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Genomic analysis of lung adenocarcinoma with micropapillary component: Identification of micropapillary-related subtypes and development of a prognostic model

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Background

Micropapillary adenocarcinoma represents a highly aggressive histologic subtype of lung adenocarcinoma (LUAD), and even a minor proportion of micropapillary component (MPC) could contribute to poor prognosis. Thus, a comprehensive analysis of the genetic features of LUAD with MPC would help better understand the cancer biology and guide future treatments.

Methods

In a previous international cohort comprising over 1500 patients, we have identified 11 genes that are significantly associated with the prognosis of LUAD. In this study, we investigated the expression patterns of these 11 genes in a total of 1592 micropapillary-containing LUAD samples from The Cancer Genome Atlas (TCGA) dataset. Furthermore, LASSO Cox regression analysis was employed to predict overall survival (OS). Patients were classified into low- and high-risk groups based on the median value of the risk score. The predictive accuracy of the scoring system was subsequently validated, and a nomogram was employed to optimize its clinical applicability range.

Results

Patients were divided into two genomic subtypes based on prognostic genes using an unsupervised clustering analysis to further investigate the special regulation mechanism. Kaplan-Meier curves demonstrated that patients in gene cluster A had significantly better overall survival (OS) times compared to those in gene cluster B. An eight-gene prognostic signature was developed using LASSO Cox regression analysis. Patients in the high-risk group exhibited a worse OS compared to those in the low-risk group (71.9 months vs. 118.5 months). Notably, patients in the high-risk group with micropapillary component had significantly worse OS compared to those in the intermediate- (HR=1.81, 95% CI 1.13-2.88, P=0.013) and low-risk groups (HR=1.03, 95% CI 0.63-1.70, P=0.910), whereas no significant difference was observed between patients without micropapillary component and the low-risk group.

Conclusions

These findings are expected to provide fresh insight into the nature of this aggressive cancer subtype, pave a new path for assessing the disease prognosis, and assist in developing personalized therapeutic strategies for patients with LUAD.

Legal entity responsible for the study

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Disclosure

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