INPLASY PROTOCOL

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Conflicts of interest: None declared. Comparison of prognosis among patients with colorectal cancer liver metastases treated by surgical resection, radiofrequency ablation and HIFU: a protocol for network meta-analysis

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Review question / Objective: Clinical treatments for colorectal cancer liver metastases are not the same. In order to clarify the impact of surgical resection, radiofrequency ablation and HIFU, we provided a decision-making basis for the clinical treatment of colon cancer liver metastasis through systematic reviews and network meta-analysis.

Condition being studied: Colorectal cancer is a malignant tumor second only to lung and breast cancer in the West. The liver is the main target organ for colorectal cancer metastasis, affecting the prognosis and survival. Surgical treatment has made great progress in colorectal cancer liver metastasis (CRLM), including radiofrequency ablation, high-intensity focused ultrasound ablation.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 May 2021 and was last updated on 12 May 2021 (registration number INPLASY202150044).

INTRODUCTION

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METHODS

Participant or population: For patients diagnosed with CRLM, there are no restrictions on gender, age, primary site, primary tumor grade, liver metastasis site, and number of metastases.

Intervention: The patients receive one of the three treatments of HR, RFA and HIFU.

Comparator: One of the three treatments of HR, RFA and HIFU.

Study designs to be included: Randomized Controlled Trial (RCT).

Eligibility criteria: Inclusion: Randomized Controlled Trial (RCT) without restriction on the use of blind methods.

Information sources: We will search the following English electronic bibliographic databases: PubMed (inception- present), Embase (inception- present), Cochrane Central Register of Controlled Trials (CENTRAL) (inception- present), CINAHL (inception- present), Web of Science (inception- present), as well as the Chinese databases: China Knowledge Network (CNKI) (inception- present), China Biomedical Literature Database(CBM) (inception- present), VIP Data(inceptionpresent), Wan Fang Data(inceptionpresent).

Main outcome(s): Main outcomes: (1) the occurrence of complication (Lung infection, incision infection, hemorrhage from liver section) (2) estimated blood loss (3) the

occurrence of relapse (local recurrence, intra-hepatic recurrence, extra-hepatic recurrence) (4) overall survival rate.

Additional outcome(s): Additional outcomes: length of hospital stays.

Quality assessment / Risk of bias analysis: The methodological quality of the final included RCT will be evaluated independently by two reviewers (YSZ, ZBZ). Any disagreements will be resolved through discussion between the two parties or decided by a third reviewer (LW). The research quality of RCTs was evaluated by two researchers using the tools recommended by Cochrane System Reviewer Manual 5.1 to assess the risk of bias16,17, and Rev Man 5.3 was used to draw the risk of bias related chart. This tool includes random methods, allocation hiding, blinding (researcher and subject), blinding (outcome measurer), complete outcome data, selective reporting of results, and other sources of bias. Each aspect can be further classified as low risk, high risk or unclear risk.

Strategy of data synthesis: In this study, Stata software was used for data analysis and comparison, and relative risk (RR) and 95% confidence interval (95% CI) were used as the analysis statistics of binary variables. Use inconsistency test to detect whether there is inconsistency between direct evidence and indirect evidence. The inconsistency test was performed by node analysis, and if P>0.05, the consistency model was used for analysis. At the same time, the node splitting method is used to check the local inconsistency. When direct evidence and indirect evidence are inconsistent, use RevMan 5.3 for direct comparison. If P>0.05, it is considered that there is no overall inconsistency; if the 95% CI of the ROR contains 1, it is considered that there is no local inconsistency, otherwise there is local inconsistency18. Heterogeneity is judged by the prediction interval graph. If the 95% CI and 95% prediction interval (95% Pr I) both contain 1 or both do not contain 1, then it is considered that there is no statistical heterogeneity, otherwise, there is statistical

heterogeneity. By calculating the area evaluation under the cumulative ranking curve (SUCRA).

Subgroup analysis: If the evidence is sufficient, we will conduct a subgroup analysis to determine the differences between different genders, ages, primary sites, primary tumor grades, and metastasis methods.

Sensitivity analysis: We will exclude lowquality studies for sensitivity analysis.

Country(ies) involved: China.

Keywords: Colorectal cancer, liver metastases, treat, network meta-analysis.

Contributions of each author:

Author 1 - Yushan Zhou. Author 2 - Zubang Zhou. Author 3 - Minghua Zhang. Author 4 - Ya'e Xue. Author 5 - Xueting Zhang. Author 6 - Li Wang.