

# INPLASY PROTOCOL

To cite: Qu et al. The presence of a cribriform pattern is related to poor prognosis in lung adenocarcinoma after surgical resection: A meta-analysis. Inplasy protocol 202340110. doi: 10.37766/inplasy2023.4.0110

Received: 29 April 2023

Published: 29 April 2023

**Corresponding author:**  
Ming Du

ljdyt1103@sina.com

**Author Affiliation:**  
Department of Cardiothoracic Surgery, the First Affiliated Hospital of Chongqing Medical University.

**Support:** None.

**Review Stage at time of this submission:** Data analysis.

**Conflicts of interest:**  
None declared.

## The presence of a cribriform pattern is related to poor prognosis in lung adenocarcinoma after surgical resection: A meta-analysis

Qu, HR<sup>1</sup>; Li, JF<sup>2</sup>; Zeng, R<sup>3</sup>; Du, M<sup>4</sup>.

**Review question / Objective:** We perform a meta-analysis to comprehensively assess the prognostic value of cribriform pattern in lung adenocarcinoma patients after surgical resection.

**Condition being studied:** In 2011, a new histological classification for this disease was proposed by the American Thoracic Society and the European Respiratory Society (IASLC/ATS/ERS), which included five major histological subtypes (lepidic, acinar, papillary, solid, and micropapillary), and later adopted by the World Health Organization. According to the criteria of the new classification system, the cribriform pattern (CP) is included in the acinar subtype, defined as invasive back-to-back fused tumor glands with poorly formed glandular spaces lacking intervening stroma or invasive nests of tumor cells that produce glandular lumina without solid components. Studies have shown that the CP is related to poor prognosis in lung adenocarcinoma. These reported the negative impact of the cribriform pattern in ADC after pulmonary resection has not been validated in larger studies.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 April 2023 and was last updated on 29 April 2023 (registration number INPLASY202340110).

### INTRODUCTION

**Review question / Objective:** We perform a meta-analysis to comprehensively assess the prognostic value of cribriform pattern in lung adenocarcinoma patients after surgical resection.

**Condition being studied:** In 2011, a new histological classification for this disease was proposed by the American Thoracic Society and the European Respiratory Society (IASLC/ATS/ERS), which included five major histological subtypes (lepidic, acinar, papillary, solid, and micropapillary),

---

and later adopted by the World Health Organization. According to the criteria of the new classification system, the cribriform pattern (CP) is included in the acinar subtype, defined as invasive back-to-back fused tumor glands with poorly formed glandular spaces lacking intervening stroma or invasive nests of tumor cells that produce glandular lumina without solid components. Studies have shown that the CP is related to poor prognosis in lung adenocarcinoma. These reported the negative impact of the cribriform pattern in ADC after pulmonary resection has not been validated in larger studies.

## METHODS

**Search strategy:** (component OR predominant OR pattern OR subtype OR minor) AND (resect OR resection OR operate OR operation OR lobectomy OR sublobectomy) AND (cancer OR carcinoma OR tumor) AND (lung OR pulmonary) AND cribriform.

**Participant or population:** Lung adenocarcinoma patients after surgical resection.

**Intervention:** The presence of a cribriform pattern.

**Comparator:** Without cribriform pattern.

**Study designs to be included:** Observational studies assessing the significance of the Lung adenocarcinoma subtype for prognosis.

**Eligibility criteria:** Inclusion criteria for selecting the studies for this meta-analysis were as follows criteria: (1) the research subjects were patients with confirmed L-ADC after surgical resection ; (2) specimens were evaluated by the comprehensive and detailed histological diagnostic model according to the new IASLC/ATS/ERS classification; (3) OS and/or DFS should be evaluated in the study; (4) the hazard ratio (HR) of OS and/or DFS was obtained through multivariate Cox regression analysis; (5) only including the

largest volume when the same institution was reported in different studies. Exclusion criteria were as follows: (1) editorials, letters, reviews, abstracts, case reports, and animal experiments; (2) studies with insufficient data for estimating hazard ratio (HR) and 95% confidence interval (CI)); (3) studies published in a non-English language. (4) patients who received neoadjuvant treatment.

**Information sources:** A systematic search was conducted on the three main literature databases (PubMed, Web of Science, and Embase databases), the reference list was also checked for relevant articles.

**Main outcome(s):** The pooled DFS and OS in patients with cribriform pattern.

**Quality assessment / Risk of bias analysis:** The Newcastle-Ottawa Scale (NOS) was used to assess each of the included studies' quality by the two authors (Haoran Qu and Jianfeng Li) after scanning the full texts. The NOS consists of three parts: selection (0-4 points), comparability (0-2 points), and outcome assessment (0-3 points). NOS scores of  $\geq 6$  was regarded as high-quality studies. Any inconsistencies between the two authors were discussed with the senior author (Ming Du). Cochran's Q test and I<sup>2</sup> value were undertaken to assess the heterogeneity of the included trials. Significant heterogeneity was regarded as an I<sup>2</sup> value greater than 50% or P-value less than 0.05. The pooled HR and the 95%CI were estimated using the random-effect despite of the heterogeneity. Publication bias was evaluated by Begg's funnel plot and Egger's linear regression test if the included studies were more than ten. All P-values were two-sided. The P < 0.05 was considered statistically significant.

**Strategy of data synthesis:** We extracted HRs and 95% CIs estimated by multivariate analysis from each eligible study conducted in L-ADC patients to calculate and analyze the Ln (HR) and the standard error (SE) by using the generic inverse variance. The pooled HR and the 95%CI were estimated using the random-effect

---

despite of the heterogeneity. This comprehensive meta-analysis was performed using the Review Manager software (Rev Man, version 5.3, Copenhagen: Nordic Cochrane Centre, Cochrane Collaboration, 2014).

approved the final version of the manuscript.

Email: ljdyt1103@sina.com

**Subgroup analysis:** According to the proportion of the cribriform pattern, we divided the included studies into two subgroups, the cribriform pattern subgroup, and the cribriform pattern predominant subgroup. The effect of the cribriform pattern on OS and DFS was analyzed by using the pooled HRs and 95% CIs, respectively.

**Sensitivity analysis:** Sensitivity analyses were performed to find the source of heterogeneity.

**Language restriction:** English.

**Country(ies) involved:** China.

**Other relevant information:** None.

**Keywords:** Cribriform predominant lung adenocarcinoma; Presence of cribriform pattern; NSCLC; Postoperative; Prognosis; Meta-analysis.

**Contributions of each author:**

**Author 1 - Haoran Qu -** Put forward the idea and designed the research; Contribute to literature searching, data extraction and analysis; Wrote the manuscript; approved the final version of the manuscript.

Email: 237668087@qq.com

**Author 2 - JianFeng Li -** Contribute to literature searching, data extraction and analysis; approved the final version of the manuscript.

Email: 444292708@qq.com

**Author 3 - Rui Zeng -** Contribute to literature searching, data extraction and analysis; approved the final version of the manuscript.

Email: 550385611@qq.com

**Author 4 - Ming Du -** Contribute to research design, literature searching, data extraction and analysis; revised the manuscript;