EC PULMONOLOGY AND RESPIRATORY MEDICINE
Mini Review

The Role of Artificial Intelligence in Lung Disease Diagnosis

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Received: September 16, 2024; **Published:** October 23, 2024

Abstract

Artificial Intelligence (AI) is transforming pulmonary medicine by significantly enhancing diagnostic accuracy, prognostic capabilities, and treatment outcomes across various pulmonary diseases. Leveraging clinical data, imaging modalities, and advanced machine learning algorithms, AI enables precise disease management. Studies demonstrate AI's superiority in interpreting pulmonary function tests, accurately predicting mortality in chronic obstructive pulmonary disease (COPD), and efficiently identifying undiagnosed cases from low-dose CT scans. In asthma and interstitial lung disease (ILD), AI aids in diagnosis, phenotype classification, and exacerbation prediction, offering personalized management strategies tailored to individual patient needs. Moreover, in pulmonary infections like tuberculosis (TB) and COVID-19, AI-based systems facilitate early detection, prognosis, and management, guiding timely interventions to improve patient outcomes. Additionally, AI technologies enhance the detection and characterization of pulmonary nodules and lung malignancies, improving diagnostic accuracy and treatment decisions. This article will describe these AI methods and explore their effectiveness.

Keywords: *Lung Disease; Artificial Intelligence; Detection; Chronic Obstructive Pulmonary Disease; Interstitial Lung Disease; COVID-19; Tuberculosis*

Introduction

Artificial Intelligence (AI) is a field in computer science focused on instructing machines to emulate human intelligence and carry out tasks with expertise. Its functionalities encompass the ability to provide accurate outcomes and analyse vast datasets, surpassing the limitations of conventional statistical approaches [1]. In the field of pulmonary medicine, AI has been actively employed for nearly two decades, with its applications continually expanding. By leveraging clinical data, chest imaging, lung pathology, and pulmonary function testing, AI contributes to diagnostic processes and outcome predictions for pulmonary diseases. The use of AI-based applications empowers physicians to navigate vast datasets, enhancing the precision of pulmonary disease treatment. Given the increasing significance of AI in pulmonary medicine, it becomes imperative for healthcare practitioners managing patients with pulmonary conditions to comprehend its functioning, facilitating its integration into clinical practices for the betterment of patient care [2].

Artificial intelligence and machine learning

Overview of AI

Artificial intelligence (AI) constitutes a field within computer science dedicated to replicating human cognitive processes, encompassing thinking, learning, planning, and reasoning, with the aim of solving intricate problems. The inception of AI dates back to 1956 when scientists began conceptualising the idea of computers learning from data, marking the commencement of this evolving discipline [3]. Although the terms AI, machine learning, and deep learning are frequently used interchangeably, it is crucial to clarify their relationship to prevent misunderstandings. AI serves as the overarching concept, involving the simulation of human intelligence through computer systems. On the other hand, machine learning (ML) is a field of AI, leveraging its capacity to learn and analyse extensive datasets, often with more variables than traditional statistical methods [4]. Machine learning employs diverse algorithms, such as supervised learning, unsupervised learning, and reinforced learning [3]. In supervised learning, the computer identifies patterns with guidance, while unsupervised learning entails pattern recognition without external guidance [4]. Reinforced learning discerns and analyses data without explicit labels, utilising incremental positive or negative feedback [5]. Deep learning, a subset of machine learning, which facilitates algorithms to learn from training datasets and apply acquired knowledge to execute specific tasks on new datasets [4]. Given the escalating complexity of healthcare data, AI holds considerable potential to profoundly impact medical data analysis and the practice of medicine.

Limitations of AI

There are several limitations hindering the effective application of ML technology in the medical field. Firstly, the challenge of data availability is emphasised, encompassing issues related to obtaining sufficient and high-quality data, including text, numbers, and images. Inaccurate or insufficient data is identified as a factor that can lead to flawed model structures and biassed conclusions, undermining the reliability of ML predictions in healthcare.

Secondly, there are several concerns regarding experimental methods, emphasising the importance of robust experimental design and replication. The absence of standards for model selection is highlighted as a significant challenge, raising the potential for the misuse or abuse of ML models. Flawed experimental design is identified as a source of errors that can compromise the accuracy of conclusions drawn from ML applications in the medical domain.

Ethical concerns constitute another major limitation. Issues related to optimization, prediction, and classification are identified as potential sources of ethical problems. These problems may manifest in unequal outcomes on sensitive issues or violations of privacy, necessitating a careful consideration of ethical implications in the development and application of ML technology in healthcare.

In summary, there are several issues related to experimental design and ethical considerations. Addressing these limitations is crucial for the responsible and effective deployment of AI/ML techniques in healthcare.

Obstructive lung diseases

The diagnostic gold standard for obstructive lung diseases such as asthma and chronic obstructive pulmonary disease (COPD) typically relies on a combination of signs, symptoms, and spirometry. While artificial intelligence (AI) cannot replace the crucial role of clinicians, it can enhance their interpretation of data [2].

Dr. Wim Janssens, leading a study at the Department of Respiratory Medicine, University Hospitals Leuven, Belgium, demonstrated the superior effectiveness of AI-based software in interpreting pulmonary function tests (PFTs) compared to pulmonologists. Pulmonary function tests offer precise and measurable indicators of lung performance [6]. The study, using historical patient cases, revealed that pulmonologists exhibited variability and errors, achieving 74.4% accuracy and displaying a common disagreement ($\kappa=0.67$) in pattern recognition. Furthermore, their accuracy in diagnosing respiratory diseases was 44.6%. In contrast, the AI software surpassed pulmonologists, achieving 100% accuracy in pattern interpretation and an 82% correct diagnosis rate. This research implies that AI could offer more precise and consistent PFT interpretations, potentially serving as a valuable decision support tool in clinical practice [7].

COPD

As per the 2023 reports from the World Health Organisation (WHO), COPD stands among the leading three causes of global mortality [8]. Chronic Obstructive Pulmonary Disease (COPD) is a chronic inflammatory lung disease that causes restricted airflow in the lungs [9].

A study by Moll., *et al.* introduces a machine learning mortality prediction model, MLMP-COPD, for patients with Chronic Obstructive Pulmonary Disease (COPD). The model, based on clinical, spirometric, and imaging features, outperforms existing indexes (BODE, BODE modifications, and ADO) in predicting all-cause mortality across two COPD cohorts. Key predictors include the 6-minute walk distance, FEV1% predicted, age, and the pulmonary artery-to-aorta ratio from imaging. The study highlights the potential of machine learning to enhance mortality prediction for COPD patients, providing a web-based tool for exploring the model's features and predictions [10].

Although spirometry remains the definitive diagnostic standard for COPD, research indicates the potential use of artificial intelligence and deep learning in screening patients for this condition.

The study by Tang., *et al*. suggests that utilising deep residual networks in low-dose computed tomography (CT) scans of smokers and ex-smokers can effectively identify undiagnosed cases of chronic obstructive pulmonary disease (COPD). In a proof-of-concept investigation, the researchers employed artificial intelligence, specifically deep residual networks, to automatically detect COPD in a dataset of low-dose CT scans initially conducted for early lung cancer detection. The proposed approach demonstrated clinically acceptable performance, achieving an area under the receiver operating characteristic curve (AUC) of 0.889 in cross-validation experiments. An AUC of 0.889 indicates that, on average, the model has an 88.9% chance of correctly distinguishing between COPD and non-COPD cases during cross-validation, demonstrating robust diagnostic capability. The study suggests that this deep learning method could serve as an effective tool for COPD detection in individuals undergoing CT screening for lung cancer [11].

Furthermore, AI has been used to define and analyse the characteristics of individuals who have been diagnosed with COPD. The COPD Genetic Epidemiology Study (COPDGene) spans a decade, gathering extensive data on chest imaging, spirometry, and molecular aspects. It has significantly contributed to understanding and predicting diverse chronic obstructive pulmonary disease (COPD) subtypes, emphasising the continuum of COPD manifestations and the role of machine learning in uncovering novel biological insights [12]. The study by Fischer., *et al*. introduces an AI-based algorithm for automated lung lobe segmentation and emphysema quantification on chest CT scans. Significantly correlating with Global Initiative for Chronic Obstructive Lung Disease (GOLD) severity stages, especially in the left upper lobe, it provides valuable insights for defining and analysing characteristics in individuals already diagnosed with COPD, contributing to a comprehensive understanding of the disease's manifestations and progression [13]. Moreover, machine learning-based strategy has been used for early detection of exacerbations in patients with COPD. The algorithm utilises a comprehensive set of patient characteristics, including demographics, comorbid conditions, history, symptoms, and vital signs, to predict the likelihood of a COPD flare-up and recommend appropriate responsive actions. The goal is to offer effective, on-demand decision support for COPD patients, enabling timely intervention and reducing the impact of exacerbations on patient health [14].

Asthma

Asthma, characterised by intermittent and reversible obstructive lung symptoms and encompassing various phenotypes, stands to benefit from the application of artificial intelligence (AI) [15]. AI has the potential to enhance the diagnosis, classification of phenotypes, prediction of asthma exacerbations, and assessment of treatment responses in this respiratory condition [2].

Asthma, characterised by its heterogeneous nature, encounters issues of both underdiagnosis and overdiagnosis, particularly in socioeconomically disadvantaged regions. Remarkably, a substantial proportion, ranging from 20% to 73%, eludes detection, while approximately 30% to 35% of individuals identified as asthma sufferers do not manifest the condition authentically [16].

To address this concern, a retrospective birth cohort study employed Electronic Health Records (EHRs) and Predetermined Asthma Criteria. This study successfully introduced a novel natural language processing algorithm designed for pediatric asthma diagnosis, demonstrating commendable sensitivity (97%), specificity (95%), positive predictive value (90%), and negative predictive value (98%). The test cohort comprised 497 children, with a 31% prevalence of asthma. The algorithm's efficacy was further validated by applying it to records from an additional 497 children (median age, 2.3 years) at a different hospital, revealing comparable sensitivity (92%), specificity (96%), and positive (89%) and negative (97%) predictive values. This confirmed the algorithm's reliability in diagnosing paediatric asthma within an external EHR system. However, it is imperative for the algorithm to undergo additional validation in an adult cohort [17,18]. In another cross-sectional study, a Natural Language Processing (NLP) algorithm called NLP-API was developed to automatically identify paediatric patients meeting Asthma Predictive Index (API) criteria from Electronic Health Records (EHRs). The primary purpose was to autonomously identify paediatric patients satisfying the criteria outlined in the Asthma Predictive Index for the diagnosis of asthma. Tested on 427 subjects with an average age of 5.3 years from Olmsted County, the NLP-API exhibited a sensitivity of 86%, specificity of 98%, and positive and negative predictive values of 88% and 98%, respectively. The algorithm demonstrated construct validity by associating asthma status with known risk factors. NLP-API has the potential to enhance asthma care and research by facilitating population management and large-scale studies focused on children meeting API criteria [19]. Moreover, a neural network model leveraging 13 clinical characteristics was formulated using data gleaned from EHR. This model exhibited exceptional performance, accurately identifying 100% of asthma patients within a cohort of 254 individuals [20].

Regarding the classification of asthma phenotypes, utilising both a machine learning approach and cluster analysis, the most responsive phenotype to corticosteroids was observed in individuals with characteristics such as low pulmonary function, high serum eosinophils, nasal polyps, and late-onset asthma. Conversely, the least corticosteroid-responsive phenotype was identified in young, obese females with early-onset asthma. This finding aligns with the rationale that corticosteroid responses in asthma treatment are heterogeneous, emphasising the need for a comprehensive understanding of contributing factors. The referenced study employed a multiview learning approach, employing multiple-kernel k-means clustering on various clinical variables. The analysis revealed four distinct asthma clusters with differential corticosteroid responses, providing valuable insights for precision management of the disease [21].

In an additional investigation, Qin., *et al*. harnessed deep learning algorithms on high-resolution computed tomography (HRCT) chest images to assess small airway function in asthmatic children facing small airway obstruction. The study, aimed at evaluating the clinical efficacy of various glucocorticoid administration methods, employed the Res-Net deep learning algorithm for feature extraction and image reconstruction. Among 118 hospitalised asthmatic children with acute exacerbation, the study categorised them into glucocorticoid aerosol inhalation group (group A), glucocorticoid combined with bronchodilator aerosol inhalation group (group B), and oral hormone therapy group (group C). The deep learning model effectively measured airway wall thickness, showing improvements in small airway function and inflammation post-treatment. Notably, oral corticosteroids demonstrated superior efficacy over aerosol inhalation, emphasising the potential of the Res-Net model for clinical evaluation and segmentation of CT image information in enhancing asthma care [22].

Interstitial lung disease

Interstitial lung disease (ILD) serves as a comprehensive descriptor encompassing various pathological processes leading to inflammation and fibrosis in the pleura and parenchyma [2].

Deep learning algorithms are pivotal in diagnosing Interstitial Lung Disease (ILD) by analysing HRCT chest images. In a study led by Walsh., *et al*. a database of 1157 HRCT images illustrating diffuse fibrotic lung disease was classified using the 2011 American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society (JRS)/Latin American Thoracic Association (ALAT) guidelines and Fleischner Society diagnostic criteria. Notably, the algorithm, with a median accuracy of 73.3% compared to 70.7% for 91 thoracic radiologists, excelled in interpreting HRCT images. This highlights the algorithm's potential as an efficient and reproducible tool for ILD diagnosis, particularly valuable for patient stratification in clinical trials and offering valuable insights into image interpretation in the medical field [23].

Chloe., *et al*. investigated the effectiveness of a content-based image retrieval (CBIR) system utilising deep learning algorithms in diagnosing interstitial lung disease (ILD) through chest CT images. Focusing on patients with confirmed ILD, including usual interstitial pneumonia (UIP), nonspecific interstitial pneumonia (NSIP), cryptogenic organising pneumonia, and chronic hypersensitivity pneumonitis, the CBIR system significantly improved diagnostic accuracy and interreader agreement among eight readers with varying experience levels. Despite limitations, such as covering only four major ILD categories and potential overstatement of performance, the system's reliance on deep learning allowed for the quantification of structural characteristics, particularly benefiting UIP and NSIP cases. The study concluded that the proposed CBIR system, with its deep learning integration, holds promise in enhancing ILD diagnosis, particularly in settings lacking thoracic imaging expertise, offering valuable radiologic decision support [24].

Various studies have employed artificial intelligence (AI) algorithms to assess high-resolution CT (HRCT) images of patients with interstitial pulmonary fibrosis, successfully quantifying airway volumes and parenchymal lesions. A specific study aimed to address the growing need for accurate prognostic estimation in idiopathic pulmonary fibrosis (IPF) by developing an AI-based image analysis software, AIQCT. Utilising 304 HRCT scans for training, AIQCT automatically categorised and quantified parenchymal patterns and airways. The software's accuracy was validated against visual scores and demonstrated significant correlations. When applied to 120 IPF patients, bronchial and normal lung volumes, quantified by AIQCT, independently correlated with survival, providing additional prognostic insights beyond traditional measures like the gender-age-lung physiology stage of IPF. Despite certain study limitations, AIQCT's ability to quantify clinically relevant lesions suggests its potential as a valuable tool for IPF prognosis assessment [25].

Pulmonary infections

Tuberculosis

Tuberculosis (TB) continues to exert a substantial toll on lives in numerous regions globally. The diverse manifestations of TB in chest radiography pose a persistent diagnostic challenge. In 2016, a breakthrough occurred with the inception of the initial computer-aided diagnosis (CAD) system designed to enhance TB detection [2]. Over time, researchers have crafted numerous computer-aided diagnosis (CAD) algorithms capable of identifying diverse radiographic manifestations in tuberculosis (TB), such as cavitary and focal TB [26]. Beyond the realm of diagnosis, artificial intelligence (AI) proves valuable in various facets of tuberculosis (TB) care. AI has been proposed as a tool for scrutinizing medical records, recognizing symptomatic patterns, conducting surveillance, and assessing factors that could potentially contribute to the challenges associated with treatment and medication adherence failures in TB [27].

Doshi., *et al*. highlight innovative approaches in utilizing AI-based software to enhance global TB patient care and management. In patient care, digital technologies address the challenge of medication adherence through tools like electronic medication monitors and virtual directly observed treatment via video (VDOT) [28]. The integration of artificial intelligence in VDOT, with its ability to recognize individual patterns and gestures, offers a promising solution to enhance both privacy and efficiency. Additionally, AI presents opportunities in transforming smartphones into clinical instruments and supporting diagnostic and treatment decisions through cognitive computing [29,30].

In the realm of surveillance, AI has the potential to review disaggregated patient records, tracing unique signatures within large datasets even when personal identifiers are unavailable. This approach can significantly contribute to TB surveillance by identifying clinical manifestations, predicting treatment failure, and detecting outbreaks early on. In program management, AI's role in "connected diagnostics" becomes prominent, aiding in remotely monitoring diagnostic machines, interpreting results data, and consolidating information from various diagnostic processes [31].

COVID-19

In recent years, the global landscape has been significantly impacted by the COVID-19 Pandemic [32]. Between 2020 and 2022, global morbidity and mortality rates had surged due to the ongoing experimentation with treatment options for COVID-19. This challenge was addressed with AI software developed to assist in early diagnosis and prognosis of individuals afflicted by COVID-19 [2]. Li., *et al*. conducted a comprehensive, multi-center retrospective study, developing the COVID-19 detection neural network-a deep learning model with the primary objective of distinguishing CT findings indicative of COVID-19 infection from those associated with community-acquired pneumonia. Additionally, the study highlighted the necessity of a multidisciplinary diagnostic approach for viral pneumonias, emphasising the importance of a comprehensive strategy due to overlapping chest CT imaging findings with other chest diseases, ultimately enhancing the efficacy of patient treatment [33].

Another study utilised a deep-learning convolutional neural network (CNN) to stage the severity of COVID-19 lung infection based on radiologists' severity scores obtained from portable chest X-rays. The CNN, designed with convolutional, activation, batch normalisation, max pooling, and dense layers, effectively predicted disease severity on a graded scale. Transfer learning, involving a pre-trained VGG16 model, optimised predictions, enhancing efficiency without sacrificing performance. This approach demonstrates potential for efficient triage, risk assessment, resource allocation, and disease monitoring in the context of COVID-19 [34]. This can help in early prognostication of the disease, which can lead to making early treatment decisions.

The described ML algorithm in the READY clinical trial is designed to predict the need for invasive mechanical ventilation in COVID-19 patients within 24 hours of their initial hospital encounter. The algorithm utilises inputs such as diastolic and systolic blood pressure, heart rate, temperature, respiratory rate, oxygen saturation, white blood cell count, platelet count, lactate, blood urea nitrogen, creatinine, and bilirubin. Its development involved a multicenter approach, enrolling patients across five U.S. health systems. Notably, the algorithm's performance surpassed that of the commonly used scoring system MEWS, demonstrating higher sensitivity and specificity. Its accuracy in identifying patients requiring mechanical ventilation provides valuable early prognostication, aiding in patient triage and resource allocation. The algorithm's reliance on routinely available vital sign and lab data, along with its ability to predict outcomes within a short timeframe, positions it as a promising tool for improving COVID-19 patient care and minimising the risks associated with emergency interventions [35].

Moreover, researchers have crafted advanced deep learning algorithms that play a crucial role in discerning protein structures and configurations. The information generated by this algorithm has proven indispensable in the progress of the COVID-19 vaccine [36].

Pulmonary nodules and lung malignancy

Despite recent advances in the treatment of pulmonary malignancies, the World Health Organization considers them among the deadliest of all solid malignancies, with lung cancer alone responsible for a higher number of deaths than any other form of cancer globally, registering 1.76 million reported deaths in 2018 [37]. Timely and precise diagnosis remains crucial for enhancing patient outcomes. Utilising deep learning algorithms, Computer-Aided Diagnosis (CAD) systems serve as a support tool for radiologists in examining CT images through lung segmentation. This approach facilitates a more targeted analysis, enabling the detection and classification of nodules with increased accuracy.

Siemens Healthcare employs a cutting-edge algorithm that integrates statistical finite element analysis and three-dimensional lung segmentation within adversarial neural network training. The algorithm addresses challenges in automatically detecting lobar fissures on CT scans due to their slender morphology, indistinct boundaries, and potential confusion with disease-related abnormalities, particularly in cases of fibrosis. Traditional anatomical knowledge-based methods often prove inadequate for pathological lungs. The

Siemens algorithm utilises a statistical finite element shape model of lobes, deforming onto an individual's lung shape through principal component analysis to predict likely fissure locations. Testing on 20 CT scans demonstrates the algorithm's success in estimating fissure locations, outperforming anatomy-based segmentation methods in both healthy and fibrotic subjects [38].

Chauvie., *et al*'s study compared machine learning algorithms for lung cancer detection in chest digital tomosynthesis (DTS), revealing that neural networks significantly enhanced the positive predictive value (PPV). Despite this improvement, a drawback of deep learning is its inconsistent identification of malignant versus benign nodules. The study aimed to address this issue by boosting PPV using radiomics features within the SOS clinical trial. Logistic regression, Random Forest, and a neural network were applied to develop predictive models. Results demonstrated the neural network as the most effective, showcasing high PPV (0.95) and substantial sensitivity (0.90). Combining visual analysis with the neural network could reduce false positives in DTS, offering improved diagnostic accuracy for radiologists [39].

The issue of spatial and temporal heterogeneity in solid cancers, presenting challenges for invasive biopsy-based molecular assays, offers a significant opportunity for non-invasive imaging. The evolving field of medical imaging, characterised by innovations in hardware, imaging agents, standardised protocols, and imaging analysis methodologies, is moving towards quantitative imaging. Radiomics, an approach involving the high-throughput extraction of numerous quantitative features from radiographic images, addresses this challenge. The method utilises features from one image to develop data-characterization algorithms, contributing to the identification of nuanced malignancy characteristics often overlooked by human experts. Combining Radiomics with deep learning holds promise in providing radiologists worldwide with a diagnostic advantage in detecting pulmonary malignancies, offering a non-invasive means to capture intra-tumoral heterogeneity. However, the efficacy of Radiomics requires further validation in multi-centric settings and laboratory environments [40].

Afshar., *et al*. introduced DRTOP, a deep learning-based Radiomics model addressing limitations in hand-crafted radiomics for predicting time-to-event outcomes in lung cancer patients. By utilising raw CT and PET scans without pre-defined feature constraints and eliminating the need for precise tumour segmentation, DRTOP demonstrated significant predictive capabilities in an experiment involving 132 lung cancer patients. CT-based features were identified as predictors for overall survival, distant control, and local control, while PET-based features predicted overall survival and recurrence-free survival. Concordance indices suggested DRTOP's accuracy was comparable or superior to hand-crafted radiomics in predicting clinical outcomes. The proposed deep learning model showcased potential for personalised lung cancer management by outperforming traditional radiomics approaches [41].

Conclusion

The utilisation of AI and machine learning algorithms remains a dynamic and pertinent subject within pulmonary medicine. In the medical domain, human errors, such as missed, delayed, or inaccurate diagnoses, can result in significant health and economic repercussions. AI emerges as a valuable tool to address these challenges, facilitating swift, precise, and early diagnosis, prognosis, and treatment of pulmonary diseases. However, the apprehension and lack of confidence in incorporating AI into clinical practice may impede its widespread adoption in healthcare. Overcoming these hurdles necessitates a collaborative effort between physicians and AI developers, emphasising the importance of a robust and extensive database for well-performing AI algorithms. While AI cannot replace the expertise of clinicians, it can augment their capabilities, contributing to enhanced patient care and global healthcare standards.

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