

# INPLASY

## Correlation of Cell-in-Cell structure with prognosis in solid tumors

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### ADMINISTRATIVE INFORMATION

**Support** - XJZT24LY09; 2021JZ-29; 2023-JC-QN- 0965.

**Review Stage at time of this submission** - Preliminary searches.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY2024100020

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 6 October 2024 and was last updated on 6 October 2024.

### INTRODUCTION

**Review question / Objective** The purpose of this study was to investigate the effect of the number of Cell-in-Cell structures on the difference in prognosis of solid tumors. The study method selected was a retrospective non-randomized study to evaluate the difference in overall survival of patients with high Cell-in-Cell structure and low Cell-in-Cell structure.

**Condition being studied** The included studies were eligible patients with solid tumors, and Cell-in-Cell data were collected.

### METHODS

**Search strategy** Search for relevant articles in PubMed and Web of science databases. Relevant keywords, phrases, and MeSH terms have been adapted to suit the specific requirements of each database. An example of a retrieval strategy is the one used for PubMed: (((Cell-in-Cell Structure OR

cytophagocytosis OR cell cannibalism OR entosis OR emperitosis)) AND ((tumor OR tumour OR cancer OR neoplasms))) AND ((prognosis OR prognostic)). The retrieved articles are then cross-checked to ensure that all possible studies are retrieved.

**Participant or population** Solid tumor patients who underwent cell-in-cell data acquisition.

**Intervention** Patients with a high level of Cell-in-Cell structure.

**Comparator** Patients with a low level of Cell-in-Cell structure.

**Study designs to be included** Retrospective non-randomized studies.

**Eligibility criteria** Overall survival data of patients with solid tumors. Inclusion criteria included full-text available studies in adult patients (> 18 years of age) with solid tumors receiving surgery alone,

surgery and adjuvant (chemical) radiation therapy, radiation therapy alone, or a combination of chemoradiotherapy. The study required survival analysis and CICs statistics, including extractable overall survival (OS), hazard ratio (HR). The exclusion criteria are as follows: non-English language; No full text; Insufficient reported data; Unextractable data; The types of articles are reviews, case reports, conference abstracts, letters to the editor, or book chapters.

**Information sources** PubMed and Web of science databases.

**Main outcome(s)** Overall survival.

**Quality assessment / Risk of bias analysis** National Institute for Health and Clinical Excellence (NICE) Quality assessment.

**Strategy of data synthesis** Revman software is selected for data analysis. Data from each study were transcribed in tabular form. Binary variables are reported by count and percentage. The primary endpoint is OS. OS is defined as the time from the date of diagnosis (or the start of treatment) until death from any cause. The effect size of HR was used to measure the impact of CICs on survival. If the authors provided data, HR and 95% confidence intervals (CI) were extracted directly from each study. HR was extracted from the single-factor model in cases where both single-factor and multi-factor analyses were reported. Otherwise, they are estimated indirectly using the method described by Tierney et al. (Tierney et al. 2007). HR greater than 1 indicates poor survival in patients with high CICs, while HR less than 1 indicates survival benefit in patients with high CICs. A logarithmic transformation of HR is performed before combining the effect size estimates. Calculated by inverse variance, a cumulative hazard ratio of 95% CI was provided for reported outcomes. Heterogeneity among studies was assessed by the following method (I<sup>2</sup>). According to the Cochrane evaluator manual, I<sup>2</sup> was evaluated as follows: I<sup>2</sup> ≤ 40%, low heterogeneity; I<sup>2</sup> ranged from 41% to 60% with moderate heterogeneity. I<sup>2</sup> ranges from 61% to 100%, with significant heterogeneity (Higgins JPT 2023). Given the observational nature of most of the included studies, we decided to adopt a statistically conservative approach. If heterogeneity exists in I squared, random effects model is selected; otherwise, fixed effects model is selected. STATA software was selected for data analysis. If I squared, heterogeneity was considered, random effects model was selected; otherwise, fixed effects model was selected.

**Subgroup analysis** No subgroup analysis was performed.

**Sensitivity analysis** Sensitivity analysis was performed using Revman software, and sensitivity was reflected by observing the change of effect size after deleting one of the literatures.

**Country(ies) involved** China.

**Keywords** Cell-in-Cell structure; solid tumors; overall survival; prognostic factors.

#### Contributions of each author

Author 1 - Haoyi Zi - Author 1 drafted the manuscript.

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