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Review Article

Artificial Intelligence: Predicting Patient Outcomes and Treatment Response in Lung Cancer

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Abstract

Lung cancer, the leading cause of cancer-related mortality, prompts innovative strategies for prognosis and personalized treatment. This review delves into the evolving landscape of advanced Non-Small Cell Lung Cancer (NSCLC) treatment, emphasizing the integration of Artificial Intelligence (AI) to process vast diagnostic and treatment data. AI's synergy with TNM staging proves pivotal, linking histopathologic images to survival outcomes. Highlighting AI's role in understanding lung cancer prognosis and predicting treatment responses, studies showcase its potential in histopathologic image analysis, radiomics, and genomic features. Findings include successful differentiation of survival outcomes in adenocarcinoma and squamous cell carcinoma, predicting responses to tyrosine kinase inhibitors and immunotherapy, and developing deep learning radiomic biomarkers for tumor mutational burden prediction. AI discerns prognostic details within sub-genotypes and also assists in predicting EGFR and KRAS mutations. Encompassing histopathologic image analysis, radiomics, and predictive modeling, the review highlights AI's multifaceted utility in lung cancer management. Studies collectively affirm AI's potential to advance prognostic assessments and refine personalized treatment approaches. The implications extend beyond the current landscape, suggesting transformative impacts on future clinical capabilities.

Keywords: Lung cancer, Artificial intelligence, Prognostic assessment, Personalized treatment, Histopathologic images, Radiomics, Genomic features, Machine learning, Deep learning

Abbreviations: NSCLC: Non-Small Cell Lung Cancer; TNM: Tumor, Node, Metastasis; AI: Artificial Intelligence; TCGA: The Cancer Genome Atlas; TMA database: Stanford Tissue Microarray Database; CNN: Convolutional Neuronal Networks; TKI: Tyrosine Kinase Inhibitor; AUC: Area Under Curve; AUROC: Area Under the Receiver Operating Characteristic Curve; ICI: Immune Checkpoint Inhibitor; SCAV: Selective Class Average Voting; OS: Overall Survival; CT Scan: Computerized Tomography Scan; PET Scan: Positron Emission Tomography Scan; SVM: Support Vector Machine; TMB: Tumor Mutational Burden; TMBRB: Tumor Mutational Burden Radiomic Biomarker

Introduction

Lung cancer stands as the primary cause of cancer-related mortality, accounting for 1.8 million deaths in 2020 [1]. However, the landscape of treatment for patients with advanced Non-Small Cell Lung Cancer (NSCLC) has expanded significantly with the emergence of precision medicine, offering a diverse array of treatment options informed by genetic insights [2]. Amidst the extensive data generated during diagnosis and treatment, the integration of Artificial Intelligence (AI) proves pivotal in streamlining the synthesis of extensive datasets from varied sources, including imaging scans, electronic health records, and genomic profiles, thereby contributing to the field of oncology [3,4]. The progress in lung cancer treatment entails tailored options for each pathologic subtype. The prognosis of this intricate disease is shaped by various factors, with TNM staging playing a crucial role in stratification, decision-making, and prognosis assessment [5]. Within this framework, the integration of artificial intelligence with TNM staging presents a specific avenue, notably in linking histopathologic images with survival outcomes [6]. In the management of lung cancer, an important objective is understanding the overall prognosis of the disease and predicting its response to different therapies. Artificial intelligence assumes a

critical role in achieving these objectives, enhancing our capability to predict lung outcomes and treatment responses.

Discussion

In a study, *Yu, et al*. analyzed 2,186 histopathology whole-slide images from lung adenocarcinoma and squamous cell carcinoma patients, employing machine learning to extract and identify 9,879 quantitative image features. The study successfully differentiated shorter-term from longer-term survivors in stage I adenocarcinoma ($P<0.003$) and squamous cell carcinoma ($P=0.023$) within the TCGA dataset, with validation in the TMA cohort reinforcing its predictive capabilities ($P<0.036$ for both tumor types). The findings underscore the potential of automatically derived image features in precision oncology for predicting lung cancer patients' prognoses [7]. In a study by *Li, et al*. Convolutional Neuronal Networks (CNN) were used to analyze histopathologic images, revealing a significant association between the interaction strength of tumor cells and stromal cells and a favorable prognosis ($P=0.05$) [8]. AI continues to contribute to advancing prognostic insights through lung cancer radiomics [9,10]. CT-based radiomics nomograms can predict lymph vascular invasion and Overall Survival (OS) in NSCLC patients and stratify patients into low risk and high-risk group which can potentially aid in guiding personalized treatment strategies before surgery [10]. PET-CT scans have also stratified patients using hand-crafted radiomics [11] and deep learning features [12]. In another study, the integration of genomic features with radiomics and clinical data demonstrated a remarkable improvement in model performance. The Area Under the Receiver Operating Characteristic Curve (AUROC) increased from 0.79 in clinical to 0.87 when incorporating radiomic and genomic features. This emphasizes AI's capacity to establish meaningful relationships between imaging findings and molecular characteristics of tumors [13,14]. Advancement in Tyrosine Kinase Inhibitors (TKI) and immunotherapy highlights the significance of molecular tumor characterization in enabling tailored precision therapy [15]. A machine learning model deep learning semantic signature improved survival by predicting tumor progression risk after EGFR-TKI therapy in Stage IV EGFR Variant-Positive NSCLC [16]. In a study, Radiomics was utilized to predict treatment response in advanced NSCLC patients receiving Immune Checkpoint Inhibitors (ICIs). The CT scan radiomic characteristics employed in the study demonstrated the capability to predict treatment response and survival [17]. In another study, the researchers utilized machine learning to assess changes in radiomic texture (DelRADx) on CT scans before and after ICI therapy in Non-Small Cell Lung Cancer (NSCLC) patients. The DelRADx patterns successfully predicted response to ICI therapy and OS. These findings suggest that DelRADx could serve as a valuable tool for identifying early functional responses in NSCLC patients undergoing ICI therapy [18].

In the study by *Moreno, et al*. the challenge of predicting EGFR and KRAS mutations in lung cancer is addressed using an ensemble approach, including Selective Class Average Voting (SCAV). Despite a small dataset, the method significantly enhances the performance of both machine learning models and CNNs. Improved sensitivity and AUC are observed for EGFR mutation prediction, reaching an AUC of 0.846 in the deep learning approach. Similar notable improvements are noted for KRAS mutation prediction in both machine learning and deep learning models. The study highlights the efficacy of ensembles, particularly SCAV, in accurate mutation prediction from small image datasets, with implications for future application with larger datasets to enhance clinical capabilities [19]. In the study conducted by Kureshi et al., machine learning techniques, including Support Vector Machine (SVM) and decision tree classifiers, were utilized to assess multiple factors in predicting tumor response in EGFR-positive NSCLC patients treated with erlotinib or gefitinib. The resulting data-driven decision support model exhibited a predictive accuracy of 76% and an AUC of 0.76 [20]. In this study by *He, et al*. a deep learning radiomic biomarker (TMBRB) was developed from CT images for predicting Tumor Mutational Burden (TMB) in advanced Non-Small-Cell Lung Cancer (NSCLC). By using a 3D-densenet model and 1020 deep learning features, TMBRB effectively differentiated between High-TMB and Low-TMB patients, demonstrating robust performance in both the training (AUC: 0.85) and test cohorts (AUC: 0.81). Its predictive capabilities extended to stratifying patients for immunotherapy response with different overall survival and progression-free survival [21]. The scope of AI extends to discerning prognostic details within sub-genotypes of identified mutations. In a study focused on early-stage lung adenocarcinoma, researchers developed a fusion-positive tumor prediction model that proficiently predicts the TMB status and identifies EGFR/TP53 mutations. The median AUC values for these predictions were 0.606, 0.604, and 0.586, respectively [22]. Additionally, some machine learning models successfully predicted EGFR and KRAS mutations based on radiomic features [23,24]. Immunotherapies targeting PDL-1 and PD-1 have improved survival in a subset of patients with advanced lung cancer [15]. A study demonstrated that radiomics markers derived from baseline CT scans undergoing PD-1/PD-L1 inhibitor treatment for advanced NSCLC patients can help in discerning patients prone to hyper progression [25]. In another study, the integration of AI has facilitated the prediction of tumor histology and assessment of PD-1/PL-L1 status, contributing to predicting responses to immunotherapy. In a study of 194 patients undergoing PD-1/PD-L1 inhibitor treatment for stage IIIB-IV NSCLC, researchers utilized baseline PET/CT data and developed multiparametric imaging histological signature models, accurately predicting the likelihood of sustained clinical improvement from immunotherapy [26].

Conclusion

In summary, the integration of Artificial Intelligence into lung cancer management holds significant promise for advancing prognostic assessments and refining personalized treatment approaches. The discussed studies, spanning diverse methodologies such as histopathologic image analysis and predictive modeling, collectively demonstrate the multifaceted utility of AI.

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None.

Conflict of Interest

None.

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