# INPLASY PROTOCOL

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# Efficacy of anatomic versus nonanatomic hepatectomy in patients with BCLC A stage hepatocellular carcinoma: A systemic review and meta-analysis

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**Review question / Objective:** Hepatectomy is currently the main radical treatment for hepatocellular carcinoma. Hepatectomy includes anatomic and non-anatomic hepatectomy. Since hepatocellular carcinoma spreads in the liver along the portal vein system, anatomic hepatectomy following portal vein anatomy can theoretically remove the primary tumor and its peripheral tumor more thoroughly than non-anatomic hepatectomy. However, it remains controversial whether AR is better than NAR in patients with BCLCA stage hepatocellular carcinoma without large vessel invasion. Some reports have confirmed the survival advantage of AR, however, others studies have found no significant difference in HCC recurrence or overall survival rates between the two types of HCC after resection. This controversy has continued for many years, with no consensus yet. The objective of this meta-analysis was to clarify the efficacy of anatomic versus nonanatomic hepatectomy in patients with BCLC A stage hepatocellular carcinoma.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 September 2021 and was last updated on 06 September 2021 (registration number INPLASY202190018).

## INTRODUCTION

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than NAR in patients with BCLCA stage hepatocellular carcinoma without large vessel invasion. Some reports have confirmed the survival advantage of AR, however, others studies have found no significant difference in HCC recurrence or overall survival rates between the two types of HCC after resection. This controversy has continued for many years, with no consensus yet. The objective of this meta-analysis was to clarify the efficacy of anatomic versus nonanatomic hepatectomy in patients with BCLC A stage hepatocellular carcinoma.

**Condition being studied:** a) Some reports have confirmed the survival advantage of AR, but others studies have found no significant difference in HCC recurrence rate or overall survival rate between the two types of HCC after resection.This controversy has lasted for many years, and there has been no unified consensus so far. With the rapid development of precision medicine in recent years, more and more relevant articles have been published. b) Although there are a large number of relevant meta-analyses, they do not strictly limit the inclusion criteria, leading to other potential factors affecting the authenticity of the results. such as, biological characteristics of tumor, incidence of cirrhosis, hepatitis incidence, etc. c) In recent years, strict inclusion and exclusion criteria have been formulated in some studies that have issued, and population baselines have been corrected by PSM (Propensity Score Matching ), which greatly increases the reliability of studies.

## METHODS

**Participant or population:** BCLC A stage hepatocellular carcinoma.

**Intervention:** Anatomic resection, AR.

**Comparator:** Non-anatomic resection, NAR.

**Study designs to be included:** Randomized controlled trials and observational studies.

**Eligibility criteria:** a) Comparison of AR and NAR in HCC patients with single and no macrovascular invasion; b) Randomized controlled trials and observational studies; c) Language is English or Chinese; d) Reported 1 -, 3 -, and 5-year OS(overall survival) and DFS (disease-free survival).

**Information sources:** PubMed, Embase and Cochrane library.

**Main outcome(s):** 1year, 3year, 5year overall survival (OS), and 1year, 3year, 5year disease-free survival (DFS) rates.

**Quality assessment / Risk of bias analysis:** The quality of the included studies was assessed independently by two authors (S HX, D F) according to the Cochrane collaboration's tool for randomized controlled trials and the NOS for observational studies of propensity matched.

**Strategy of data synthesis:** Binary variables are synthesized by random effect model or fixed effect model via odds ratio(OR), continuous variables are synthesized by weighted mean difference or standardized mean difference. Quantitative analysis $I^2$ test is used for heterogeneity analysis. When $I^2$ is 0%, it is considered that there is no heterogeneity between studies, when $I^2<25\%$, there is mild heterogeneity between studies, when $25\%<I^2<50\%$,there is moderate heterogeneity between studies, and when $50\% <I^2<75\%$, it is considered that there is a high degree of heterogeneity between studies. In principle, meta analysis can be carried out only when there is no heterogeneity between the included studies, or when the heterogeneity is mild. If the homogeneity is low, we choose the fixed effect model; if the homogeneity is high, we choose the random effect model , or do not do meta analysis. Results will be assessed using forest plots and presented as ORs for the main outcome and secondary outcomes. When $I^2 50\%$, meta regression analysis and subgroup analysis can be used to deal with heterogeneity, or only descriptive evaluation can be made. Finally, the sensitivity analysis of the results will be

carried out to include and exclude those studies that are not sure whether they meet the inclusion criteria or not. If the influence analysis is carried out, the results do not change greatly, indicating that the results are more credible; on the contrary, if we get a large difference or even the opposite conclusion after exclusion, indicating that the feasibility of the results is low. we should be very careful in interpreting the results and drawing conclusions. Publication bias will be assessed by a funnel plot for meta-analysis and quantified by the Egger method. Statistical analysis will be conducted using R software for Windows v4.0 (R version 4.0.3 (2020-10-10) Copyright (C) 2020 The R Foundation for Statistical Computing. package = "meta").

**Subgroup analysis:** We will make a subgroup of Group of baseline with PSM.

**Sensitivity analysis:** Sensitivity analysis of the results will be carried out to include and exclude those studies that are not sure whether they meet the inclusion criteria or not. If the influence analysis is carried out, the results do not change greatly, indicating that the results are more credible; on the contrary, if we get a large difference or even the opposite conclusion after exclusion, indicating that the feasibility of the results is low.

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

**Keywords:** anatomic hepatectomy, nonanatomic hepatectomy, hepatocellular carcinoma.

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