A novel ferroptosis-related lncRNAs signature for prognosis prediction in patients with lung squamous cell carcinoma

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Abstract

Background: Lung squamous cell carcinoma (LUSC) is the second most common histological subtype of lung cancer, and the prognosis of most LUSC patients are so far still very poor. Ferroptosis is a newly defined form of cell death, and involved in LUSC progression and treatment. However, there is no research to establish a ferroptosis-related lncRNAs signature for patients with LUSC. This study aims to establish a predictive model to elucidate the relationship between ferroptosis and prognosis of LUSC patients, to explore the potential value of ferroptosis in therapeutic options.

Methods: Based on the expression profiles of ferroptosis-related lncRNAs, a LASSO cox regression model was established for the prognosis of LUSC. The validation of ferroptosis-related lncRNAs prognostic signature was assessed Kaplan-Meier survival analysis, receiver operating characteristic curve (ROC) analysis, decision curve analysis (DCA) of the risk factors, and risk survival status plot. The predictive independence was validated via univariate and multivariate cox regression analysis. A nomogram was established and verified by calibration curves and ROC. The enriched signaling pathways were predicted via GSEA. Immune cells, functions, and checkpoints were assessed between high risk and low risk group based on ferroptosis-related lncRNAs signature.

Results: 16 ferroptosis-related lncRNAs were found to be independent prognosis factors for LUSC, including MIR3945HG, AC016924.1, LUCAT1, LINC02600, LINC02555, C10orf55, AC104248.1, AL591686.1, AL606489.1, LINC01322, MIR22HG, AC026704.1, AP006545.2, LINC01508, SRP14-AS1, and AL122125.1. Kaplan-Meier analysis revealed the high-risk ferroptosis-related lncRNAs signature associated with poor prognosis. The ROC and DCA of the ferroptosis-related lncRNAs signature showed great performance compared with other traditional clinical features in predicting the prognosis. Besides, the survival status plot showed that the risk score of patients was inversely proportional to their survival rate. The risk score and stage proved to be the independent predictors for OS. A nomogram combining the signature and stage was constructed. The nomogram-predicted probability of 3- and 5-year survival approached the actual survival time. Several immune-related pathways were enriched in the high-risk group. The signature was distinctly associated with the immune cells, functions, and checkpoints.

Conclusion: A novel and reliable ferroptosis-related lncRNAs signature that can effectively classify LUSC patients into high risk and low risk groups in terms of prognosis was developed. Targeting ferroptosis may be a therapeutic option in LUSC.

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