Application of artificial intelligence in diagnosis of pulmonary tuberculosis

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Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*. Although the diagnostic technology of pulmonary tuberculosis (PTB) has advanced, accurate and differential diagnoses of PTB are still challenging. In recent years, the rapid development of artificial intelligence (AI) and its wide application in the medical field have provided new opportunities for diagnosing and treating TB and PTB. The machine learning model of AI has not only helped physicians improve diagnostic accuracy, but also enabled them to make early preventive diagnoses for individuals at increased risk of infection. Furthermore, AI can guide physicians to formulate targeted treatment strategies for PTB patients with different conditions.

AI-assisted chest X-ray (CXR) imaging: A lot of mature AI software has been applied to TB diagnosis in recent years. The specific AI-combined strategy is shown in Supplementary Figure 1, http://links.lww.com/CM9/B897. A previous meta-analysis showed that although the sensitivity and specificity of each software may differ under certain conditions, the accuracy of physician-only and computer-aided diagnosis (CAD) software-based diagnoses was similar, and the use of CAD software significantly reduced the variability caused by different experiences and work fatigue. The early exploration of CAD in the prevention and treatment of PTB can be traced back to 1968, and the widespread use of AI technology for TB prevention and control began in 2016 [Supplementary Figure 2, http://links.lww.com/CM9/B897].

Although the performances of different softwares may differ, they all have high sensitivity and can help doctors improve the sensitivity and specificity of diagnosis. Developing an AI-based automated screening platform in remote and resource-poor regions can significantly reduce the waiting time for patients to receive diagnostic reports, improve the efficiency of hospital outpatient clinics, and increase the accuracy of disease diagnosis. Research found that the sensitivity, specificity, positive predictive value, negative predictive value (NPV), and diagnostic accuracy of the AI-assisted system were higher than those of the physician alone.[1] Another study compared the performance of AI automated image reading technology and manual image reading in identifying pathogen-positive PTB patients, and the results showed that among 47 pathogen-positive PTB patients, 14 cases were misdiagnosed by senior experts and 5 cases were misdiagnosed by AI.[2] These data suggested that the sensitivity of AI reading was approximately 20% higher than that of human reading. However, it should be noted that false positives can be caused by many lesions with similar imaging appearances but different clinical information, resulting in a misdiagnosis rate of 10%. The comparisons of the performance of different CXR-assisted diagnosis softwares for PTB and diagnostic efficiency of CXR-assisted diagnosis software and doctors are listed in Supplementary Table 1, http://links.lww.com/CM9/B897. In summary, AI-assisted CXR diagnosis has potential advantages in the rapid localization and quantification of PTB lesions, which can not only accurately identify microscopic lesions often missed by the human eye, but also assist in the diagnosis and improve the detection rate of PTB.

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AI-assisted CT imaging diagnosis: CT is superior to CXR in identifying parenchymal lesions and showing active features of PTB (e.g., cavities, parenchymal abnormalities, and lobular central nodules). In recent years, relevant AI systems have been developed to assist in reading chest CT images to help internists improve the accuracy and sensitivity of CT diagnosis of PTB, and existing AI algorithms can improve the classification accuracy of five types of PTB images by 71%.[3] In addition, it has been suggested that AI can automatically identify pulmonary abnormalities 1000 times more efficiently than doctors. Interestingly, one study compared the sensitivity and accuracy of AI and physicians in CT reading of PTB patients, and found that the sensitivity and accuracy of AI reading were 95.49% and 90.4%, respectively, while the sensitivity and accuracy of physicians reading were 93.8% and 92.8%, respectively.[4] The performance comparisons of various CT-assisted diagnosis softwares for PTB and the diagnostic efficacy of both CT-assisted diagnosis software and medical practitioners are documented in Supplementary Table 2, http://links.lww.com/CM9/B897. Thoss data suggest that the algorithms can help doctors improve the sensitivity and accuracy of CT scans in PTB diagnosis.

AI-assisted other examinations: *Mycobacterium tuberculosis* can be detected by sputum smear or culture. Fluorescent microscopy is one of the most accurate methods for sputum smear examination, with a sensitivity of over 70%. However, there are still false negative sputum smear results in 20–40% of cases. Although bronchoscopic biopsy can be used for further investigation, it is usually not recommended as a routine screening test because of its invasive nature and low sensitivity (only 42–63%). Research found that AI has certain advantages in pathological diagnosis, which can reduce the false negatives and misdiagnosis rates related to human error.[5] A previous study investigating the use of AI-assisted pathology in transbronchial lung biopsy (TBLB) showed that the sensitivity of AI-assisted test was significantly higher than that of conventional bacteriology when detecting acid-fast bacilli (AFB) alone (86% *vs.* 29%, $P = 0.046$), and the specificity of AI-assisted pathology was 100%.[6] All in all, AI-assisted pathology is more sensitive to identifying AFB in samples collected via bronchoscopy than conventional bacteriological tests, and the sensitivity of sputum smears can be improved by using AI automatic microscope. Furthermore, T cells spot test (T-SPOT) is a commonly used immune test to diagnose TB infection in clinical practice. Previous studies have found that blood T-SPOT test combined with pulmonary CT image and AI-based diagnosis system can improve diagnostic accuracy.[7]

AI-assisted differential diagnosis of PTB and other diseases: In some cases, the imaging-based differential diagnosis of PTB can be challenging, especially for doctors with limited experience. In such cases, AI can serve as a necessary supplement and establish standardized lesion classification, thus increasing the overall accuracy of diagnosis. Previous studies related to this topic have been summarized in Supplementary Table 3, http://links.lww.com/CM9/B897. It has been known that peripheral lung cancer and PTB nodule have similar shapes on CT scans. Different AI models can automatically extract abstract features through image classification by comparing them to the maximum and average CT values of AI parameters. Content-based image retrieval with a convolutional Siamese neural network (CBIR-CSNN) can be used to differential diagnosis using CT image. In addition, the depth learning nomograph algorithm can also be used to determine tuberculous granuloma and pulmonary adenocarcinoma, and the area under the curve (AUC) is higher than 80%. Clinical experiments have verified that the accuracy of AI in differentiating benign and malignant lesions has improved, reaching as high as 88.9%.[8] Chest CT is also a conventional diagnostic method for silicosis, which shows similar characteristics to those seen in miliary TB. The differentiation between both diseases often requires additional efforts. A previous study investigated the prediction model of silicosis and TB based on machine learning algorithms, statistical analysis, and data mining, and showed that the accuracy of diagnosis was 83.1%,[9] indicating the important role of AI in differential diagnosis. Pneumonia is a common lung disease, and the accuracy of sputum smear to differentiate pediatric pneumonia and PTB is less than 50% due to the low bacterial content. Therefore, the diagnosis mainly depends on radiological examination. AI was also helpful in the differential diagnosis of pneumonia and TB, with the diagnostic accuracy as high as 97.7%,[10] whereas physicians only achieved an accuracy of 79.9%. Furthermore, AI has an excellent performance in the differential diagnosis of PTB from COVID-19 and non-tuberculous mycobacteria pulmonary disease (NTM-PD). A multicenter study evaluated the performance of a deep learning system (DLS) using six independent test sets consisting of different patient populations and two diseases (TB and COVID-19).[11] The high sensitivity operating point of the DLS showed comparable performance to board-certified radiologists in ruling out normal CXRs. The DLS achieved negative predictive values (NPVs) ranging from 0.85 to 0.95 for general abnormalities, 0.88 to 0.98 for TB, and 0.56 to 0.85 for COVID-19. These NPVs are similar to the NPVs of radiologists, which ranged from 0.67 to 0.87 for general abnormalities, 0.74 to 0.88 for TB, and 0.62 to 0.78 for COVID-19.[11]

Similarly, a retrospective study also evaluated the performance of radiologists with and without AI assistance in distinguishing COVID-19-infected pneumonia from other pulmonary diseases (such as TB and common pneumonia) by CT scans and found that in 694 cases, the accuracy, sensitivity, and specificity of AI were 91.4%, 91.8%, and 90.9%, respectively.[12] Compared to doctor-only based diagnosis, the accuracy and sensitivity increased by 1% and 4.7% with AI assistance. It has been established that a deep learning-based AI model can improve radiologists' performance in distinguishing COVID-19 from other pulmonary infections. It's important to note that, the clinical symptoms of NTM-PD are similar to those of PTB. Therefore, PTB can easily be misdiagnosed based on clinical presentation alone, especially in the early stages. However, NTM-PD and PTB have different characteristics in radiology.

AI-assisted prediction of PD prognosis: With the help of AI technology, doctors can not only determine the characteristics related to treatment failures of each patient, such as drug allergy, imaging manifestation, microbiological examination results, education level, and employment, but also identify those high-risk patients at an early stage. Sauer *et al*[13] used machine learning to identify features associated with TB treatment failure and to predict patients at high risk of treatment failure based on baseline demographic and clinical characteristics, and found that drug allergy patterns, imaging results, microscopic Ziehl–Neelsen stain results, education level, and employment status were associated with treatment failure. By identifying patients with a high risk of treatment failure, we can pay more attention to these patients to reduce the risk and prevent the occurrence of drug-resistant tuberculosis (DR-TB). The classification method modeled by AI can predict the treatment outcome of specific patients at the beginning of TB treatment. The random forests (RFs) model had the highest prediction accuracy, reaching 76%. The support vector machine (SVM) model had the highest precision and specificity at 73.05% and 95.71%, respectively. The sensitivity of artificial neural network (ANN) was the highest at 68.5%. AI-assisted machine learning can predict the treatment outcome of TB to help doctors better evaluate the benefit of treatment and encourage patients to receive regular anti-TB treatment, thus reducing the rate of treatment interruption.

Problems and challenges of AI-assisted diagnosis of TB: The application of AI in the diagnosis of PTB has exhibited significant potential for enhancing accuracy and efficiency. Nonetheless, the development and implementation of AI-assisted diagnosis tools for PTB face various challenges and problems, including limited availability and quality of data, lack of standardization, ethical considerations and bias, interpretability and explainability, and integration into clinical workflow. Besides, relatively high false-positive results may occur due to the characteristics of AI-assisted diagnosis, such as its inability to comprehensively analyze patients' clinical symptoms, focusing on detecting small lesions and reducing missed diagnoses. Addressing the aforementioned challenges is crucial to maximize the potential of AI-assisted diagnosis in improving accuracy, efficiency, and patient outcomes. Collaborative efforts involving clinicians, researchers, policymakers, and regulatory bodies are essential to overcome these challenges and ensure successful integration of AI into routine clinical practice for PTB diagnosis.

In conclusion, AI is important in diagnosing PTB and can improve the diagnostic accuracy, sensitivity, and specificity of CXR- and CT-based tests. In addition, AI plays an excellent auxiliary role in image feature extraction and sputum smear diagnosis in the microbiological examination. Moreover, AI can automatically facilitate lesion labeling and classification, assisting doctors in performing differential diagnoses and helping predict the prognosis of PTB. However, the development and implementation of AI in PTB face various challenges and problems that need to be addressed in the future.

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Conflicts of interest

None.

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