## INPLASY PROTOCOL

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Review question / Objective: Since the first clinical study in 1995, the clinical application of percutaneous radiofrequency ablation (RFA) for early-stage hepatocellular carcinoma (HCC) has been expanding. Currently, RFA and surgical resection are recognized as a treatment method for early-stage HCC, and RFA has been widely used as a minimally invasive method for treating early-stage HCC. Many studies have proven that RFA is as effective as surgery in treating early stage HCC. In addition, thermal ablation is a radical treatment for small HCC in addition to hepatectomy, and RFA is the first-line treatment for this technique, which is recommended by every liver research association. In prospective studies of Milan criteria-eligible patients with HCC receiving unipolar RFA as the only first-line therapy, three-year local tumor progression of 8%-26% has been reported. A new No-touch RFA (NTRFA) technique has been gaining attention in recent years for its advanced concept, which overcomes the shortcomings of conventional RFA and provides a greater range and volume of necrosis. Although many studies have provided encouraging results, studies on the prognosis and complications of NTRFA for HCC remain scarce. In this study, we performed a single-arm meta-analysis to determine the pooled proportion of local tumor progression-free survival, recurrence-free survival, overall survival, and adverse events for NTRFA in patients with small HCC in order to provide a reliable pooled proportion for subsequent studies.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 July 2022 and was last updated on 23 July 2022 (registration number INPLASY202270101).

## **INTRODUCTION**

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studies have proven that RFA is as effective as surgery in treating early stage HCC. In addition, thermal ablation is a radical treatment for small HCC in addition to hepatectomy, and RFA is the first-line treatment for this technique, which is recommended by every liver research association. In prospective studies of Milan criteria-eligible patients with HCC receiving unipolar RFA as the only first-line therapy, three-vear local tumor progression of 8%-26% has been reported. A new Notouch RFA (NTRFA) technique has been gaining attention in recent years for its advanced concept, which overcomes the shortcomings of conventional RFA and provides a greater range and volume of necrosis. Although many studies have provided encouraging results, studies on the prognosis and complications of NTRFA for HCC remain scarce. In this study, we performed a single-arm meta-analysis to determine the pooled proportion of local tumor progression-free survival, recurrence-free survival, overall survival, and adverse events for NTRFA in patients with small HCC in order to provide a reliable pooled proportion for subsequent studies.

**Condition being studied: Literature** inclusion criteria: (1) study type: randomized controlled trials (RCTs), clinical controlled trials, uncontrolled prospective trials, prospective observational studies, and retrospective studies; (2) subjects: patients aged 18 years or older with hepatocellular carcinoma less than 5 cm treated with no-touch radiofrequency ablation, regardless of sex, race, or etiology; (3) interventions: no-touch radiofrequency ablation ; (4) the article reported the outcome indicators. Literature exclusion criteria (1) other study types such as reviews and case reports; (2) non-English literature, duplicate publications or conference abstracts; (3) animal studies.

## **METHODS**

Participant or population: patients aged 18 years or older with hepatocellular carcinoma less than 5 cm treated with no-

touch radiofrequency ablation, regardless of sex, race, or etiology.

Intervention: No-touch radiofrequency ablation.

Comparator: None.

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

**Eligibility criteria:** (1) other study types such as reviews and case reports; (2) non-English literature, duplicate publications or conference abstracts; (3) animal studies.

Information sources: Pubmed, enbase, Cochrane Library.

Main outcome(s): The primary outcome was Local tumor progression-free survival, and the secondary outcomes were RFS, OS, and adverse events.

Quality assessment / Risk of bias analysis: Since only single-group studies were included in the literature search, the JBI critical appraisal quality assessment of the cage selles study was used as a quality assessment tool.

Strategy of data synthesis: Where possible and appropriate, we performed metaanalyses of quantitative and qualitative data using windows R4.0.1. The combined proportions were calculated using the 'meta' package. We used a random effects model because the clinical and methodological aspects are likely to be different between these studies. The I2 statistic was used to assess heterogeneity between effect sizes for individual studies and was defined as low (25-50%), medium (50-75%), or high (>75%). If a meta-analysis of the results was not possible, we described the results qualitatively.

## Subgroup analysis: None.

**Sensitivity analysis:** To address the impact on effect estimates, we tested the results by performing sensitivity analyses.

Language: English.

Country(ies) involved: China.

Other relevant information: None.

Keywords: Hepatocellular carcinoma,Notouch Radiofrequency ablation, Local tumor progression-free survival.

Contributions of each author: Author 1 - Fei Du. Author 2 - Li Ren.