Chronic Obstructive Pulmonary Diseases:
Journal of the COPD Foundation®

Perspective

Integrating Artificial Intelligence in the Diagnosis of COPD Globally: A Way Forward

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Abstract

The advancement of artificial intelligence (AI) capabilities has paved the way for a new frontier in medicine, which has the capability to reduce the burden of COPD globally. AI may reduce health care-associated expenses while potentially increasing diagnostic specificity, improving access to early COPD diagnosis, and monitoring COPD progression and subsequent disease management. We evaluated how AI can be integrated into COPD diagnosing globally and leveraged in resource-constrained settings. AI has been explored in diagnosing and phenotyping COPD through auscultation, pulmonary function testing, and imaging. Clinician collaboration with AI has increased the performance of COPD diagnosing and highlights the important role of clinical decision-making in AI integration. Likewise, AI analysis of computer tomography (CT) imaging in large population-based cohorts has increased diagnostic ability, severity classification, and prediction of outcomes related to COPD. Moreover, a multimodality approach with CT imaging, demographic data, and spirometry has been shown to improve machine learning predictions of the progression to COPD compared to each modality alone. Prior research has primarily been conducted in high-income country settings, which may lack generalization to a global population. AI is a World Health Organization priority with the potential to reduce health care barriers in low- and middle-income countries. We recommend a collaboration between clinicians and an AI-supported multimodal approach to COPD diagnosis as a step towards achieving this goal. We believe the interplay of CT imaging, spirometry, biomarkers, and sputum analysis may provide unique insights across settings that could provide a basis for clinical decision-making that includes early intervention for those diagnosed with COPD.

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Abbreviations:

AI=artificial intelligence; **AUC**=area under the curve; **CanCOLD**=Canadian Cohort Obstructive Lung Disease; **COPD**=chronic obstructive pulmonary disease; **COPDGene®**=COPD Genetic Epidemiology study; **CT**=computed tomography; **ECLIPSE**=Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints; **GOLD**=Global initiative for chronic Obstructive Lung Disease; **HICs**=high-income countries; **IEAs**=image expression axes; **$IEA_{emphysema}$**=emphysema axis IEA; **IEA_{airway}**=airway axis IEA; **LMIC**=low- and middle-income countries; **mMRC**=modified Medical Research Council dyspnea scale; **PFT**=pulmonary function test; **SGRQ**=St George's Respiratory Questionnaire; **SPIROMICS**=SubPopulations and InteRmediate Outcome Measures in COPD Study; **TB**=tuberculosis; **WHO**=World Health Organization

Funding Support:

Not applicable

Citation:

Robertson NM, Centner CS, Siddharthan T. Integrating artificial intelligence in the diagnosis of COPD globally: a way forward. *Chronic Obstr Pulm Dis*. 2024;11(1):114-120. doi: https://doi.org/10.15326/jcopdf.2023.0449

Publication Dates:

Date of Acceptance: September 22, 2023
Published Online Date: September 26, 2023

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Keywords:

COPD; artificial intelligence; prediction; machine learning; computer tomography

Introduction

An estimated 328 million people have chronic obstructive pulmonary disease (COPD) worldwide, and COPD is expected to become the leading cause of death[1] by 2030. The advancement of artificial intelligence (AI) capabilities has paved the way for a new frontier of medicine that has the potential to reduce morbidity and mortality rates associated with noncommunicable diseases globally, including COPD. AI is defined as computers performing high-order tasks that previously required human intellect. Types of AI include machine learning machine learning, deep learning, and artificial neural networks. There has been an increasing uptake of AI due to its advantages of reliability, processing speeds, cost-effectiveness, ability to decipher complex issues, and skill to analyze large amounts of data issues.[2] AI has the potential to improve the efficiency and access to high-quality health care services.[3,4] For this reason, the role of AI in medicine has generated significant interest, especially in the early detection of COPD progression in at-risk populations and improving the diagnosis of COPD.[5-9] The question remains: *how can AI be integrated into COPD diagnosis globally and leveraged in resource-constrained settings?*

Artificial Intelligence in COPD Diagnosis

AI is currently being explored in diagnosing and phenotyping COPD through auscultation, pulmonary function testing (PFT), and imaging. Deep learning has been used to analyze 12-channel lung sounds on auscultation among 41 participants with varying levels of COPD severity in Turkey.[10] Altan and colleagues[10] found high accuracy and classification performance above 94% with an area under the curve (AUC) value of 0.9659. AI's role in improving COPD identification and classification with a simple tool like auscultation may allow for easy adoption in resource-constrained settings. Moreover, a multicenter European intervention recently assessed the preferential and differential diagnostic accuracy of PFTs with collaboration between pulmonologists and explainable AI.[11] The authors found an overall increase in the mean preferential and differential diagnosis percentage with the supplementation of AI compared to pulmonologists alone. However, for some pulmonologists, the supplementation of AI with pulmonologist expertise appeared deleterious to their diagnostic accuracy.[11] This highlights the importance of clinical expertise in clinical decision-making and in providing extensive training with the AI framework before integrating it in clinical settings. Additionally, further studies are ultimately warranted to determine if clinical AI decision support technology improves longitudinally with AI integration into clinical settings.

Research integrating imaging modalities, such as computer tomography (CT), has been coupled with AI to monitor and stage COPD.[7,8,11-13] Hasenstab and colleagues have utilized CT quantification to measure the percentage of lung emphysema and air trapping as an emerging COPD diagnostic tool.[7] The CT machine learning model had a similar performance in COPD staging as spirometry in Global initiative for chronic Obstructive Lung Disease (GOLD) staging. Furthermore, CT imaging coupled with AI can provide utility in predicting COPD-related outcomes. An analysis including 8983 participants from the COPD Genetic Epidemiology (COPDGene®) study and the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) cohort studies used a deep learning approach to evaluate CT images among smokers with COPD.[9] Almost 50% of COPDGene participants were accurately GOLD staged and 75% were labeled within one GOLD stage.[9] This study characterized well-performing and calibrated AI models that could predict patients with COPD who were most likely to have COPD exacerbation events and those with the highest mortality.[9] AI also classified these participants into emphysema categories to extrapolate and effectively predict performance on the 6-minute walk distance test and the St George's Respiratory Questionnaire (SGRQ) measuring health-related quality of life.[8] AI can be a beneficial tool for characterizing unique aspects of imaging that are consistent with high-risk groups and patients with COPD. Therefore, AI analysis of CT imaging in patients with COPD can further be employed for overall risk stratification in clinical settings, which can have important implications for COPD management and treatment. Furthermore, AI analysis can inform the progression and prognosis of COPD.

While these studies have shown promise in diagnosing, stratifying, and predicting outcomes of COPD, there are limitations to this approach. Unfortunately, AI algorithm utility can be constrained by data quality and quantity. The quality of AI models depends on the training data and these studies often lack patient diversity and can have small sample sizes. There is a need for larger prospective cohort studies recruiting diverse patient populations to increase quality and transferability to the general population. Many of these studies are secondary analyses of large prospective cohorts of patients with COPD risk factors (i.e., COPDGene, ECLIPSE, and Canadian Cohort Obstructive Lung Disease [CanCOLD] studies). Recognizing the limitations of AI can preclude its overuse and misuse, especially to prevent erroneous associations without appropriate clinical context. Clinicians should critically evaluate AI performance and results for clinical context.

Clinician expertise can complement AI as a solution to this. A potential concern for some is the black box problem where only the input and output are understood. Learning by example is one of the most powerful and not fully comprehended forces that drive intelligence. For example, our brain recognizes patterns to understand experiences, but we do not fully understand the neural networks taken to reach the designated outcome.[14] AI can be thought of in a similar manner. Nonetheless, it is critical that clinicians provide substantial oversight to ensure proper use. Another concern of AI in overall COPD management is overdiagnosis. These imaging studies often include analysis of CT imaging of COPD, which is cost-prohibitive in some medical settings. However, the AUC value of CT imaging in identifying COPD was 0.89 and the positive predictive value was 0.847 in a sample of 2153 participants with CT imaging in the ECLIPSE cohort.[15] These results clearly depict the capacity to advance precision medicine with AI.

The Multimodal Diagnostic Approach

Although studies highlight the potential of AI in imaging alone, using a multimodality approach may further enhance COPD diagnostic capabilities and provide a solution to these cited limitations. A recent population-based study of the CanCOLD cohort found that the combination of quantified CT imaging (texture-based radiomic features), demographic data, and spirometric measurements improved machine learning prediction of progression to COPD compared to each modality alone.[12]

Similarly, biomarkers associated with lung abnormalities consistent with emphysema and airway-predominant COPD features may present an avenue for AI to diagnose COPD and monitor COPD progression. A recent study by Chen and colleagues analyzed CT imaging and utilized deep learning of blood RNA-seq gene expression to determine similarities in inflammatory patterns and lung structural changes called image-expression axes (IEAs) in 1223 participants from the COPDGene study.[13] The emphysema axis IEA ($IEA_{emphysema}$) was associated with lower lung function, a higher proportion of neutrophils, and radiological central emphysema. The airway axis IEA (IEA_{airway}) was associated with thicker airways and a higher white blood cell count. Participants classified as high $IEA_{emphysema}$/IEA_{airway} had worse outcomes including the highest SGRQ scores, highest modified Medical Research Council dyspnea scale (mMRC) scores, and the shortest 6-minute walk test distances.[13] This study distinguished multiple IEAs related to specific inflammatory pathways associated with emphysema and airway-predominant COPD. Emerging research combining CT imaging, blood transcriptomics, and phenotypic data can be applied to AI to increase our understanding of the influence of lung structure and systemic inflammatory mechanisms implicated in COPD. The addition of sputum[16] and biomarker analysis[17] may be utilized in conjunction with the aforementioned features to further enhance the capabilities of AI to diagnose COPD and predict COPD exacerbations and outcomes. This information could be used as a prognostic indicator in COPD and implicated in the emerging *treatable trait* strategy in COPD treatment.[18]

The Need and Utility of Artificial Intelligence in Low- and Middle-Income Countries

Globally, there is great interest in defining early-onset COPD among at-risk individuals (e.g., SubPopulations and InteRmediate Outcome Measures in COPD Study-[SPIROMICS] Study of Early COPD Progression) and early detection of COPD in order to initiate timely treatment. *The Lancet's* Commission "Towards the Elimination of COPD" similarly advocates for early identification of COPD among populations at high risk for developing COPD based on symptoms and risk factors using technology in low- and middle-income countries' (LMIC) health care systems.[19] The Lancet Commission calls for the prevention and detection of early-stage COPD using diagnostic methods such as blood and radiological biomarkers before irreversible changes have developed. Similarly, they suggest computer-assisted CT and biomarker interpretation with AI to increase the feasibility of implementation in resource-constrained settings.[19] However, most studies assessing AI capacities in COPD diagnosis have predominantly taken place in high-income countries (HICs). A recent scoping review of the use of AI for the delivery of essential health services across World Health Organization (WHO) regions identified 81.3% (n=74) of studies occurring in HIC settings.[4] Similarly, a systematic review of AI in COPD management found that 63% (n=42) of studies occurred in HICs.[20] However, the burden of COPD is disproportionately concentrated in LMICs.[1] There is a unique interplay of COPD risk factors in LMICs including biomass smoke exposure, ambient air pollution, malnutrition, and prior tuberculosis (TB) infection, which may influence COPD phenotype. Therefore, studies in HICs may have reduced generalizability to global populations, specifically in LMICs due to significant variation in the COPD endotype and pathophysiology. Increasing the inclusion of ethnic and COPD endotype diversity into AI-related research would allow greater transferability to the global population. For this reason, we advocate for population-based data collection in LMIC settings to generate an AI algorithm.

Many LMICs face barriers to high-quality health care delivery that include limited radiological equipment and a shortage of long-term medical professionals, such as radiologists and pulmonologists.[21] Altogether this leads to high rates of under-diagnosis and misdiagnosis of COPD observed in national and international surveys in LMICs.[22]

Moreover, prior research by the European Respiratory Society has shown that chest CTs are as available or more available than spirometry in many global settings.[18] Therefore, with radiological imaging, AI can help reduce barriers to care by identifying negative radiological exams and labeling appropriate exams that require further review by the appropriate medical professionals. Additionally, this approach could be broadly integrated into other biological and clinical tests and exams. Using AI may help overcome the shortage of health care providers and may help improve patient care alike in LMICs. AI can assist in the diagnosis and assessment of COPD to improve patient care and enhance diagnostic capabilities.[5] For example, AI technology has high sensitivity and specificity in the detection of TB through AI-supported detection of acid-fast stained TB bacillus, reducing the workload of health care workers and enhancing disease surveillance in China and Pakistan.[17,23] AI has been used primarily in infectious disease monitoring and management in LMICs with increasing use in non-communicable disease interventions such as diabetes and cancer.[23-26]

There are few studies to date in LMICs integrating AI in the diagnosis of COPD.[4] These limited studies include small sample sizes of under 400 participants located in Turkey, Brazil, India, China, and Bosnia and Herzegovina focusing on COPD diagnosis and classification of COPD severity.[27-31] Most AI interventions focused on developing algorithms to evaluate COPD decision support systems using demographic data, spirometry, and biomarkers to collaborate with clinicians.[27-31] This further highlights the potential acceptability and role of AI in supporting clinicians, especially in resourced-constrained settings. These AI algorithms were highly accurate (over 80%) in diagnosing COPD and predicting related outcomes such as acute exacerbation risk, disease severity indices, and hospitalization.[30,31] Thus, we recognize the need for larger population-based studies in LMICs to build AI infrastructure where the burden of COPD is higher and can have the greatest impact on the global COPD burden.

Applying and Integrating Artificial Intelligence in Clinical Practice

COPD is the optimal condition for AI application due to its chronic progressive nature with complex genetic and environmental interactions, fluctuating presentations over time, and a vast array of multimodal testing available. Clinician expertise and knowledge to provide patient-specific COPD diagnosis is essential. AI will likely not be a replacement for clinical judgment for the foreseeable future. Nonetheless, it is fundamental to develop an AI approach that can be implemented in LMICs to help address barriers to high-quality health care. Prior research has shown that machine learning can be effectively implemented in LMIC settings with robust routine health information readily available but often underused.[32,33] AI infrastructure development in LMICs is currently supported by the WHO and international organizations through capacity-building and training programs.[34] In fact, the WHO has recently made AI a top priority calling for the development and implementation of AI to address challenges in global settings.[35] The WHO asserts that AI can improve clinical decision-making made by health care providers and assist in disease screening and evaluation in resource-constrained settings such as in LMICs.[31] To mitigate the growing burden of COPD in LMICs, a multivariate approach that utilizes available resources may be more effective. For example, utilizing sputum and biomarker analysis may provide unique insights into the lung microbiome to facilitate COPD endotype diagnosis and risk assessment of COPD exacerbations that imaging may not detect alone. Not only may this approach improve clinical decision-making, but this approach is also typically low-cost.

We summarize our proposed approach to apply and integrate AI in clinical practice in Figure 1. We recommend an emphasis on improving access to quality health care services to diagnose COPD in resource-constrained settings such as in LMICs as this is of the utmost importance globally. We suggest clinical collaboration between clinicians with an AI-supported multimodal approach to COPD diagnosis as a step towards achieving this. We believe the interplay of CT imaging, spirometry, biomarker analysis, and sputum analysis may provide unique insights across settings that could provide a basis for clinical decision-making that includes early intervention for those diagnosed with COPD. Clinician expertise is irreplaceable and supplementing with AI technology can improve COPD endotype classification and predict disease trajectory, which may improve COPD outcomes.

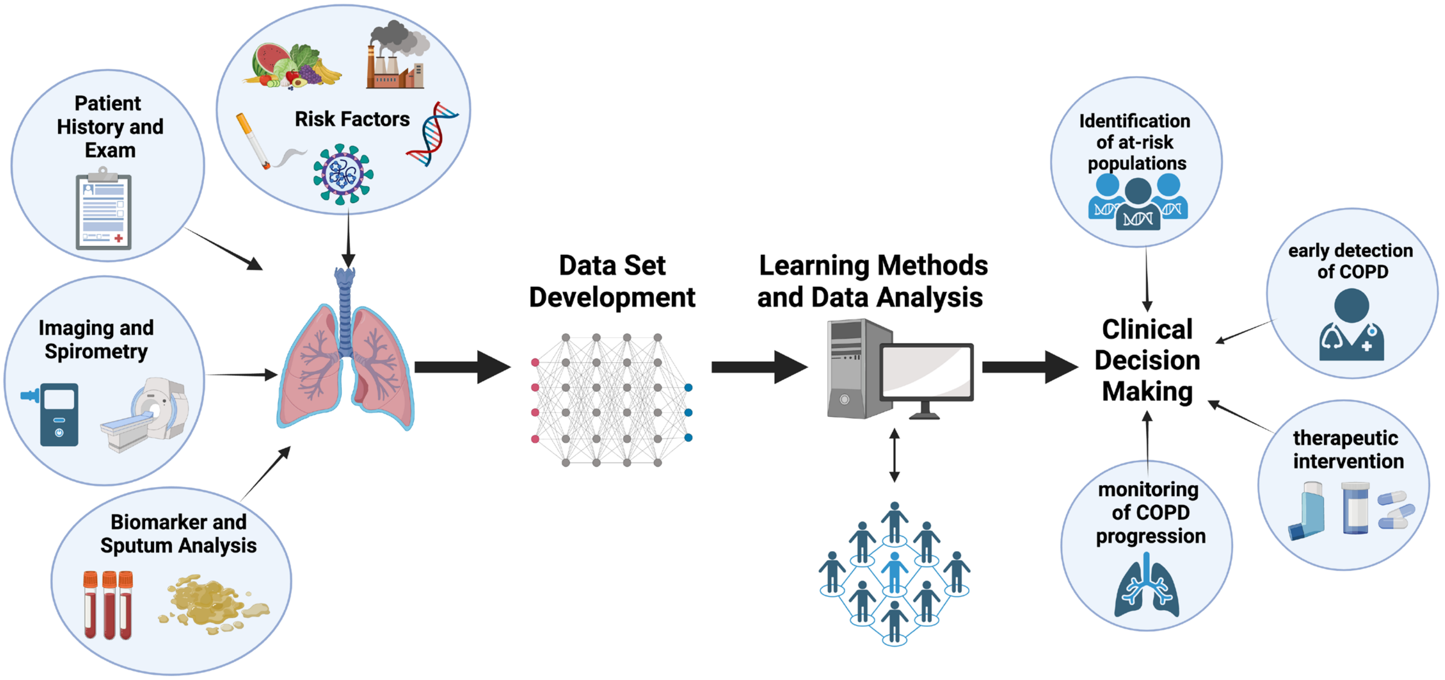
Acknowledgements

Author contributions: All authors contributed to concept and design, analysis and interpretation, and drafting and revising the manuscript for important intellectual content. All authors approved the final version of the manuscript for publication.

Declaration of Interests

The authors have no competing interests to declare.

Figure 1. An Approach to Apply and Integrate Artificial Intelligence in Clinical Practice



COPD=chronic obstructive pulmonary disease

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