

INPLASY PROTOCOL

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Review Stage at time of this submission: Formal screening of search results against eligibility criteria.

Conflicts of interest:
None.

INTRODUCTION

Review question / Objective: 1. Whether R1 margin negatively influences the survival of gastric cancer after curative intent resection. 2. Which subgroups are most impacted by R1 margin and which are not?

Condition being studied: Generally, complete resection with cancer cell

Impact of surgical margin status on the survival outcome after surgical resection of gastric cancer: a protocol for systematic review and meta-analysis

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Review question / Objective: 1. Whether R1 margin negatively influences the survival of gastric cancer after curative intent resection. 2. Which subgroups are most impacted by R1 margin and which are not?

Condition being studied: Generally, complete resection with cancer cell negative (R0) margin has been accepted as the most effective treatment of gastric cancer and positive resection (R1/R2) margin has been associated with decreased survival to varied degrees. However, the independent impact of microscopical positive (R1) margin on long-term survival may be confounded.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 May 2020 and was last updated on 08 May 2020 (registration number INPLASY202050028).

negative (R0) margin has been accepted as the most effective treatment of gastric cancer and positive resection (R1/R2) margin has been associated with decreased survival to varied degrees. However, the independent impact of microscopical positive (R1) margin on long-term survival may be confounded.

METHODS

Search strategy: A systematic search of PubMed, Embase, and the Cochrane Central Register of Controlled Trials databases will be performed from their inception to 30 April 2020 to identify randomized controlled trials, cohort studies, case-control and cross-sectional studies focusing on the impact of R1 margin on survival of gastric cancer after curative intent resection.

Participant or population: Patients who have undergone curative intent resection for gastric cancer diagnosed by pathological examination will be included. Gastric cancer patients underwent palliative intent resection will be excluded.

Intervention: The exposure will be postoperatively R1 margin confirmed by permanent pathologic section (PPS), which means cancer cells are identified microscopically by PPS at the linear, circular, proximal, or distal resection margin.

Comparator: R0 margin confirmed by PPS.

Study designs to be included: Studies with randomized controlled, cohort, case-control, or cross-sectional designs.

Eligibility criteria: 1. Studies with randomized controlled, cohort, case-control, or cross-sectional designs estimating the impact of margin status on gastric cancer survival after curative intent resection. 2. Studies reporting OS or DFS of R1 and R0 groups. 3. Studies published in English. 4. Studies including only human participants. 5. There will be no restrictions on publication year.

Information sources: A systematic search of PubMed, Embase, and the Cochrane Central Register of Controlled Trials databases will be performed. We will also manually search the references of relevant articles to further identify eligible studies, and their full texts will be retrieved.

Main outcome(s): OS of R1 and R0 margin group, or relevant data to estimate it.

Quality assessment / Risk of bias analysis: Two independent reviewers will assess the methodological quality and risk of bias of included studies using the Cochrane Collaboration's risk of bias tool for RCTs and the risk of bias In Non-randomized studies of Interventions (ROBINS-I) tool for non-randomized studies.

Strategy of data synthesis: We will import extracted data into Rev Man 5.3 software for data synthesis. A fixed-effect model will be used when heterogeneity is low, otherwise, a random-effect model will be chosen. When substantial heterogeneity is detected, subgroup analysis and sensitivity analysis will be performed to investigate its possible sources.

Subgroup analysis: Subgroup analyses are planned as follows: 1. Study carried out in: Asia and other regions; 2. Tumor stage: early gastric cancer (EGC) and advanced gastric cancer (AGC); 3. Lymphadenectomy: $\leq D1$ and $\geq D2$; 4. HR (estimating OS or DFS) extracted from: multivariate analysis and univariate analysis; 5. Proximal cancer (tumor in the gastroesophageal junction, cardia, or fundus).

Sensitivity analysis: We will apply the leave-one-out sensitivity analysis to evaluate the robustness of the results.

Language: We will include studies published in English.

Country(ies) involved: China.

Keywords: Surgical margin; Gastric cancer; Survival; Meta-analysis.

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