INPLASY PROTOCOL

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Surgical Prognostic Factors of Second Primary Lung Cancer: A Systematic Review and Meta-analysis

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Review question / Objective: The objective of this study was to explore the effects of different surgical strategies and potential prognostic factors on the prognosis of patients with SPLC through a systematic review and meta-analysis. Prognostic factors included surgical approach, type of SPLC (Synchronous and metachronous), histology, disease-free interval (DFI), tumor size, CT morphology, lymph node metastasis status, smoking status, gender.

Condition being studied: With the development of imaging technology and better survival after primary lung cancer, the detection rate of second primary lung cancer (SPLC) has been increasing. At present, the staging and treatment of the second primary lung cancer are still controversial. Although surgery is widely accepted as the main treatment method, there is no unified diagnostic criteria and diagnosis and treatment strategy. The objective of this study was to explore the effects of different surgical strategies and potential prognostic factors on the prognosis of patients with SPLC through a systematic review and meta-analysis.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 November 2022 and was last updated on 10 November 2022 (registration number INPLASY2022110047).
**Condition being studied:** With the development of imaging technology and better survival after primary lung cancer, the detection rate of second primary lung cancer (SPLC) has been increasing. At present, the staging and treatment of the second primary lung cancer are still controversial. Although surgery is widely accepted as the main treatment method, there is no unified diagnostic criteria and diagnosis and treatment strategy. The objective of this study was to explore the effects of different surgical strategies and potential prognostic factors on the prognosis of patients with SPLC through a systematic review and meta-analysis.

**METHODS**

**Search strategy:** Through a comprehensive online search of three databases (MEDLINE, EMBASE and Cochrane), we determined the research on the prognostic factors of SPLC between January 2000 and August 2022. The combination of search terms is as follows:(second primary lung cancer OR multiple primary lung cancer OR MPLC OR SPLC OR separate primary lung cancer OR multifocal lung cancer) AND (wedge resection OR segmentectomy OR lobectomy OR sublobar resection OR pneumonectomy OR surgery OR operative).

**Participant or population:** The selected study meets the following criteria: (1) The definition of SPLC must be clear in the study; (2) Cases with metachronous and/or metachronous SPLC included in the study; (3) The first primary tumor and SPLC should be removed by surgery; (4) Five year OS shall be provided (calculated from SPLC surgery). Studies meeting the following criteria were excluded: (1) Editorials, letters, comments, meeting summaries and case reports; (2) Research published in languages other than English; (3) Primary malignant tumors or intrapulmonary metastatic tumors of other organs were included in the study; (4) The prognosis data is incomplete or the risk ratio (HR), 95% CI cannot be extracted.

**Intervention:** Surgery.

**Comparator:** This experiment is not a control experiment.

**Study designs to be included:** Retrospective study.

**Eligibility criteria:** The selected study meets the following criteria: (1) The definition of SPLC must be clear in the study; (2) Cases with metachronous and/or metachronous SPLC included in the study; (3) The first primary tumor and SPLC should be removed by surgery; (4) Five year OS shall be provided (calculated from SPLC surgery). Studies meeting the following criteria were excluded: (1) Editorials, letters, comments, meeting summaries and case reports; (2) Research published in languages other than English; (3) Primary malignant tumors or intrapulmonary metastatic tumors of other organs were included in the study; (4) The prognosis data is incomplete or the risk ratio (HR), 95% CI cannot be extracted.

**Information sources:** Computer searches MEDLINE, EMBASE, Cochrane databases. The retrieval time range is from 2000 to 2022.

**Main outcome(s):** Hazard ratio (HR) and 95% confidence interval (CI) for each prognostic factor.

**Quality assessment / Risk of bias analysis:** The Newcastle-Ottawa Scale (NOS) was used to assess each of the included studies quality by two independent authors. The NOS consists of three parts: selection (0-4 points), comparability (0–2 points), and outcome assessment (0–3 points). NOS scores of ≥5 were regarded as high-quality studies.

**Strategy of data synthesis:** In case we perform a meta-analysis heterogeneity will be explored with the Cochran's Q test and $I^2$ test. If the Cochran's Q test is < 0.05 we will consider that the meta-analysis presents a high degree of heterogeneity. And if the $I^2$ test is < 50% we will use a fixed effect model. If the $I^2$ test is > 50% we will use a random effect model. A Forest plot will be performed for each prognostic
factor. Publication bias will be evaluated with the Egger’s test for each forest plot. A sensitivity analysis will be carried out to evaluate the robustness of the results for each forest plot.

**Subgroup analysis:** Subgroup analysis was carried out according to the type of SPLC (synchronous or metachronous).

**Sensitivity analysis:** A sensitivity analysis will be carried out to evaluate the robustness of the results for each forest plot.

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

**Keywords:** Second primary lung cancer, Surgery, Prognosis, Meta-analysis.

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