INPLASY PROTOCOL

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None.

Clinical efficacy of Laparoscopic liver resection versus radiofrequency ablation for smell hepatocellular carcinoma: a systematic review and meta-analysis

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Review question / Objective: **Clinical efficacy of Laparoscopic liver resection versus radiofrequency ablation for smell hepatocellular carcinoma.**
Condition being studied: **Hepatocellular carcinoma (HCC) is the fifth-most common cancer in the worldwide and due to its highly malignant nature, it has become the second leading cause of cancer death. There are several treatment available for the HCC, such as liver transplantation, hepatic resection, ablative therapies , transcatheter hepatic arterial chemoembolization (TACE) and molecular-targeted drugs in Internal Medicine. For the HCC within the Milan criteria, liver transplantation remains the recommended treatment of choice. Due to the suitable donors of liver transplantation are rare and liver transplantation requires high cost and waiting period, the application of liver transplantation is limited. Liver resection and radiofrequency ablation (RFA) should remain the first options for curative treatment of HCC. Especially in the treatment of small liver cancer, laparoscopic liver resection (LLR) not only has the advantages of quick recovery and less blood loss from minimally invasive surgery, but also can remove part of normal liver tissue which can reduce the impact of tumor microvascular infiltration. However, the existing research which comparing LLR and RFA in the treatment of small hepatocellular carcinoma have produced conflicting results.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 June 2020 and was last updated on 14 June 2020 (registration number INPLASY202060051).

INTRODUCTION

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METHODS

Participant or population: Inclusion criteria: (1)the inclusion patients should be diagnosed with hepatocellular carcinoma by American Association for the Study of Liver Diseases (AASLD) standard, and also confirm with Milan small hepatocellular carcinoma criteria(the diameter of single HCC nodule is smaller than 5 cm or up to 3 nodules that are each smaller than 3 cm in diameter) or the University of California, San Francisco (UCSF) criteria (the diameter of a single tumor smaller than 6.5 cm or up to 3 nodules that were each smaller than 4.5 cm in diameter) (2)published studies should comparing LLR and RFA(including percutaneous RFA and laparoscopic RFA) in smell hepatocellular carcinoma among adults (3) the type of studies was include Randomized Controlled Trials, Retrospective study, Non-randomized Controlled Trials (4)report at least one outcome indicator of interest and no other surgical procedures or anti-tumor treatment were performed (5)the highest quality and most complete study was included if one article was published on multiple journal. Exclusion criteria (1) the publication type was case report, review, meta-analysis, non-clinical study and letter (2) study with no available full-text or lack of interested long-term and recent outcomes.

Intervention: To compare the treatment of smell hepatocellular carcinoma with Laparoscopic liver resection and radiofrequency ablation.

Comparator: Two different radiofrequency ablation treatments were compared: percutaneous radiofrequency ablation (P-RFA) and laparoscopic radiofrequency ablation(L-RFA).

Study designs to be included: RCTs; prospective observational studies; retrospective observational studies.

Eligibility criteria: (a) Report at least one significant outcome indicator without any other surgical or antitumor treatment; (b) When an article is published in more than one journal, it includes the highest quality and most complete research. (c) No full text is available or studies with interesting long-term and recent results are lacking will be exclude.

Information sources: PubMed, Embase, Web of Science, MEDLINE, Cochrane Library, Scopus database and the China Biomedical Literature Database (CBM)

Main outcome(s): The interested long-term outcomes in this study were overall survival (OS)、disease-free survival (DFS) and local recurrence between the LLR and RFA groups. The recent outcomes of interest were operation time、blood loss、hospitalization duration and overall postoperative complications.

Additional outcome(s): None.

Data management: A systemic search was performed by two independent researchers by using PubMed、Embase、Web of Science、MEDLINE、Cochrane Library、Scopus database and the China Biomedical Literature Database (CBM) for those from inception to May 2019 without any other limits. The following medical subject headings (MeSH) terms include "Radiofrequency Ablation", "Laparoscopy", "Hepatectomy", "Carcinoma, Hepatocellular", "Small Hepatocellular Carcinoma". The MeSH terms and free text terms were utilized to locate articles, combined with the boolean operators AND/OR to made an appropriate search strategy. The results generated by the retrieval were export as bibliography import into NoteExpress (v3.2.0) for further comment, and the disagreement was decided by the third researcher. Then we extracted all the effect quantities of interest and made an Excel sheet.

Quality assessment / Risk of bias analysis: We will assess methodological quality, or risk of bias, for each individual study based on the Cochrane Risk of Bias tool for RCTs, and the Newcastle-Ottawa Scale for observational studies. (low risk)These studies had the least bias, and the results were considered valid. These studies adhered to the commonly held concepts of high quality, including the following: a clear description of the population, setting, approaches, and comparison groups; appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; a low dropout rate; and clear reporting of dropouts. (moderate risk)These studies were susceptible to some bias, but not enough to invalidate the results. They did not meet all the criteria required for a rating of good quality because they had some deficiencies, but no flaw was likely to cause major bias. The study may have been missing information, making it difficult to assess limitations and potential problems. (high risk)These studies had significant flaws that might have invalidated the results. They had serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.

Strategy of data synthesis: A systemic search was performed by two independent researchers by using PubMed, Embase, Web of Science, MEDLINE, Cochrane Library, Scopus database and the China Biomedical Literature Database (CBM) for those from inception to May 2019 without any other limits. The following medical subject headings (MeSH) terms include "Radiofrequency Ablation", "Laparoscopy", "Hepatectomy", "Carcinoma, Hepatocellular", "Small Hepatocellular Carcinoma". The MeSH terms and free text terms were utilized to locate articles, combined with the boolean operators AND/OR to made an appropriate search strategy. The results generated by the retrieval were export as bibliography import into NoteExpress (v3.2.0) for further comment, and the disagreement was decided by the third researcher. Then we extracted all the effect quantities of interest and made an Excel sheet. Calculation for time-to-event variables was carried out using the hazard ratios (HRs) and 95% confidence intervals (CIs). We calculated the mean differences (MDs) for continuous outcomes and risk ratios (RRs) with 95% confidence intervals (CIs). Engauge Digitizer (v10.8) and method described by Tierney will be used to estimate HR from the available statistic and Kaplan-Meier curves if the inclusion studies didn't provide HR. If the studies only provide medians and interquartile ranges rather than mean±standard deviation (SD), we will calculate mean±SD used the method by Wangand Luo.

Subgroup analysis: (a) Two different radiofrequency ablation treatments were compared: percutaneous radiofrequency ablation (P-RFA) and laparoscopic radiofrequency ablation(L-RFA) . (b) Whether the number of tumors is a single.

Sensibility analysis: One by one exclusion study was performed for sensitivity analysis.

Language: English.

Country(ies) involved: China.

Keywords: Small hepatocellular carcinoma; Laparoscopic liver resection; Radiofrequency ablation; Overall survival; Disease-free survival.

Contributions of each author:

Author 1 - Bo-Wen Xu - research design, literature retrieval, analyzing of data, drafting this manuscript and polishing it.
Author 2 - Jian-hua Chang - literature retrieval, analyzing of data.
Author 3 - Qiong Li - analyzing of data, revising it critically.
Author 4 - Yu-Xuan Zhao - analyzing of data, revising it critically.
Author 5 - Xu-Ting Zhi - research design; revising it critically, funding this manuscript, approving the submitted version.