INPLASY PROTOCOL

To cite: Wu et al. Role of surgical resection on hepatic metastasis of gastrointestinal stromal tumor: A systematic review and meta-analysis. Inplasy protocol 2021100009. doi: 10.37766/inplasy2021.10.0009

Received: 02 October 2021

Published: 02 October 2021

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Support: **Zhejiang Liver Cancer Diagnosi.**

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

Conflicts of interest:
None declared.

Role of surgical resection on hepatic metastasis of gastrointestinal stromal tumor: A systematic review and meta-analysis

Wu, Z[1]; Zhang, B[2]; Liu, C[3]; Liu, Y[4].

Review question / Objective: **1. Participants (P): The subject's histological examination confirmed liver metastasis of gastrointestinal stromal tumor, or liver metastasis was confirmed by CT (computed tomography), MRI (magnetic resonance imaging) and/or positron emission tomography . 2. Interventions (I) and comparisons (C): Surgery combined with TKI treatment and TKI alone. (3) Outcomes (O): OS or PFS. (4) Study design(S): Observational cohort studies and randomized controlled studies(RCTs).**

Information sources: **Two researchers conducted systematic literature searches in PubMed, EMBASE, Cochrane Library and Wanfangdata, using a combination of the following terms: "gastrointestinal stromal tumor", "GIST or GISTs", "hepatectomy or Hepatectomies"", "liver or hepatic", "Metastasis", "Metastasis Resection","surgery ", no language restrictions. All studies are carefully evaluated to determine duplicate data. The full text of potentially qualified studies will be screened and evaluated by examiners for inclusion. Any disagreements regarding research qualifications between them will be resolved through discussions with a third researcher.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 02 October 2021 and was last updated on 02 October 2021 (registration number INPLASY2021100009).

INTRODUCTION

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and comparisons (C): Surgery combined with TKI treatment and TKI alone. (3) Outcomes (O): OS or PFS. (4) Study design(S): Observational cohort studies and randomized controlled studies(RCTs).

Condition being studied: Gastrointestinal stromal tumor (GIST) is the most common sarcoma of the digestive tract. 15%-50% of patients have metastases at the time of diagnosis, so complete resection is difficult. For locally high-risk GIST patients, despite complete resection, nearly 40% of patients still have tumor recurrence within 2 years. The liver and peritoneum are the most common sites of metastasis, accounting for approximately 65% and 20% of the total, respectively. Imatinib is a tyrosine kinase inhibitor (TKI) and is the first-line treatment for advanced GIST. In clinical trials, it achieved high disease control rates and significantly extended survival. Despite its effectiveness, nearly 50% of patients developed drug resistance after 2 years of treatment. The limitations of TKI treatment prompted a reassessment of surgery for advanced GIST. Therefore, surgery combined with TKI for the treatment of liver metastases from GIST may be a choice that can improve the survival of patients. The purpose of this study is to evaluate the difference in the effect of liver resection combined with TKI therapy and TKI therapy alone on the survival of patients with GIST liver metastasis.

METHODS

Search strategy: We conduct systematic literature searches in PubMed, EMBASE, Cochrane Library and Wanfangdata, using a combination of the following terms: "gastrointestinal stromal tumor", "GIST or GISTs", "hepatectomy or Hepatectomies"", "liver or hepatic", "Metastasis", "Metastasis Resection","surgery ""gastrointestinal stromal tumor", "GIST or GISTs", "hepatectomy or Hepatectomies"", "liver or hepatic", "Metastasis", "Metastasis Resection","surgery ".

Participant or population: Inclusion criteria1. Participants (P): The subject's histological examination confirmed liver metastasis of gastrointestinal stromal tumor, or liver metastasis was confirmed by CT (computed tomography), MRI (magnetic resonance imaging) and/or positron emission tomography. 2. Interventions (I) and comparisons (C): Surgery combined with TKI treatment and TKI alone(3) Outcomes (O): OS or PFS.(4) Study design(S): Observational cohort studies and randomized controlled studies(RCTs).Exclusion criteria1. Meeting abstracts, letters, case reports, comments, or non-clinical studies with no data available.2. Studies with a follow-up time of less than 3 years. 3. Exclude other patients with concurrent malignant tumors. 4. Lack of research on survival data such as OS or PFS.

Intervention: The liver is the most common metastatic site for gastrointestinal stromal tumors. TKI is the main drug for the treatment of gastrointestinal stromal tumors. Therefore, compare liver resection combined with TKI and TKI therapy alone. Patients receiving TKI therapy alone will be considered as the baseline group.

Comparator: Intervention group: surgical resection combined with TKI for the treatment of liver metastases from gastrointestinal stromal tumors.Control group: TKI alone in the treatment of metastatic gastrointestinal stromal tumors with liver metastases. Surgery combined with TKI, TKI alone.

Study designs to be included: The heterogeneity of the included trials was assessed by Cochran Q test and measured by I^2 statistics. The interpretation of I^2 values was by assigning I^2 values of 0-25%, 25-50%, and 75% as low, medium, and high. The random effects dersimonan-laird method was used to calculate mixed HRs and 95% ci. According to the study design, sample size, race, survival analysis and average follow-up to explore and explain the differences (heterogeneity) between the results of different studies, and evaluate the publication bias.

Eligibility criteria: Inclusion criteria1. Participants (P): The subject's histological examination confirmed liver metastasis of gastrointestinal stromal tumor, or liver metastasis was confirmed by CT (computed tomography), MRI (magnetic resonance imaging) and/or positron emission tomography .2. Interventions (I) and comparisons (C): Surgery combined with TKI treatment and TKI alone(3) Outcomes (O): OS or PFS.(4) Study design(S): Observational cohort studies and randomized controlled studies(RCTs).Exclusion criteria1. Meeting abstracts, letters, case reports, comments, or non-clinical studies with no data available.2. Studies with a follow-up time of less than 3 years.3. Exclude other patients with concurrent malignant tumors.4. Lack of research on survival data such as OS or PFS.

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Main outcome(s): Overall Survival (OS): The time from intervention treatment (surgery combined with TKI or TKI alone) to death due to any cause. Progression-free survival (PFS): The time from the start of intervention treatment (surgery combined with TKI or TKI alone) to the progression of tumor (in any aspect) or death (for any reason).Main outcome will be patient survival and disease free survival following diagnosis. The survival will be defined as time since diagnosis.

Quality assessment / Risk of bias analysis: The Newcastle-Ottawa Scale (NOS) will be used to assess the risk of bias in the included non-randomized clinical studies (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp). The NOS scoring criteria award scores related to group comparability, study group selection, exposure determination, and adequacy of outcome evaluation and cohort follow-up.

Strategy of data synthesis: The heterogeneity of the included trials was assessed by Cochran Q test and measured by I^2 statistics. The interpretation of I^2 values was by assigning I^2 values of 0-25%, 25-50%, and 75% as low, medium, and high. The random effects dersimonan-laird method was used to calculate mixed HRs and 95% ci. According to the study design, sample size, race, survival analysis and average follow-up to explore and explain the differences (heterogeneity) between the results of different studies, and evaluate the publication bias.

Subgroup analysis: Perform subgroup analysis based on the level of heterogeneity. If the heterogeneity is high, set the subgroup according to the result.

Sensitivity analysis: Sensitivity analysis: OS/RFS: Conduct a sensitivity analysis to see if any research affects the final results. The results show that missing documents have no significant impact on the final results, indicating that our conclusions are reliable.

Language: No language limits.

Country(ies) involved: China.

Other relevant information: Zujian Wu, Zhejiang Chinese Medical University. Bing Zhang, Tongde Hospital of Zhejiang Province. Changfeng Liu, Tongde Hospital of Zhejiang Province. Yusu Liu, Zhejiang Chinese Medical University.

Keywords: "gastrointestinal stromal tumor", "GIST or GISTs", "hepatectomy or Hepatectomies"", "liver or hepatic",

“Metastasis", "Metastasis Resection”, "surgery ".

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