# INPLASY PROTOCOL

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Corresponding author: Lingkai Zhang

ekko2731@foxmail.com

# **Author Affiliation:**

Graduate School of Qinghai University.

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# No-touch versus conventional radiofrequency ablation prognosis for hepatocellular carcinoma below 5cm: a systematic review and meta-analysis

Zhang, LK<sup>1</sup>; Du, F<sup>2</sup>; Ren, L<sup>3</sup>.

Review question / Objective: The purpose of this study was to systematically evaluate the prognosis of no-touch radiofrequency ablation (NT-RFA) and conventional radiofrequency ablation (RFA) for hepatocellular carcinoma (HCC) less than 5cm.

Eligibility criteria: Literature inclusion criteria: (1) Study type: Randomized controlled trials (RCTs), clinical controlled trials, uncontrolled prospective trials, prospective observational studies, and retrospective studies; (2) Subjects: HCC patients over 18 years old were included, regardless of gender, race and etiology; (3) Intervention measures: No-touch radiofrequency ablation and radiofrequency ablation; (4) The included patients were diagnosed as hepatocellular carcinoma according to imaging or clinical criteria, with Child-Pugh grade A or B, whose tumor diameter was smaller than 5cm. (5) The study reported LTP or OS or complications. Exclusion criteria: (1) Reviews, comments, letters and case reports; (2) No-English literature, duplicate publications or conference abstracts; (3) Single-arm study on no-touch ablation; (4) Studies on animals.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 July 2022 and was last updated on 24 July 2022 (registration number INPLASY202270104).

# INTRODUCTION

**Review question / Objective:** The purpose of this study was to systematically evaluate the prognosis of no-touch radiofrequency ablation (NT-RFA) and conventional radiofrequency ablation (RFA) for hepatocellular carcinoma (HCC) less than 5cm. **Condition being studied:** Early-stage hepatocellular carcinoma (HCC) is considered a curable stage of HCC, and timely treatment and effective intervention for patients who with this disease can improve the survival and prognosis of HCC patients. At present, the first-line treatment of early-stage HCC recommended by major liver associations in the world includes hepatectomy, liver transplantation, microwave ablation (MWA) and radiofrequency ablation (RFA). Although surgical resection is still the main choice for the treatment of early-stage HCC patients, ablation is recommended when patients cannot undergo hepatectomy. RFA is widely used all over the world because of its low invasion, security, economy and effectiveness. Traditional intratumoral monopolar RFA can only produce limited necrotic areas, and even if ablation areas overlap, it will lead to uneven tumor necrosis . Therefore, local tumor progression (LTP) is often caused by incomplete ablation or satellite nodules . A retrospective study by Kim et al. showed that after using RFA to treat HCC, the cumulative incidence of LTP in 5 years was as high as 27%. In order to avoid the above problems, some scholars try to use non-touch radiofrequency ablation (NT-RFA) technology to further improve the local curative effect. In NT-RFA, multiple electrodes are inserted outside the tumor and then activated sequentially to form an ablation zone. This technique makes the tumor itself inviolable and reduces the incidence of LTP. A randomized clinical trial by Park et al. indicated that the cumulative incidence of LTP in the NT-RFA group was significantly lower than the traditional RFA group, and NT-RFA was the only predictor of LTP in multivariate analysis. Based on the results, Park et al. believe that NT-RFA is a more beneficial treatment option for patients with liver cancer. As far as we know, there is no systematic meta-analysis to compare the effects of NT-RFA and traditional RFA on the cumulative incidence of LTP, OS and complications in patients. The purpose of this study was to compare the prognosis of patients with early-stage HCC treated by two ablation techniques.

# **METHODS**

Participant or population: HCC patients over 18 years old were included, regardless of gender, race and etiology.

Intervention: Non-touch radiofrequency ablation.

**Comparator:** conventional radiofrequency ablation.

Study designs to be included: Randomized controlled trials (RCTs), clinical controlled trials, uncontrolled prospective trials, prospective observational studies, and retrospective studies.

Eligibility criteria: Literature inclusion criteria: (1) Study type: Randomized controlled trials (RCTs), clinical controlled trials, uncontrolled prospective trials, prospective observational studies, and retrospective studies; (2) Subjects: HCC patients over 18 years old were included, regardless of gender, race and etiology; (3) Intervention measures: No-touch radiofrequency ablation and radiofrequency ablation; (4) The included patients were diagnosed as hepatocellular carcinoma according to imaging or clinical criteria, with Child-Pugh grade A or B, whose tumor diameter was smaller than 5cm. (5) The study reported LTP or OS or complications. Exclusion criteria: (1) Reviews, comments, letters and case reports; (2) No-English literature, duplicate publications or conference abstracts; (3) Single-arm study on no-touch ablation; (4) Studies on animals.

Information sources: PubMed, Cochrane Library and Embase databases.

Main outcome(s): Local tumor progression.

Additional outcome(s): Overall survival and complications.

Quality assessment / Risk of bias analysis: The data were extracted from the included literature using a pre-developed data extraction form, which included basic information about the included studies (Author, age, sample size, demographic characteristics, laboratory tests, tumor characteristics), outcome (LTP, OS and complications) and assessment of the risk of bias. Finally, the two researchers reviewed the data and any differences were resolved through discussion. Evaluate the quality of the studies on the basis of the Newcastle-Ottawa scale. Strategy of data synthesis: In our study, due to the limitation of the number of studies included, we are unable to evaluate publication bias and meta regression to determine the source of heterogeneity when the heterogeneity is high. R 4.0.3 ("metafor" package) were used for the statistical analyses.

#### Subgroup analysis: None.

Sensitivity analysis: We assessed the heterogeneity of the included studies using I2, and if I2 was  $\leq$ 50%, a meta-analysis with a fixed effects model was applied. If 50% $\leq$  I2 $\leq$ 100%, a meta-analysis with a random effects model was applied.

Language: English.

Country(ies) involved: China.

Keywords: no-touch radiofrequency ablation, conventional radiofrequency ablation, hepatocellular carcinoma, prognosis.

# Contributions of each author:

Author 1 - Lingkai Zhang. Email: ekko2731@foxmail.com Author 2 - Du Fei. Author 3 - Li Ren. Email: renli xn@163.com