5%, 95.2%, and 60%, respectively, on skin, nails, and hair; while the specificities were 91.4%, 100%, and 100%, respectively. It was as skillful as human inspectors; though, performance on hair samples needed improvement.

Collectively, these studies underscore the evolving role of AI in clinical, onychoscopic, and histopathological analysis of onychomycosis, with enhanced diagnostic accuracy and workflow efficiency [Table 2 and Supplementary Table 3].[15-24] However, AI should complement, not replace, the expertise of dermatologists and pathologists.

Subungual melanoma

Melanoma involving the nail unit often remains a diagnostic challenge. Winkler *et al*.[25] investigated the diagnostic performance of a CNN in identifying melanomas of various subtypes and localizations. The CNN demonstrated high sensitivity (>93.3%) and specificity (>65%) in identifying superficial spreading melanoma (SSM), lentigo maligna melanoma (LMM), and nodular melanoma (NM). However, the sensitivity was lower (83.3%) for acrolentiginous melanomas (AM), though with high specificity (91.0%). Interestingly, the CNN exhibited limited performance in identifying mucosal melanomas (sensitivity: 93.3%, specificity: 38.0%) and subungual melanomas (sensitivity: 53.3%, specificity: 68.0%). The corresponding ROC-AUC values were 0.754 and 0.621, respectively, suggesting the limited capability of CNNs in diagnosing mucosal and subungual melanomas. It also highlights the potential for improvement through additional training.

Chen *et al*.[26] conducted a study to establish an intelligent precursor system for non-invasive monitoring of nail pigmentation, with an aim to minimize the need for nail biopsy. About 550 onychoscopic images were allocated to the training and test set (10:1 ratio) by using k-fold cross-validation. A DL model, developed using the Pytorch framework and optimized based on the U-Net image segmentation module (to analyze the contour of the entire nail plate and pigmented areas), assessed specific indicators following the "ABCDEF" rule. Its performance was compared with evaluations by clinical experts. The image segmentation module achieved automatic segmentation of the pigmented area and the entire nail plate, with dice coefficients of 0.8711 and 0.9652, respectively; while the DL model demonstrated consistency with evaluations by clinical experts on five qualitative indicators. Thus, the AI system could accurately segment the pigmented area and provide medically interpretable index analysis, potentially serving as an intelligent follow-up system for monitoring nail pigmentation.

Nail psoriasis

While the diagnosis of nail psoriasis may be less of a challenge, scoring its severity is time-consuming. There

Table 2: Summary of AI applications in the diagnosis of onychomycosis

Authors	Year	Sample Size	Aims & Objectives	Methods	Results	Conclusions/Comments
Boon *et al*.[15]	2006	117 abnormal nails including 128 images	Evaluate computer-assisted microscopy in the diagnosis of onychomycosis	Neural network scanning (NNS) system	- 50 cases were positive, and 47 were negative by both methods. - In 20 cases NNS failed to present images of fungi found in histologic sections. - 67 out of 117 cases (57%) require screening by light microscopy.	NNS can significantly reduce the number of histopathology slides to be screened by light microscopy proving highly valuable in high-throughput diagnostic laboratories.
Han *et al*.[17]	2018	A1 set– 4557 images, A2 set– 484 images (Onychomycosis, onychodystrophy, Healthy Controls)	Investigate the efficacy of DL for diagnosing onychomycosis	Deep learning analysis of full-field photographs	Accuracy: 87.9% (Sensitivity: 83.3%, Specificity: 92.6%)	DL offers promising results for onychomycosis diagnosis using clinical photographs. However, external validation on larger datasets is warranted.
Aishwarya *et al*.[24]	2020	300 images (diseased and unaffected nails)	Evaluate a deep CNN to diagnose onychomycosis	Deep CNN (VGG-19)	Accuracy: 98.6% Logistic regression: 97.9% Support vector machines: 97.1%	VGG-19 can diagnose onychomycosis with an accuracy of 98.6%.
Kim *et al*.[19]	2020	90	Evaluate the diagnostic abilities of a deep NN and onychoscopic examination in diagnosing onychomycosis	Faster-RCNN (region-based CNN	Algorithm Sensitivity: 70.2% and Specificity: 72.7% ($p<0.001$) Onychoscopy Sensitivity: 72.7% and Specificity: 72.9%	The algorithm achieved comparable diagnostic accuracy with experienced dermatologists and onychoscopic examination
Decroos *et al*.[23]	2021	For training – 528 cases For diagnostic accuracy and comparison – 199 cases	Develop and evaluate the diagnostic accuracy of the DL system for diagnosis of onychomycosis	Convolutional neural network (CNN)	Sensitivity: 94.1%, Specificity: 98%)	DL system demonstrated non-inferiority to analog diagnosis (with a non-inferiority margin of 5%) in terms of specificity and AUROC analysis. AI encountered challenges in recognizing spores and exhibited confusion between serum or aggregated bacteria and fungal elements.
Gao *et al*.[21]	2021	292 samples (236 skin samples, 50 nail samples, 6 hair samples)	Design and explore the application of an automated microscope for fungal detection in skin specimens	ResNet-50-based image processing model	Sensitivity: Skin - 99.5%, Nails - 95.2%, Hair - 60% Specificity: Skin – 91.4%, Nails - 100%, Hair - 100%	The performance of the automated microscope was comparable to human inspectors; however, its sensitivity in detecting fungal elements in hair samples was lower.
Jansen *et al*.[16]	2022	664 histologic whole-slide images (hematoxylin and eosin and periodic acid Schiff stains)	Evaluate U-NET-based segmentation approach to detect fungal elements on digitized histologic sections of human nail specimens compared to dermatopathologists	U-NET-based CNN	Sensitivity: 94%, Specificity: 77%	ML-based algorithms applied to real-world clinical cases can perform with sensitivity comparable to human pathologists.
Zhu *et al*.[18]	2022	1155 onychoscopic images (603 onychomycosis,	Evaluate DL-based diagnostic models for	Faster-RCNN (region-based convolutional	Accuracy: 87.5% (Sensitivity: 78.5%, Specificity: 93%)	DL-based diagnosis models showed superior diagnostic accuracy to dermatologists.

Contd...

Table 2: Contd...

Authors	Year	Sample Size	Aims & Objectives	Methods	Results	Conclusions/Comments
		221 nail psoriasis, 104 traumatic onychodystrophy, and 227 normal images	onychomycosis in onychoscopy	neural network		
Yilmaz *et al*.[20]	2022	160 microscopic images (KOH mount) of onychomycosis and 297 microscopic images of normal nails	Evaluate a deep NN for automatic fungal element detection in nail KOH mount	Deep NN structure (VGG16 and InceptionV3)	VGG16 showed Accuracy: 88.10±0.8% (Sensitivity: 75.04±2.73%, Specificity: 92.67±1.17%) InceptionV3 showed Accuracy: 88.78±0.35% (Sensitivity: 74.93±4.52%, Specificity: 93.78±1.74%)	Automated systems are capable of detecting fungi in microscopic images employing the proposed DL models.
Düzayak S *et al*.[22]	2023	76 (diseased and healthy nails)	Evaluate diagnostic accuracy of onychomycosis using classical ML algorithm	Artificial NN, support vector machine, ensemble decision trees	Accuracy: 97.25% (Sensitivity: 96%, Specificity: 98%)	Conventional ML algorithms perform at par compared to DL algorithms. The proposed model may help the dermatologist as a decision support system in the clinic.

are many objective scoring systems available based on the detection of nail bed or matrix features and their counting.[27] AI can assist in this tedious task. Folle *et al*.[28] developed and assessed the clinical utility of NN for modified Nail Psoriasis Severity Index (mNAPSI) score assessment in a diverse dataset of 177 patients (1154 nails) having rheumatoid arthritis (38%), psoriatic arthritis (34%), psoriasis without arthritis (10%), and no specific diagnosis (18%). The NN showed strong performance with an ROC-AUC of 0.88 and an accuracy of 0.55. There was a high positive Pearson correlation (90.0%) with human annotations, indicating potential clinical utility. AI could also be used for assessment of other severity indices, and deployment in patient-friendly mobile applications, enabling remote monitoring, reducing the need for clinic visits.

AI in nail fold capillaroscopy

The proximal nail fold is a valuable site for assessing capillary microcirculation in-vivo and non-invasively. Nailfold capillaroscopy (NFC) is of diagnostic as well as prognostic value, especially in connective tissue diseases (especially systemic sclerosis) and lifestyle diseases (including diabetes and arterial hypertension).[29-33] However, qualitative and quantitative analysis requires good-quality NFC images and is time-consuming. AI has been found useful in circumventing both these hurdles.[29-33] AI applications in NFC are summarized in Table 3.[29-33]

Nail in systemic disease

Nail is rightfully known as the "window to systemic disease." Fingernails and toenails may be the first to exhibit symptoms of systemic illness due to low oxygen supply. Easy accessibility makes them convenient for examination, repeated examination, and diagnosis, reducing the need for specialized equipment. The shape, texture, and color of human nails often provide insights into underlying diseases or nutritional imbalances. Digital image processing techniques to identify such alterations may facilitate the effortless prediction of various diseases.[34]

NFC images can also be used to characterize neutropenia non-invasively. This is an advantage when frequent and repetitive monitoring is needed, for example, in patients on chemotherapy. Pablo-Trinidad *et al*.[35] evaluated an AI screening tool for severe neutropenia in 44 patients undergoing high-dose chemotherapy followed by autologous stem cell transplantation (ASCT). It included a compact microscopy system to capture high-resolution, high-frame-rate videos of superficial capillaries, with an automated software pipeline to analyze the videos, detect nailfold capillaries, count optical-absorption gaps (proxies for flowing neutrophils), and calculate the Leuko index (a non-invasive measure to estimate white blood cell concentration based on optical markers in capillary imaging). This was compared with actual leukocyte counts from blood drawn at specific times. It was seen that with at least three suitable capillaries identified, the automated system achieved a high classification accuracy (AUC: 0.95). The percentage agreement between its results and reference neutrophil counts increased from 69.8% to 90.9% as more capillaries were analyzed per session, helping accurately detect severe neutropenia. The system could also be adapted for differential detection of white blood cell subtypes.

Indi *et al*.[36] devised a novel system for early disease detection through human nail image analysis. A training dataset of 100 nail images of 20 patients with specific diseases was used for an AI system focused on extracting color features for diagnostic inference in cardiovascular diseases, diabetes, liver diseases, and anemia. Evaluation

Table 3: Summary of AI applications in Nail fold capillaroscopy

Authors	Year	Sample Size	Aims and Objectives	Method used	Results	Conclusions/ Comments
Karbalaie *et al*.[33]	2018	475 NFC Images	To evaluate image enhancement technique for NFC	Elliptical Broken Line (EBL) method	Observers preferred the visual quality of AI-enhanced images. Improved intra- and inter-observer reliability with image enhancement.	The study lacks details on the methodology and sample size. Image enhancement improves the visibility of capillary details for better assessment.
Nitkunanathanajah *et al*.[32]	2020	23 SSc patients 19 healthy controls	To assess microcirculation using Optoacoustic Imaging (OAI)	Raster-scanning optoacoustic mesoscopy (RSOM); OAI involves the use of AI combined with ultrasound and optical imaging to visualize and quantify capillaries in three dimensions (3-D)	RSOM provided higher-resolution 3D images than dermoscopy. Identified characteristic SSc vasculopathy in RSOM images. Significant differences in vascular volume between the SSc and control groups (P<0.0005).	RSOM offers promising visualization and quantification of nailfold capillaries in 3-dimensions. This was preliminary work; further research is needed to assess clinical utility.
Liu *et al*.[31]	2020	50 NFC Images	To develop DL method for capillary segmentation	Res-Unet (deep neural network)	Accuracy: 91.72%, Dice Score: 97.66%	Res-Unet is effective for capillary segmentation in NFC images. Limited sample size; thus, it needs validation on larger datasets
Shah *et al*.[30]	2023	120 participants (diabetic/non-diabetic with, cardiovascular disease/no disease)	To investigate NFC for diabetes & cardiovascular risk prediction	Convolutional Neural Networks (CNNs)	High accuracy for diabetes diagnosis (AUROC: 0.84). Potential to predict cardiovascular events in diabetic patients (AUROC: 0.65).	NFC with CNN analysis holds promise for diabetes screening and cardiovascular risk assessment. More research is needed to validate in larger cohorts.
Garaiman *et al*.[29]	2023	289 SSc patients	To analyze NFC images for microangiopathy using DL	Vision Transformer (ViT) algorithm	AUC: 81.8%–84.5% for microangiopathic changes. Accuracy: 85.8%–93.5% for scleroderma patterns. Processing time: 0.19 s/image.	ViT demonstrates robust performance in identifying microangiopathy in NFC images. Lacks comparison with established diagnostic methods

metrics to measure performance included genuine acceptance rate (GAR) and false acceptance rate (FAR). The study reported an average diagnostic accuracy of 65% as compared to the training data, demonstrating the potential of color-based nail image analysis in early disease diagnosis. Similar studies by Sharine *et al*.[37] and Kumar *et al*.[38] also reinforced the potential of nail color features for early disease diagnosis. Tolentino *et al*.[39] utilized an image processing system incorporating image segmentation, color thresholding, and shape analysis, using a tablet, high-definition webcam, and USB LED light for image capture and processing. The system could diagnose six patients with cardiovascular diseases (coronary occlusion, congestive heart failure, and congenital heart disease), matching with the diagnoses of attending specialists, achieving 100% accuracy. These studies outline the development of low-cost disease-detecting devices, beneficial for small healthcare units and remote operations, providing non-invasive and early diagnosis by analyzing fingernails.

AI in Management of Nail Disorders

AI also has the potential to revolutionize the management of nail disorders, though lesser published evidence exists as

Table 4: Role of AI in the management of nail disorders

Field of patient management	AI Tools	Utility in onychology
Counselling	Chatbots	AI-powered chatbots provide patients with readily available, evidence-based information on nail disorders including causes, symptoms, treatment options, and self-care tips. This can empower patients, address basic concerns, and potentially reduce unnecessary clinic visits.
	Personalized Advice Platforms	AI algorithms can analyze a patient's specific nail diagnosis and medical history to generate personalized advice on lifestyle modifications, hygiene practices, and relevant product recommendations.
Clinician Efficiency (Especially w.r.t. repeat examinations e.g., melanoma detection)	AI-assisted Decision Support Systems	AI systems can analyze nail images, highlighting potentially concerning features and suggesting differential diagnoses, allowing clinicians to focus on more complex aspects while managing such patients.
	Automated Image Analysis for Repeat Examination	Automation of analysis of follow-up nail images, e.g., suspected melanoma, or monitoring response in chronic conditions like nail psoriasis. AI can flag potential changes requiring further investigation.
AI-driven Monitoring of Treatment Response	Sequential Image Analysis for Monitoring	To monitor response to treatment, AI can analyze serial images of nails undergoing treatment to identify subtle improvements or signs of treatment failure. This can prompt adjustments in the treatment plan. AI-aided image analysis can help reduce hospital visits.
Facilitating Remote Care	AI-powered telediagnosis platforms	AI can facilitate remote consultations in areas with limited access to dermatologists. Patients upload high-quality nail images for analysis by AI algorithms, followed by a remote consultation with a clinician if needed. This reduces unnecessary hospital visits. The same approach can be used for treatment monitoring of patients living in remote areas.

of now. Going with developments in other fields, AI may be utilized for counseling, improving clinician efficiency, facilitating remote care, and monitoring treatment response. Some relevant aspects are summarized in Table 4.[40,41]

Future Directions/Challenges

AI opens up newer avenues for research in onychology by enabling large-scale data analysis, image-based analysis, identification of novel biomarkers in nail specimens (metabolomics), and exploration of disease mechanisms. Future research efforts are likely to focus on developing AI-driven diagnostic tools for rare or complex nail conditions, investigating the genetic basis of nail disorders, and optimizing treatment strategies through predictive modeling. However, several key challenges impede its successful integration into the clinical practice of onychology [Supplementary Table 4].[42] Ensuring regulatory compliance, addressing data privacy and security issues, and integrating AI technologies seamlessly into existing healthcare workflows may offer the way forward.

Conclusions

AI systems in onychology are exhibiting diverse applications in patient care, and medical research. Ongoing research and development is sure to bring up further innovations and enhancements with respect to onychology. However, integration into clinical practice should be guided by a collaborative approach between AI developers and nail experts, ensuring the best possible outcomes for patients. Due to inherent advantages in the field of onychology, AI has a huge potential regarding integration into routine nail management. Potential benefits include early detection, timely intervention, and personalized management, especially as the nail offers a window to both systemic and dermatologic diseases. However, challenges exist in the form of data scarcity, variability in image quality, and complex nail pathologies. Additional issues include lack of interpretability, ethical concerns, and potential workflow disruptions, complicating its widespread adoption.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Applications of AI in healthcare

AI Systems/Tools	Applications in healthcare
Diagnostic Systems	Aid scrutiny of medical images (e.g., X-rays, MRIs, CT scans) to pinpoint irregularities or anomalies. For example, deep learning systems, especially convolutional neural networks (CNNs), are used to detect various cancers, including breast and lung cancers, with high precision and efficiency.
Predictive Analytics	Employ machine learning (ML) algorithms to predict patient outcomes, disease progression, and treatment responses based on historical patient data. Help clinicians make well-informed decisions and tailor treatment plans for improving outcomes. Integrate longitudinal patient data, real-time monitoring, and genomic data for precision medicine applications.
Natural Language Processing (NLP) Systems	Parse and extract clinical insights from unstructured medical texts (clinical notes, research papers, electronic health records (EHRs), etc.) to create clinical summaries, which aid healthcare decision-making.
Robotics and Surgical Assistance	Heighten surgical precision, minimize invasiveness, and reduce human error during surgery. Execute intricate surgeries with improved dexterity and autonomy, including robotic-assisted laparoscopic procedures, robot-guided neurosurgery, and ARTAS iX system, to harvest healthy hair follicles during hair transplantation.[3]
Drug Discovery and Development	Expedite drug discovery by analyzing extensive datasets, predicting molecular interactions, and identifying potential drug candidates. Recent advancements involve integrating deep learning (DL) models for tasks such as virtual screening, *de novo* drug design, and predictive modeling of drug efficacy and toxicity.
Clinical Decision Support Systems (CDSS)	Furnish clinicians with evidence-based recommendations, guidelines, and alerts at the point of care, aiding informed decision-making. Recent developments include the integration of real-time patient data, ensuring interoperability with EHR systems, and implementing personalized risk assessment models.
Remote Monitoring and Telemedicine	Enable continuous tracking of patient health parameters, facilitating early detection of health issues and timely intervention. Recent developments include the integration of wearable devices, sensors, and AI algorithms for tasks such as remote patient triage, virtual consultations, and managing chronic diseases.

Supplementary Table 2: Basic terminology used with AI in healthcare			
Fundamental Concepts		Advanced AI Architectures and analytics	
Machine Learning (ML)	Subfield of AI with algorithms that learn from data without explicit programming. Common ML algorithms in medicine include decision trees, support vector machines, and random forests.	Neural Networks (NNs)	AI computational models are similar to the biological structure of the brain. Composed of interconnected nodes (artificial neurons) that process information through weighted connections. NNs learn by adjusting these weights based on training data.
Deep Learning (DL)	Subfield of ML that utilizes artificial neural networks (ANNs) with multiple layers, for complex pattern recognition. DL, just like the brain, deciphers information through labeling and assigning to various categories.	Convolutional neural networks (CNNs)	A form of DL architecture, well suited to analyzing visual data, including medical images.
Transfer Learning (TL)	Subfield of ML that utilizes knowledge gained from solving one problem to solving a different, but related, problem. It allows the model to transfer the knowledge from the source task to the target task, improving performance and reducing the requirement of labeled data.	Deep neural network	A complex artificial NN comprising multiple layers of interconnected nodes. It is designed to learn intricate patterns and representations from large-scale data, enabling tasks such as medical image analysis, disease diagnosis, and patient outcome prediction, with high accuracy and efficiency.
Supervised learning	It involves training ML models with labeled patient data to predict outcomes or make diagnostic decisions.	Recurrent neural networks (RNNs)	Another form of deep learning NN which is adept at processing temporal and sequential data like text or videos
Unsupervised Learning	A type of ML where the AI model learns patterns from unlabelled data. It can be used for anomaly detection in medical images.	Transformers	Specific type of NN architecture excelling at natural language processing (NLP) tasks. They are used for analyzing clinical text such as EHRs to enable patient risk stratification and automated report generation.
Semi-supervised learning	Involves training of ML models using a combination of labeled and unlabeled patient data, particularly useful when labeled data may be scarce or expensive to obtain.	Generative Pre-trained Transformers (GPTs)	These are large language models (LLMs), pretrained on massive amounts of text data. They can help generate personalized patient education material or summarize medical literature. These are currently not widely deployed in clinical practice.
Reinforcement Learning	A type of ML where an AI model learns by interacting with the environment and receiving rewards or penalties for its actions. This has applications in medical robotics or developing personalized treatment strategies.	Youden Index	It is a statistical measure that quantifies the effectiveness of a diagnostic test, representing the ability to correctly identify positive cases while minimizing false positives.
Training Data	Labeled data used to train AI models. Each data point comprises features (relevant characteristics) and a corresponding label (known outcome).	F1 score	It is an evaluation metric for classification tasks, such as disease diagnosis or patient outcome prediction, particularly useful when the dataset has imbalanced class distributions. Its value ranges from 0 to 1, with higher values indicating better performance.
Validation Data	Separate datasets are used to objectively evaluate the performance of a trained AI model on unseen data.	Matthews correlation coefficient	It evaluates the performance of binary classification models, specifically in scenarios with imbalanced datasets. Its value ranges from − 1 (complete disagreement between predictions and observations) to + 1 (perfect prediction). A 0 indicates random prediction.
Model Evaluation Metrics	Quantitative measures are used to assess the performance of an AI model. These include accuracy, sensitivity, specificity, and area under the curve (AUC).	Dice coefficient	It quantifies the overlap between the delineated regions of interest (ROIs) in medical imaging, such as tumor or organ boundaries, with 1 indicating perfect agreement and 0 indicating no overlap.
Feature Extraction	Identifying and extracting relevant characteristics (features) from raw data for analysis by AI models.	Jaccard Index/ Intersection over Union (IoU)	It quantifies the overlap between manually delineated and algorithmically segmented ROIs by calculating the ratio of the intersection area to the union area of the two regions.

Supplementary Table 3: Comparative sensitivity and specificity for AI diagnosis versus conventional diagnostic methods in onychomycosis

Method		Sensitivity (%)	Specificity (%)	Advantages	Disadvantages
KOH mount examination[20]	AI	75.0±2.7	92.7±1.2	High accuracy, rapid diagnosis, reduces human error	Requires high-quality data and well-trained models
	Dermatologist	74.8±19.5	74.3±18.0	Accessible, cost-effective	Variability in interpretation; potential for false negatives
Histopathological examination[23]	AI	94.1	98	High accuracy, quick processing, scalable	Limited to algorithm capabilities, data quality dependent
	Dermatopathologist	97.25	94.6	Gold standard, comprehensive analysis, detailed histopathological findings	Time-consuming, expensive, requires specialized training

Supplementary Table 4: Challenges in integrating AI into onychology

Challenges	Description
Data scarcity	Limited availability of nail image datasets restricts model development.
Heterogeneity	Variability in image quality, lighting, and patient demographics can compromise generalizability and accuracy.
Complexity of nail pathologies	Variable morphology, color, and texture of nail disorders pose challenges for accurate discrimination by AI algorithms. Models need to be robust and specific as the nail unit has a limited number of clinical signs as manifestations of most diseases.
Lack of interpretability	Many AI models lack transparency and interpretability, hindering trust and acceptance in clinical settings.
Regulatory and ethical concerns	Compliance with data privacy regulations and ethical principles (e.g., patient consent and confidentiality) is crucial for AI implementation in onychology.
Workflow disruptions and training	Adoption of AI technologies may cause disruptions in workflows, require additional training, and increase workload unless integrated seamlessly with electronic health records (EHRs) and clinical decision support systems (CDSS).
Need for further research	Robust validation studies, interdisciplinary collaboration, and addressing ethical considerations are still needed in AI research for onychology.