Repeat hepatic resection versus percutaneous ablation for the treatment of recurrent hepatocellular carcinoma: meta-analysis

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Abstract

Background: The efficacy of repeat hepatic resection (rHR) in the treatment of recurrent hepatocellular carcinoma compared with radiofrequency or microwave ablation after resection of the primary tumour remains controversial. A systematic review and meta-analysis were performed to compare the safety and efficacy of these procedures.

Methods: PubMed, Embase, Scopus, Cochrane Library, and China National Knowledge Infrastructure databases were systematically searched to identify related studies published before 10 October 2021. Overall and recurrence-free survival after different treatments were compared based on pooled hazard ratios with a random-effects model.

Results: Two randomized clinical trials and 28 observational studies were included, involving 1961 and 2787 patients who underwent rHR and ablation respectively. Median perioperative mortality in both groups was zero but patients in the rHR group had higher median morbidity rates (17.0 per cent) than those in the ablation group (3.3 per cent). rHR achieved significantly longer recurrence-free survival than ablation (HR 0.79, 95 per cent c.i. 0.70 to 0.89, P < 0.001), while both groups had similar overall survival (HR 0.93, 95 per cent c.i. 0.83 to 1.04, P = 0.18).

Conclusion: rHR and ablation based on radio- or microwaves are associated with similar overall survival in patients with recurrent hepatocellular carcinoma after resection of the primary tumour.

Introduction

Hepatic resection and radiofrequency or microwave ablation are commonly used to treat patients with hepatocellular carcinoma (HCC) satisfying the Milan criteria (single nodule 5 cm or less, or up to three nodules less than 3 cm each, and no macrovascular invasion or distant metastasis)1–3. The 5-year recurrence rate is as high as 49–60 per cent among patients with early-stage HCC4–6. Given that HCC recurrence remains the leading cause of HCC-related deaths7, more effective treatment strategies are needed for recurrent HCC. Common therapies include repeat hepatic resection (rHR), radiofrequency or microwave ablation, liver transplantation, transarterial chemoembolization (TACE), radiotherapy, and administration of tyrosine kinase inhibitors. Although there are no definitive recommendations for the treatment of recurrent HCC7–9, rHR, ablation, and liver transplantation are considered the main curative approaches. The clinical application of liver transplantation is limited due to strict indications, lack of donors, and high treatment costs. In addition, meta-analyses on the safety and efficacy of rHR and ablation in patients with recurrent HCC within or beyond Milan criteria have provided conflicting conclusions10–13. In the present study, an updated systematic review with meta-analysis was performed to make recent comparisons of the safety and efficacy of rHR and microwave or radiofrequency ablation to treat recurrent HCC.

Methods

Study search

This meta-analysis was conducted according to the PRISMA Guidelines (Supplementary Material)14. A systematic search of PubMed, Embase, Scopus, Cochrane Library, and China National Knowledge Infrastructure databases was performed by two independent reviewers to retrieve articles published before 15 April 2021 using the following keywords: ‘hepatocellular carcinoma’ AND (‘recurrence’ OR ‘recurrent’) AND (‘repeat hepatectomy’ OR ‘repeat hepatic resection’, OR ‘re-hepatectomy’) AND ‘ablation’. The same search was repeated in October 2021 to identify studies published between 15 April and 10 October 2021. The search results were screened based on titles and abstracts, and appropriate articles were selected based on inclusion and exclusion criteria (see following section). The reference lists of relevant publications were also reviewed manually to identify additional potentially relevant articles.

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Inclusion and exclusion criteria
To be eligible for inclusion, studies had to involve patients with recurrent HCC after curative resection, followed by treatment with rHR, involving microwave ablation or radiofrequency ablation; compare the safety and/or efficacy of ablation and rHR for recurrent HCC, involve patients with recurrent HCC without macrovascular invasion or extrahepatic metastasis; and report one or more of the target outcomes of overall survival (OS), recurrence-free survival (RFS), or perioperative morbidity, or mortality. Eligible studies were included in the present meta-analysis even if patients received TACE or other treatments after rHR or ablation. In the case of studies with overlapping patient samples, only the largest study was included.

Exclusion criteria included studies comparing hepatectomy and ablation for primary or metastatic liver cancer; single-arm studies or studies where each treatment arm contained fewer than 10 patients; and studies in which patients received other therapies, such as TACE, radiotherapy, or tyrosine kinase inhibitors after HCC recurrence and before rHR or ablation.

Quality assessment and data extraction
The eligibility of the included studies was assessed before data extraction. The quality of the randomized and non-randomized clinical trials (RCTs) was assessed, by use of the Cochrane Handbook for Systematic Evaluation of Interventions or the Newcastle–Ottawa Scale15. The following data were extracted independently by the two reviewers: first author name, sample size, age, sex, number and size of recurrent tumours, time to first recurrence, presence of liver cirrhosis, follow-up interval, perioperative morbidity, and mortality, as well as OS, RFS, and their hazard ratios (HRs). Disagreements were resolved by discussion or assessment by a third author.

Primary and secondary outcomes
The primary outcome was OS, defined as the interval from rHR or ablation to treat recurrent HCC until death from any cause or until last follow-up. Secondary outcomes were perioperative mortality or morbidity and RFS, which was defined as the interval from rHR or ablation to treat recurrent HCC until HCC re-recurrence or death.

Statistical analysis
Meta-analysis was performed with Review Manager version 5.3 (Cochrane Collaboration, Oxford, UK). Continuous data were reported as medians and quartiles, while differences between the two treatment groups were assessed for significance with the Mann–Whitney U test. Statistical heterogeneity was assessed with the $I^2$ test. OS and RFS between the two groups were compared based on pooled HRs calculated with a random-effects model. Differences with $P<0.05$ were considered statistically significant. Whenever possible, unadjusted, or adjusted HRs were extracted from the original text of each study or estimated from Kaplan–Meier curves as described16. If both unadjusted and adjusted HRs were reported, the adjusted ratios were used. Median OS and RFS at 1, 3, and 5 years were estimated with bubble charts, where the size of each bubble represented the sample size of the given study17. The impact of individual studies on aggregate estimates was assessed through sensitivity analysis, in which the analysis was repeated after removing one study at a time. Funnel plots were also used to identify potential publication bias.

Results
Study selection
After searching the indicated databases, a total of 767 studies were identified as potentially eligible, of which 185 were duplicates. Of the remaining 582 studies, 540 were excluded based on review of titles and abstracts, leaving 42 for full-text review. Of these 42 studies, 27 met the inclusion criteria and the rest were excluded due to duplicate publication or because they were single-arm studies, studies where each treatment arm contained fewer than 10 patients, studies with no outcome data, or studies on patients with recurrent HCC with macrovascular invasion. Two of the 27 selected studies were RCTs18,19 and 25 were observational comparisons20–44. Three additional studies were identified during the repeat literature search45–47. Overall, 30 studies were included in the meta-analysis (Fig. 1).

Characteristics of included studies
One of the selected studies was conducted in Germany23 and the rest in China, Japan, Taiwan, Hong Kong, and Singapore18–22,24–47. Data were collected from 4748 patients, of whom 1961 were treated with rHR and 2787 with ablation (Table 1). Only one study involving 66 patients reported the use of microwave ablation43, whereas the remaining 26 applied radiofrequency ablation18–42,44–47. According to the Cochrane Handbook for Systematic Evaluation of Interventions, both RCTs were of high quality (Table S1). The Newcastle–Ottawa Scale score was above 5 for all non-RCTs, indicating acceptable quality (Table S2).

Perioperative morbidity and mortality
Perioperative morbidity rates were reported in 18 studies18–20,22–24,27,30–33,35,36,40,42,44–46. Median morbidity rate was higher in the rHR group (17.0 per cent, range 5.5–88.2 per cent) than in the ablation group (3.3 per cent, range 0–36.3 per cent). Common morbidities in the rHR group included hepatic insufficiency, pleural effusion, ascites, and biliary fistula, whereas bile leakage and abdominal haemorrhage were the most frequent morbidities in the ablation group. Perioperative mortality rates were reported in 21 studies18–24,28,27,30–33,35,36,40–44 and no significant differences were observed in the median mortality rate between the rHR group (0 per cent, range 0–2.9 per cent) and the ablation group (0 per cent, range 0–2.1 per cent) (Table S3).

OS and RFS
HRs of OS was extracted from 20 studies. Patients in the rHR and ablation groups had similar OS (HRs 0.93, 95 per cent c.i. 0.83 to 1.04, $P=0.18$ (Fig. 2) and median OS rates at 1 year (92.3 per cent versus 92.1 per cent), 3 years (67.7 per cent versus 72.3 per cent), and 5 years (51.5 per cent versus 52.9 per cent; Fig. 3a). HRs of RFS was extracted from 17 studies. Patients in the rHR group had significantly higher RFS (HRs 0.79, 95 per cent c.i. 0.70 to 0.89, $P<0.001$ (Fig. 4) as well as higher median RFS rates at 1 year (68.3 per cent versus 63.3 per cent), 3 years (48.1 per cent versus 35.2 per cent), and 5 years (36.2 per cent versus 23.0 per cent) (Fig. 3b).

Sensitivity analysis and publication bias
Sensitivity analysis showed that excluding any one of the studies, including the one reporting microwave ablation43 did not significantly affect the pooled results (Figs S1 and S2). Similar results were obtained when all studies were meta-analysed with a random- or fixed-effect model. However, visual inspection of
### Study or subgroup  | log (Hazard ratio) | Standard error | Weight (%) | Hazard ratio IV, Random, 95% c.i. | Hazard ratio IV, Random, 95% c.i.  
--- | --- | --- | --- | --- | ---  
Chan et al.  | -0.2107 | 0.2887 | 4.0 | 0.81 (0.48, 1.43) |  
Chen et al.  | -0.1393 | 0.2725 | 4.4 | 0.87 (0.51, 1.48) |  
Chen et al.  | 0.298 | 0.263 | 4.8 | 1.35 (0.80, 2.26) |  
Chua et al.  | -0.478 | 0.3065 | 3.5 | 0.62 (0.34, 1.13) |  
Eisele et al.  | -0.1625 | 0.336 | 2.9 | 0.85 (0.44, 1.64) |  
Feng et al.  | 0.293 | 0.283 | 4.1 | 1.34 (0.77, 2.33) |  
Ho et al.  | 0.2469 | 0.4218 | 1.9 | 1.28 (0.56, 2.93) |  
Liang et al.  | 0.0677 | 0.2465 | 5.4 | 1.07 (0.66, 1.73) |  
Liu et al.  | -0.5447 | 0.5694 | 1.0 | 0.58 (0.19, 1.77) |  
Matsumoto et al.  | -0.4943 | 0.7509 | 0.6 | 0.61 (0.14, 2.66) |  
Peng et al.  | 0.0296 | 0.1827 | 9.9 | 1.03 (0.72, 1.47) |  
Ren et al.  | -0.1054 | 0.2702 | 4.5 | 0.90 (0.53, 1.53) |  
Song et al.  | -0.117 | 0.417 | 1.9 | 0.89 (0.39, 2.01) |  
Sun et al.  | -0.057 | 0.529 | 1.2 | 0.94 (0.33, 2.66) |  
Umeda et al.  | -0.844 | 0.5725 | 1.0 | 0.43 (0.14, 1.32) |  
Wang et al.  | -0.3711 | 0.1959 | 8.6 | 0.69 (0.47, 1.01) |  
Wei et al.  | 0.4318 | 0.4809 | 1.4 | 1.54 (0.60, 3.95) |  
Xia et al.  | -0.231 | 0.171 | 11.3 | 0.79 (0.57, 1.11) |  
Zhang et al.  | -0.3285 | 0.4467 | 1.7 | 0.72 (0.30, 1.73) |  
Zhong et al.  | 0.01 | 0.1126 | 26.0 | 1.01 (0.81, 1.26) |  
Total (95% c.i.)  | 100.0 | 0.93 (0.83, 1.04) |  
Heterogeneity: $t^2 = 0.00$; $\chi^2 = 14.96$, 19 d.f., $P = 0.73$; $I^2 = 0%$  
Test for overall effect: $Z = 1.35$, $P = 0.18$  

**Fig. 1 Flow diagram of selected studies for meta-analysis**  
Based on the PRISMA Guidelines.

**Fig. 2 Forest plot comparing overall survival after repeat hepatic resection or ablation**  
Meta-analysis was conducted using a random-effects model. HRs are shown with 95% confidence intervals (95% c.i.). $P = 0.25$. 

**AdditionalNote:**
- **Records identified by searching relevant databases** $n = 769$
- **Records obtained by examining other sources** $n = 6$
- **Records screened** $n = 588$
- **Records excluded** $n = 543$
- **Studies included in qualitative synthesis** $n = 30$
- **Studies included in meta-analysis** $n = 30$
- **Full-text studies excluded** $n = 15$:  
  - Single arm $n = 7$
  - Without outcome data $n = 2$
  - Sample smaller than 10 $n = 4$
  - Duplicate publication $n = 1$
  - Macrovascular invasion $n = 1$
Table 1 Characteristics of included studies

| Studies and country/region | Groups | Sample size | Age*, year | Solitary/multiple tumour | Recurrent tumour size, cm | Time to first recurrence, months* | Cirrhosis, n (%) | Follow-up months* |
|---------------------------|--------|-------------|------------|--------------------------|----------------------------|-----------------------------------|----------------|------------------|
| Chan et al. 20, Hong Kong | rHR    | 29          | 52         | 21/8                     | 2.1 (0.8–5.5)              | 12.2                              | 25 (86.2)       | 44.9             |
| Chen et al. 21, China     | rHR    | 48          | 73.5       | 28/20                    | 2.6 ± 1.135                | -                                 | 41 (85.4)       | 36.9 (2–78)      |
| Chen et al. 22, Germany   | Ablation | 57         | 73.7       | 30/27                    | 2.5 ± 1.12                 | -                                 | 49 (88.0)       | 37.3 (2–78)      |
| Eisele et al. 23, Japan   | rHR    | 77          | ≤60 (67)   | 10  | ≤3 (39)                   | 20                              | 57 (74)          | 57 (2–168)       |
| Eisele et al. 24, China   | rHR    | 82          | ≤60 (61)   | 10  | ≤3 (77)                   | 9                               | 50 (61)          | 51 (4–111)       |
| Feng et al. 25, China     | rHR    | 99          | 56.0       | 75/24                    | 3.0 (2.5–4.0)              | >1 year (79)                   | 60 (60.6)       | -                |
| Hirokawa et al. 26, Japan | rHR    | 10          | 69         | 7/3                      | 1.9 ± 0.7                  | 22.8                             | 3 (50)          | -                |
| Ho et al. 27, Taiwan      | rHR    | 21          | 67         | 16/5                     | 1.7 ± 0.6                  | 7.6                               | 8 (38)          | -                |
| Huang et al. 28, China    | rHR    | 54          | 56.3       | -                        | 2.9 ± 1.8                  | 23.9                             | 26 (48.1)       | 32 (0–79)        |
| Kawano et al. 29, Japan   | rHR    | 50          | 61.0       | -                        | 2.3 ± 1.9                  | 20.0                             | 28 (56.0)       | 27 (0–96)        |
| Kim et al. 30, Korea      | rHR    | 45          | 53         | 45/0                     | 2.0 (0.7–4.6)              | 22                               | -               | 64 (4–113)       |
| Liang et al. 31, China    | rHR    | 44          | 48.8       | 34/10                    | ≤3 (26)                    | -                                 | 33.5 ± 24.1     | -                |
| Liu et al. 32, China      | rHR    | 39          | 50.0       | 37/2                     | 2.09 ± 0.68                | 33.4                             | 37 (94.9)       | 24               |
| Lu et al. 33, China       | rHR    | 41          | 48.9       | 39/2                     | 1.82 ± 0.82                | 21.9                             | 39 (95.1)       | 24               |
| Peng et al. 34, China     | rHR    | 194         | 52.9       | 162/22                   | 1.9 ± 0.9                  | >2 years (84)                  | 96 (69.6)       | 37.6             |
| Ren et al. 35, China      | rHR    | 145         | 51         | 127/18                   | 2.0                      | ≤2 years (71)                 | 23 (3–88)       | -                |
| Saito et al. 36, Japan    | rHR    | 68          | 52         | 52/16                    | 2.0                      | ≤2 years (37)                 | 23 (3–88)       | -                |
| Song et al. 37, Korea     | rHR    | 39          | 52.5       | 32/7                     | 2.2 ± 1.1                  | 20.9                             | 23 (59)         | 36.3 (0.8–126.6) |
| Sun et al. 38, Taiwan     | rHR    | 178         | 55.4       | 156/22                   | 1.7 ± 0.6                  | 18.0                             | 130 (73.0)      | 44.7 (5.6–139.8) |
| Umeda et al. 39, Japan    | rHR    | 29          | &ge;65 (16) | -                        | 3.2 ± 0.57                | 21.2                             | -               | 48               |
| Wang et al. 40, China     | rHR    | 128         | 50.2       | 89/39                    | 2.4 ± 0.9                  | 15.1                             | 66 (51.6)       | -                |
| Xia et al. 41, China      | rHR    | 120         | 52.4       | 96/24                    | 2.9 (1.0–5.0)              | 29.5                             | 50 (41.7)       | 44.3 (4–90.6)    |
| Xiao et al. 42, China     | rHR    | 39          | ≤60 (8)    | 5/6                      | ≤5 (8)                    | ≥1 year (8)                    | -               | -                |
| Yan at al. 43, China      | rHR    | 24          | ≤60 (19)   | 11/13                    | ≤5 (23)                   | ≥1 year (23)                   | -               | -                |
| Zhang et al. 44, China    | rHR    | 22          | 68.4       | 15/7                     | 3.9 ± 0.6                  | 11.4                             | 11 (50)         | -                |
| Zhang et al. 45, China    | rHR    | 57          | 57         | 52/5                     | 3.2                      | 29                               | 39 (68.4)       | 35 (6–60)        |
| Zhang et al. 46, China    | rHR    | 51          | 60         | 48/3                     | 2.6                      | 24                               | 30 (58.8)       | 37 (7–60)        |
| Zhang et al. 47, China    | rHR    | 59          | -          | 21                       | 3.5                      | 14                               | 61 (88.4)       | -                |
| Zhang et al. 48, China    | rHR    | 27          | 47         | 25/2                     | 3.2 ± 1.1                  | 26                               | 35 (91.7)       | 32 (9–118)       |
| Zhong et al. 49, China    | rHR    | 39          | 52         | 37/2                     | 2.7 ± 1.1                  | 30                               | -               | 28 (2–79)        |
| Chua et al. 50, Singapore | rHR    | 307         | 53.2       | 229/78                   | ≥3 (172)                  | ≤1 year (80)                    | 180 (58.6)      | 54 (1–178)       |
| Wei et al. 51, China      | rHR    | 127         | 63         | 92/35                    | 3.2 (2.2–4.5)              | 28.0                             | 48 (52.2)       | -                |
| Matsumoto et al. 52, Japan| rHR    | 23          | 66         | 19/4                     | 3.2 (0.9–10.5)             | -                                | 16 (69.6)       | 43.2 (1–150)     |

*Mean or median. -, not reported; F, female; M, male; rHR, repeat hepatic resection.
funnel plots suggested the possibility of publication bias (Figs. S3 and S4).

**Discussion**

Postoperative tumour recurrence is the most important factor affecting the long-term survival of patients with HCC after hepatic resection. Previous studies have shown that rHR and ablation are the most effective methods for treating recurrent HCC, although the 5-year re-recurrence rate remains high. In the present meta-analysis, safety, and efficacy of rHR and ablation were compared using a larger sample than in previous studies. Both therapeutic approaches provided similar OS, but rHR was associated with longer RFS at the expense of higher perioperative morbidity.

Earlier meta-analyses involving studies with small samples indicated that radiofrequency and microwave ablation have similar efficacy for primary untreated HCC, suggesting that these two percutaneous techniques could be aggregated in the present analysis. Of the 30 studies selected, only 14 compared the efficacy of microwave ablation and rHR reporting similar OS, but slightly higher RFS for rHR.

The present results are consistent with the findings of previous meta-analyses, but show higher median 5-year OS (50 per cent) after both treatments than previously reported (35.2 per cent and 48.3 per cent for rHR and for ablation respectively). Four small meta-analyses concluded that rHR was associated with better OS than ablation, whereas another study reported similar RFS for the two treatments. This discrepancy may be explained by the smaller sample size of previous studies.
A recent meta-analysis of 7 RCTs and 18 matched non-RCTs concluded that hepatic resection and radiofrequency ablation were associated with similar OS for patients with primary untreated HCC satisfying the Milan criteria, but that hepatic resection may be associated with better RFS and lower rate of local recurrence\(^1\). Consistent with these results, in this meta-analysis both treatments achieved similar 1-, 3-, and 5-year OS in patients with recurrent HCC, whereas rHR was associated with considerably higher RFS. In previous studies, 14.9 per cent of patients with HCC showed insufficient margins\(^9\) and shorter time to recurrence after ablation\(^19,44\). The significant difference in RFS between the two treatment groups in the present meta-analysis might be explained by incomplete ablation. In contrast, the similar OS values might reflect the fact that some patients received one or more additional treatments after tumour recurrence or re-recurrence\(^8,45\), that led to improved OS.

Although radiofrequency ablation is commonly used to treat HCC with tumour diameter more than 3 cm, it is currently considered best for HCC tumours less than 3 cm\(^55\). Radiofrequency ablation removes HCC with diameters of 3–5 cm much less effectively than in smaller tumours, translating to greater risk of local recurrence\(^56\). The efficacy of radiofrequency ablation also decreases gradually with increasing tumour number and diameter\(^57\). These findings suggest that tumour diameter should be considered when selecting treatment options for recurrent HCC. Unfortunately, subgroup analyses based on tumour diameter or number was not possible in the present meta-analysis, as most of the included studies reported only tumour stage.

The present results should be interpreted carefully considering several limitations. Most of the included studies were observational, indicating that additional well designed RCTs should be conducted in the future. Moreover, rHR and ablation may have different indications for recurrent HCC depending on tumour diameter, location, and patient characteristics. As most of the studies reported only data for recurrent HCC within Milan criteria, these results may not be generalizable to other patients. Patients in the included studies may have received one or more additional treatments after rHR or ablation, which may have affected their prognosis. For instance, several tyrosine kinase and immune-checkpoint inhibitors have recently been identified as first- or second-line therapy for patients with advanced or unresectable HCC\(^58-61\). Thus, the combination of rHR or local ablation with such inhibitors may improve the survival of patients with recurrent HCC. Finally, potential publication bias was observed in the funnel plots. Future meta-analysis with larger sample size may change the findings of the present study.

Despite these limitations, this meta-analysis provides evidence that rHR and local ablation are associated with similar OS in patients with recurrent HCC. rHR seems to be associated with better RFS, whereas local ablation leads to lower perioperative morbidity. These nuances highlight the need for individualized, multidisciplinary strategies when treating recurrent HCC.

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J.-H.Z. and B.-H.Y. conceived the study. B.-H.Y. and Y.-K.Z. collected and analysed data. All authors drafted the manuscript, J.-H.Z. revised the manuscript, and all authors read and approved the final version for publication. B.-H.Y. and Y.-K.Z. contributed equally.

### Disclosure

The authors declare no conflict of interest.

### Supplementary material

**Supplementary material** is available at BJS Open online.

### Data availability

All supporting data are included within the main article and its supplementary files.

### References

1. Shin SW, Ahn KS, Kim SW, Kim TS, Kim YH, Kang KJ. Liver resection versus local ablation therapies for hepatocellular carcinoma within the Milan criteria: a systematic review and meta-analysis. Ann Surg 2021;273:656–666
2. Mazzarerro V, Regalia E, Doct R, Andreola S, Pulvirenti A, Bozzetti F et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. N Engl J Med 1996;334:693–699
3. Guo WX, Sun JX, Cheng YQ, Shi J, Li N, Xue J et al. Percutaneous radiofrequency ablation versus partial hepatectomy for small centrally located hepatocellular carcinoma. World J Surg 2013;37:602–607
4. Wang JH, Wang CC, Hung CH, Chen CL, Lu SN. Survival comparison between surgical resection and radiofrequency ablation for patients in BCLC very early/early stage hepatocellular carcinoma. J Hepatol 2012;56:412–418
5. European Association for the Study of the Liver. EASL clinical practice guidelines: management of hepatocellular carcinoma. J Hepatol 2018;69:182–236
6. Marrero JA, Kulik LM, Sirin CB, Zhu AX, Finn RS, Abecassis MM et al. Diagnosis, staging, and management of hepatocellular carcinoma: 2018 practice guidance by the American Association for the Study of Liver Diseases. Hepatology 2018;68:723–750
7. Korean Liver Cancer Association and National Cancer Center. 2018 Korean Liver Cancer Association–National Cancer Center Korea Practice Guidelines for the Management of Hepatocellular Carcinoma. Gut Liver 2019;13:227–299
8. Erridge S, Pucher PH, Markar SR, Maitetzi G, Athanasiou T, Darzi A et al. Meta-analysis of determinants of survival following treatment of recurrent hepatocellular carcinoma. Br J Surg 2017;104:1433–1442
9. Gavriliidis P, Askari A, Azoulay D. Survival following redo hepatectomy vs radiofrequency ablation for recurrent hepatocellular carcinoma: a systematic review and meta-analysis. HPB (Oxford) 2017;19:3–9
10. Li MJ, Deng ZJ, Liu HT, Teng YX, Hro RR, Liang XM et al. Clinical effect of re-hepatic resection versus radiofrequency ablation in treatment of recurrent hepatocellular carcinoma in Asia: a meta-analysis. J Clin Hepatol 2021;37:1103–1109
11. Liu J, Zhao J, Gu HAO, Zhu Z. Repeat hepatic resection vs radiofrequency ablation for the treatment of recurrent...
hepatocellular carcinoma: an updated meta-analysis. Minim Invasive Ther Allied Technol 2022;31:332–341
12. Yang D, Zhuang B, Wang Y, Xie X, Xie X. Radiofrequency ablation versus hepatic resection for recurrent hepatocellular carcinoma: an updated meta-analysis. BMC Gastroenterol 2020; 20:402
13. Zheng J, Cai J, Tao L, Kirihi MA, Shen Z, Xu J et al. Comparison on the efficacy and prognosis of different strategies for intrahepatic recurrent hepatocellular carcinoma: a systematic review and Bayesian network meta-analysis. Int J Surg 2020;83:196–204
14. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009;339:b2535
15. Lo CK, Mertz D, Loeb M. Newcastle–Ottawa scale: comparing reviewers’ to authors’ assessments. BMC Med Res Methodol 2014;14:45
16. Tierney JF, Stewart LA, Ghersi D, Burdett S, Sydes MR. Practical methods for incorporating summary time-to-event data into meta-analysis. Trials 2007;8:16
17. Zhao LY, Huo RR, Xiang X, Torzilli G, Zheng MH, Yang T et al. Hepatic resection for elderly patients with hepatocellular carcinoma: a systematic review of more than 17,000 patients. Expert Rev Gastroenterol Hepatol 2018;12:1059–1068
18. Liu JL, Huang D, Cao L, Wang XJ, Li JW, Chen J et al. [Laparoscopic hepatectomy versus radiofrequency ablation in treatment of recurrent hepatocellular carcinoma: a prospective randomized control study based on interim follow-up analysis]. Di San Jun Yi Da Xue Xue Bao 2019;41:467–472
19. Xia Y, Li J, Liu G, Wang K, Qian G, Lu Z et al. Long-term effects of repeat hepatectomy vs percutaneous radiofrequency ablation among patients with recurrent hepatocellular carcinoma: a randomized clinical trial. JAMA Oncol 2020;6:255–263
20. Chan AC, Poon RT, Cheung TT, Chok KS, Chan SC, Fan ST et al. Survival analysis of re-resection versus radiofrequency ablation for intrahepatic recurrence after hepatectomy for hepatocellular carcinoma. World J Surg 2012;36:151–156
21. Chen K, Liu XY, Teng YX, Li MJ, Li YS, Huang T et al. [Rehepatectomy and radiofrequency ablation for patients with recurrent hepatocellular carcinoma]. Zhong Guo Shi Yong Wai Ke Za Zhi 2019;39:1060–1064
22. Chen S, Peng Z, Xiao H, Lin M, Chen Z, Jiang C et al. Combined radiofrequency ablation and ethanol injection versus repeat hepatectomy for elderly patients with recurrent hepatocellular carcinoma after initial hepatic surgery. Int J Hyperthermia 2018;34:1029–1037
23. Eisele RM, Chopra SS, Lock JF, Glanemann M. Treatment of recurrent hepatocellular carcinoma confined to the liver with repeated resection and radiofrequency ablation: a single center experience. Technol Health Care 2013;21:9–18
24. Feng Y, Wu H, Huang DQ, Xu C, Zheng H, Maeda M et al. Radiofrequency ablation versus resection for recurrent hepatocellular carcinoma (≤5 cm) after initial curative resection. Eur Radiol 2020;30:6357–6368
25. Hirokawa F, Hayashi M, Miyamoto Y, Asakuma M, Shimizu T, Komeda K et al. Appropriate treatment strategy for intrahepatic recurrence after curative hepatectomy for hepatocellular carcinoma. J Gastrointest Surg 2011;15:1182–1187
26. Ho CM, Lee PH, Shau WY, Ho MC, Wu YM, Hu RH. Survival in patients with recurrent hepatocellular carcinoma after primary hepatectomy: comparative effectiveness of treatment modalities. Surgery 2012;151:700–709
27. Huang XH, Huang Y, Lin KC, Zeng JH, Chi MH, Liu JF et al. [The curative efficacy comparison of percutaneous radiofrequency ablation versus surgical re-resection for recurrent small hepatocellular carcinoma]. Fu Bu Wai Ke 2013;26:93–95
28. Kawano Y, Sasaki A, Kai S, Endo Y, Iwaki K, Uchida H et al. Prognosis of patients with intrahepatic recurrence after hepatic resection for hepatocellular carcinoma: a retrospective study. Eur J Surg Oncol 2009;35:174–179
29. Kim JM, Jow JW, Yi NJ, Choi GS. Living donor liver transplantation should be cautiously considered as initial treatment in recurrent hepatocellular carcinoma within the Milan criteria after curative liver resection. Ann Transl Med 2020;8:288
30. Liang HH, Chen MS, Peng ZW, Zhang YJ, Zhang YQ, Li JQ et al. Percutaneous radiofrequency ablation versus repeat hepatectomy for recurrent hepatocellular carcinoma: a retrospective study. Ann Surg Oncol 2008;15:3484–3493
31. Lu LH, Mei J, Kan A, Ling YH, Li SH, Wei W et al. Treatment optimization for recurrent hepatocellular carcinoma: repeat hepatic resection versus radiofrequency ablation. Cancer Med 2020;9:2997–3005
32. Peng Z, Wei M, Chen S, Lin M, Jiang C, Mei J et al. Combined transcatheter arterial chemoembolization and radiofrequency ablation versus hepatectomy for recurrent hepatocellular carcinoma after initial surgery: a propensity score matching study. Eur Radiol 2018;28:3522–3531
33. Ren ZG, Gan YH, Fan J, Chen Y, Wu ZQ, Qin LX et al. [Treatment of postoperative recurrence of hepatocellular carcinoma with radiofrequency ablation comparing with repeated surgical resection]. Zhonghua Wai Ke Za Zhi 2008;46:1614–1616
34. Saito R, Amemiya H, Hosomura N, Kawadera H, Maruyama S, Shimizu H et al. Prognostic significance of treatment strategies for the recurrent hepatocellular carcinomas after radical resection. In Vivo 2020;34:1265–1270
35. Song KD, Lim HK, Rhim H, Lee MW, Kim YS, Lee WJ et al. Repeated hepatic resection versus radiofrequency ablation for recurrent hepatocellular carcinoma after hepatic resection: a propensity score matching study. Radiology 2015;275:599–608
36. Sun WC, Chen IS, Liang HL, Tsai CC, Chen YC, Wang BW et al. Comparison of repeated surgical resection and radiofrequency ablation for small recurrent hepatocellular carcinoma after primary resection. Oncotarget 2017;8:104571–104581
37. Umeda Y, Matsuda H, Sadamori H, Matsukawa H, Yagi T, Fujiwara T. A prognostic model and treatment strategy for intrahepatic recurrence of hepatocellular carcinoma after curative resection. World J Surg 2011;35:170–177
38. Wang K, Liu G, Li J, Yan Z, Xia Y, Wan X et al. Early intrahepatic recurrence of hepatocellular carcinoma after hepatectomy treated with re-hepatectomy, ablation or chemoembolization: a prospective cohort study. Eur J Surg Oncol 2015;41:236–242
39. Xiao H, Chen ZB, Jin HL, Li B, Xu LX, Guo Y et al. Treatment selection of recurrent hepatocellular carcinoma with microvascular invasion at the initial hepatectomy. Am J Transl Res 2019;11:1864–1875
40. Yan K, Liu W, Qin XM, Bai GJ. [Recurrent small hepatocellular carcinoma; percutaneous radiofrequency ablation; surgical resection]. Gan Dan Yi Wai Ke Za Zhi 2020;32:286–289
41. Yin XL, Hua TQ, Liang C, Chen Z. Efficacy of re-resection versus radiofrequency ablation for recurrent Barcelona clinic liver cancer stage 0/A hepatocellular carcinoma (HCC) after resection for primary HCC. Trans Cancer Res 2019;8:1035–1045
42. Zhang H, Xu XB, He XJ, Liu CL, Zhao MY, Li WB et al. [Comparison of the efficacy between re-operation and radiofrequency ablation on postoperative recurrent carcinoma]. Xi Bu Yi Xue 2013;25:1816–1819
43. Zhang T, Li K, Luo H, Zhang W, Zhang L, Gao M. Long-term outcomes of percutaneous microwave ablation versus repeat hepatectomy for treatment of late recurrent small hepatocellular carcinoma: a retrospective study. Zhonghua Yi Xue Za Zhi 2014;94:2570–2572

44. Zhong JH, Xing BC, Zhang WG, Chan AW, Chong CCN, Serenari M et al. Repeat hepatic resection versus radiofrequency ablation for recurrent hepatocellular carcinoma: retrospective multicentre study. Br J Surg 2022;109:71–78

45. Chua DW, Koh YX, Syn NL, Chuan TY, Yao TJ, Lee SY et al. Repeat hepatectomy versus radiofrequency ablation in management of recurrent hepatocellular carcinoma: an average treatment effect analysis. Ann Surg Oncol 2021;28:7731–7740

46. Wei F, Huang Q, Zhou Y, Luo L, Zeng Y. Radiofrequency ablation versus repeat hepatectomy in the treatment of recurrent hepatocellular carcinoma in subcapsular location: a retrospective cohort study. World J Surg Oncol 2021;19:175

47. Matsumoto M, Yanaga K, Shiba H, Wakiyama S, Sakamoto T, Futagawa Y et al. Treatment of intrahepatic recurrence after hepatectomy for hepatocellular carcinoma. Ann Gastroenterol Surg 2021;5:538–552

48. Wang HL, Mo DC, Zhong JH, Ma L, Wu FX, Xiang BD et al. Systematic review of treatment strategy for recurrent hepatocellular carcinoma: salvage liver transplantation or curative locoregional therapy. Medicine (Baltimore) 2019;98:e14498

49. Facciorusso A, Di Maso M, Muscatiello N. Microwave ablation versus radiofrequency ablation for the treatment of hepatocellular carcinoma: a systematic review and meta-analysis. Int J Hyperthermia 2016;32:339–344

50. Tan W, Deng Q, Lin S, Wang Y, Xu G. Comparison of microwave ablation and radiofrequency ablation for hepatocellular carcinoma: a systematic review and meta-analysis. Int J Hyperthermia 2019;36:264–272

51. Zhang CS, Zhang JL, Li XH, Li L, Li X, Zhou XY. Is radiofrequency ablation equal to surgical resection for recurrent hepatocellular carcinoma meeting the Milan criteria? A meta-analysis. J BUON 2015;20:223–230

52. Chen X, Chen Y, Li Q, Ma D, Shen B, Peng C. Radiofrequency ablation versus surgical resection for intrahepatic hepatocellular carcinoma recurrence: a meta-analysis. J Surg Res 2015;195:166–174

53. Cai H, Kong W, Zhou T, Qiu Y. Radiofrequency ablation versus reresection in treating recurrent hepatocellular carcinoma: a meta-analysis. Medicine (Baltimore) 2014;93:e122

54. Lachenmayer A, Tinguely P, Maurer MH, Frehner L, Knöpfli M, Peterhans M et al. Stereotactic image-guided microwave ablation of hepatocellular carcinoma using a computer-assisted navigation system. Liver Int 2019;39:1975–1985

55. Lin SM, Lin CJ, Lin CC, Hsu CW, Chen YC. Randomised controlled trial comparing percutaneous radiofrequency thermal ablation, percutaneous ethanol injection, and percutaneous acetic acid injection to treat hepatocellular carcinoma of 3 cm or less. Gut 2005;54:1151–1156

56. Livraghi T, Lazzaroni S, Meloni F. Radiofrequency thermal ablation of hepatocellular carcinoma. Eur J Ultrasound 2001;13:159–166

57. Peng ZW, Zhang YJ, Chen MS, Liang HH, Li JQ, Zhang YQ et al. Risk factors of survival after percutaneous radiofrequency ablation of hepatocellular carcinoma. Surg Oncol 2008;17:23–31

58. Lan XB, Papatheodoridis G, Teng YX, Zhong JH. The upward trend in the immunotherapy utilization for hepatobiliary cancers. Hepatobiliary Surg Nutr 2021;10:692–695

59. Liu HT, Jiang MJ, Deng ZJ, Li L, Huang JL, Liu ZX et al. Immune checkpoint inhibitors in hepatocellular carcinoma: current progresses and challenges. Front Oncol 2021;11:737497

60. Chen K, Wei W, Liu L, Deng ZJ, Li L, Liang XM et al. Lenvatinib with or without immune checkpoint inhibitors for patients with unresectable hepatocellular carcinoma in real-world clinical practice. Cancer Immunol Immunother 2021; DOI: 10.1007/s00262-021-03060-w [Epub ahead of print]

61. Deng ZJ, Li L, Teng YX, Zhang YQ, Zhang YX, Liu HT et al. Treatments of hepatocellular carcinoma with portal vein tumor thrombus: Current status and controversy. J Clin Transl Hepatol 2022;10:147–158