

# INPLASY PROTOCOL

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**Review Stage at time of this submission:** The review has not yet started.

**Conflicts of interest:**  
None declared.

## Prognostic impact of margin width after R0 Hepatectomy in patients with early solitary hepatocellular carcinoma: A meta-analysis

Zhu, XY<sup>1</sup>; Yang, SZ<sup>2</sup>; Wang, S<sup>3</sup>; Shi, HX<sup>4</sup>.

**Review question / Objective:** Compared with narrow margin, wide margin can improve the clinical prognosis (RFS, OS) of patients with isolated hepatocellular carcinoma undergoing RO hepatectomy?

**Condition being studied:** R0 was any resection with a minimum 1 mm of negative margin, negative resection margin could really reduce the recurrence rate after liver resection. A number of articles found that a wide surgical Margin prolongs the prognosis of HCC patients compared to a narrower surgical margin, but still need to be considered the situation that the tumor is close to the large blood vessels and the remaining liver parenchyma is less, so that the technical operation is limited and there may be many ostoperative complications. In addition, there is little research on the hepatectomy type cutting edge width based on AR and NAR, and our research has made important explorations in these aspects.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 July 2022 and was last updated on 26 July 2022 (registration number INPLASY202270111).

### INTRODUCTION

**Review question / Objective:** Compared with narrow margin, wide margin can improve the clinical prognosis (RFS, OS) of patients with isolated hepatocellular carcinoma undergoing RO hepatectomy?

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## METHODS

### Search strategy:

PubMed: 486篇

("Carcinoma, Hepatocellular"[Mesh]) OR (((((((((((((((((((((((Carcinomas, Hepatocellular[Title]) OR (Hepatocellular Carcinomas[Title])) OR (Liver Cell Carcinoma, Adult[Title])) OR (Liver Cancer, Adult[Title])) OR (Adult Liver Cancer[Title])) OR (Adult Liver Cancers[Title])) OR (Cancer, Adult Liver[Title])) OR (Cancers, Adult Liver[Title])) OR (Liver Cancers, Adult[Title])) OR (Liver Cell Carcinoma[Title])) OR (Carcinoma, Liver Cell[Title])) OR (Carcinomas, Liver Cell[Title])) OR (Cell Carcinoma, Liver[Title])) OR (Cell Carcinomas, Liver[Title])) OR (Liver Cell Carcinomas[Title])) OR (Hepatocellular Carcinoma[Title])) OR (Hepatoma[Title])) OR (Hepatomas[Title]))) AND ("Margins of Excision"[Mesh]) OR (((((((((((((((((((((((Excision Margin\*[Title/Abstract]) OR (Excision Margins\*[Title/Abstract])) OR (Resection Margin\*[Title/Abstract])) OR (Margin, Resection\*[Title/Abstract])) OR (Margins, Resection\*[Title/Abstract])) OR (Resection Margins\*[Title/Abstract])) OR (Surgical Margins\*[Title/Abstract])) OR (Margin, Surgical\*[Title/Abstract])) OR (Margins, Surgical\*[Title/Abstract])) OR (Surgical Margin\*[Title/Abstract])) OR (Positive Surgical Margins\*[Title/Abstract])) OR (Positive Surgical Margin\*[Title/Abstract])) OR (Surgical Margin, Positive\*[Title/Abstract])) OR (Surgical Margins, Positive\*[Title/Abstract])) OR (Negative Surgical Margins\*[Title/Abstract])) OR (Negative Surgical Margin\*[Title/Abstract])) OR (Surgical Margin, Negative\*[Title/Abstract]))

OR (Surgical Margins, Negative\*[Title/Abstract])) OR (Tumor-Free Margins\*[Title/Abstract])) OR (Margin, Tumor-Free\*[Title/Abstract])) OR (Margins, Tumor-Free\*[Title/Abstract])) OR (Tumor Free Margins\*[Title/Abstract])) OR (Tumor-Free Margin\*[Title/Abstract])) AND (2000:2022[pdat])

Search strategy

Embase:177篇

#7 #3 AND #6

#6 #4 AND #5

#5 ('excision margin' OR (excision AND margin) OR 'excision margins':ti,ab,kw OR 'resection margin':ti,ab,kw OR 'margin, resection':ti,ab,kw OR 'margins, resection':ti,ab,kw OR 'resection margins':ti,ab,kw OR 'surgical margins':ti,ab,kw OR 'margin, surgical':ti,ab,kw OR 'margins, surgical':ti,ab,kw OR 'surgical margin':ti,ab,kw OR 'positive surgical margins':ti,ab,kw OR 'positive surgical margin':ti,ab,kw OR 'surgical margin, positive':ti,ab,kw OR 'surgical margins, positive':ti,ab,kw OR 'negative surgical margins':ti,ab,kw OR 'negative surgical margin':ti,ab,kw OR 'surgical margin, negative':ti,ab,kw OR 'surgical margins, negative':ti,ab,kw OR 'tumor-free margins':ti,ab,kw OR 'margin, tumor-free':ti,ab,kw OR 'tumor free margins':ti,ab,kw OR 'tumor-free margin':ti,ab,kw) AND [2000-2022]/py

#4 'surgical margin'/exp AND [2000-2022]/py

#3 #1 AND #2

#2 ('carcinomas, hepatocellular' OR (carcinomas, AND hepatocellular) OR 'hepatocellular carcinomas':ti OR 'liver cell carcinoma, adult':ti OR 'liver cancer, adult':ti OR 'adult liver cancer':ti OR 'adult liver cancers':ti OR 'cancer, adult liver':ti OR 'cancers, adult liver':ti OR 'liver cancers, adult':ti OR 'liver cell carcinoma':ti OR 'carcinoma, liver cell':ti OR 'carcinomas, liver cell':ti OR 'cell carcinoma, liver':ti OR 'cell carcinomas, liver':ti OR 'liver cell carcinomas':ti OR 'hepatocellular carcinoma':ti OR hepatoma:ti OR hepatomas:ti) AND [2000-2022]/py

#1 'liver cell carcinoma'/exp AND [2000-2022]/py

Search strategy

Cochrane:

54篇

(Carcinomas, Hepatocellular) OR (Hepatocellular Carcinomas) OR (Liver Cell Carcinoma, Adult) OR (Liver Cancer, Adult) OR (Adult Liver Cancer) OR (Adult Liver Cancers) OR (SCancer, Adult Liver) OR (Cancers, Adult Liver) OR (Liver Cancers, Adult) OR (Liver Cell Carcinoma) OR (Carcinoma, Liver Cell) OR (Carcinomas, Liver Cell) OR (Cell Carcinoma, Liver) OR (Cell Carcinomas, Liver) OR (Liver Cell Carcinomas) OR (Hepatocellular Carcinoma) OR (Hepatoma) OR (Hepatomas) in Record Title AND (Excision Margin\*) OR (Excision Margins\*) OR (Resection Margin\*) OR (Margin, Resection\*) OR (Margins, Resection\*) OR (Resection Margins\*) OR (Surgical Margins\*) OR (Margin, Surgical\*) OR (Margins, Surgical\*) OR (Surgical Margin\*) OR (Positive Surgical Margins\*) OR (Positive Surgical Margin\*) OR (Surgical Margin, Positive\*) OR (Surgical Margins, Positive\*) OR (Negative Surgical Margins\*) OR (Negative Surgical Margin\*) OR (Surgical Margin, Negative\*) OR (Surgical Margins, Negative\*) OR (Tumor-Free Margins\*) OR (Margin, Tumor-Free\*) OR (Margins, Tumor-Free\*) OR (Tumor Free Margins\*) OR (Tumor-Free Margin\*) in Title Abstract Keyword - with Cochrane Library publication date Between Jan 2000 and Mar 2022 (Word variations have been searched).

**Participant or population:** Patients with early solitary hepatocellular carcinoma (HCC) who after R0 hepatectomy did not receive any adjuvant therapy before operation and had nolarge blood vessels tumor invasion.

**Intervention:** A wide surgical margin ( $\geq 1$  cm) and a narrow surgical margin ( $< 1$  cm).

**Comparator:** Wide margin ( $\geq 1$ cm) and narrow margin ( $< 1$ cm) on postoperative recurrence-free survival (RFS) and overall survival (OS) of patients with early solitary

hepatocellular carcinoma who after R0 hepatectomy.

**Study designs to be included:** In anatomical hepatectomy group and non-anatomical hepatectomy group, the surgical margin was divided into wide surgical margin group ( $\geq 1$ cm) and narrow surgical margin group ( $< 1$ cm). The differences of treatment strategies and prognosis (OS and RFS) were compared. According to the size of the tumor and MVI of the tumor, the surgical margin was wide surgical margin group ( $\geq 1$ cm) and narrow surgical margin group ( $< 1$ cm). The differences of the two treatment strategies and prognosis (OS and RFS) were compared.

**Eligibility criteria:** Exclude studies that lack original data, duplicate data, data that cannot be analyzed or non-human data, as well as non-observational studies, studies that exclude non-primary hepatocellular carcinoma (HCC), R1/R2 hepatectomy, multiple tumors and/or macroscopic vascular invasion.

**Information sources:** Embase、PubMed and Cochrane Library Database.

**Main outcome(s):** Main outcome is survival outcome, that is, recurrence-free survival rate (RFS) and overall survival rate (OS).

**Additional outcome(s):** Secondary results are recurrence, that is, time recurrence rate and recurrence pattern.

**Quality assessment / Risk of bias analysis:** The Newcastle-Ottawa Scale (NOS) was used to evaluate the quality and bias risk.

**Strategy of data synthesis:** RevMan 5.4 software estimates the relative risk (RR) and 95% confidence interval (CI), and evaluates the heterogeneity among the studies by forest map and I2 value.

**Subgroup analysis:** Tumor characteristics (MVI) were analyzed in subgroups, and the type of hepatectomy (AR and NAR) was also analyzed in subgroups.

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**Sensitivity analysis:** Delete the literature that leads to the obvious increase of heterogeneity, and the heterogeneity will be significantly reduced. The fixed effect model will be preferred to combine the effect quantity, while the random effect model will be used if the heterogeneity is still slightly larger.

**Language restriction:** None.

**Country(ies) involved:** China/Qinghai University.

**Keywords:** hepatocellular carcinoma; surgical margin; R0 Hepatectomy; microvascular invasion; prognostic.

**Contributions of each author:**

**Author 1 - zhu xiaoying -** Propose research ideas, Prepare the first draft, collect and organize data.

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**Author 2 - yang shizhong -** set overall research goals, and oversee and lead the planning and execution of research activities.

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**Author 3 - wang su -** Enabled the development of selection criteria, and risk of bias assessment strategies to validate the conclusions and other elements of the research findings as a whole.

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**Author 4 - shi hengxin -** Provided statistical expertise, read, provided feedback and approved the final manuscript.

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