REVIEW

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Radiofrequency ablation versus laparoscopic hepatectomy for hepatocellular carcinoma: a systematic review and meta-analysis



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Abstract

Background Although laparoscopic hepatectomy (LH) and radiofrequency ablation (RFA) are the 2 principal minimally invasive surgical approaches and the first line of treatments for patients with hepatocellular carcinoma (HCC). It is not clear which one has greater safety and efficacy. In this meta-analysis, we aim to compare the safety and effectiveness of LH versus RFA for patients with HCC, especially where perioperative and postoperative outcomes differrent.

Methods In PROSPERO, a meta-analysis with registration number CRD42021257575 was registered. Using an established search strategy, we systematically searched Web of Science, PubMed, and Embase to identify eligible studies before June 2023. Data on operative times, blood loss, length of stay, overall complications, overall survival (OS) and recurrence-free survival (RFS) were subjected to meta-analysis.

Results Overall, the present meta-analysis included 8 retrospective and 6 PSM studies comprising 1,848 patients (810 and 1,038 patients underwent LH and RFA). In this meta-analysis, neither LH nor RFA showed significant differences in 1-year and 3-year OS rate and 5-year RFS rate. Despite this, in comparison to the RFA group, LH resulted in significantly higher 1-year(p<0.0001) and 3-year RFS rate (p=0.005), higher 5-year OS rate (p=0.008), lower local recurrence rate (p<0.0001), longer length of stay(LOS) (p<0.0001), longer operative time(p<0.0001), more blood loss (p<0.0001), and higher rate of complications (p=0.001).

Conclusions Comparative studies indicate that LH seemed to provide better OS and lower local recurrence rate, but higher complication rate and longer hospitalization.

Keywords Hepatocellular carcinoma, Laparoscopic hepatectomy, Liver resection, Radiofrequency ablation, Metaanalysis

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Introduction

As the prevalence of hepatocellular carcinoma (HCC) increases, it has become the third leading cause of cancer-related death worldwide [1]. At present, there are many treatments available for HCC, including hepatectomy, liver transplantation, TACE, RFA, microwave coagulation, molecular targeted drugs and radiotherapy [2–4]. Hepatectomy and liver transplantation are generally recognized as most effective methods for the treatment of HCC, but liver transplantation can't be widely carried out due to the shortage of donor livers [5]. In recent years, minimally invasive surgery represented by laparoscopic hepatectomy (LH) and RFA has gradually become a new choice for the treatment of early-stage HCC. The use of LH and RFA is effective and a potentially curative treatment for early-stage HCC, and can provide a cure or prolong survival [6-8]. Laparotomy is often used for LH because of its complexity. Nevertheless, LH has become increasingly popular since Reich et al. reported it in 1991 [9]. Several literature reviews have affirmed RFA's safety and efficacy, highlighting RFA's advantages over open hepatectomy in terms of less blood loss, shorter operation times, and faster recovery times [10, 11]. And, few robust trials have compared the longterm oncological outcomes of LH with RFA and existing results are also not consistent. Although there has been very limited studies comparing surgical and oncological outcomes between LH and RFA for HCC [12, 13], some high-quality studies weren't included in these reviews. In this study, we compared long-term outcomes and perioperative outcomes between LH and RFA for HCC.

Methods

This meta-analysis was performed by the PRISMA guidelines and the protocol of this study was registered in PROSPERO(CRD42021257575).

Literature search and study selection

Two independent researchers (CJ, QF performed a systematic search of PubMed, EMBASE, and Web of Science in accordance with PRISMA guidelines for the studies that provided comparisons between RFA(percutaneous or laparoscopic RFA) and LH for HCC [14]. The combinations of following terms were used: "radiofrequency ablation" or "RFA", "laparoscopic", "laparoscopic hepatectomy", "liver resection", or "minimally invasive", "HCC";"hepatocellular carcinoma" or "liver cancer". Additional studies were gained by manually searching the references of eligible studies.

Inclusion and exclusion criteria

A review and screening of all titles and abstracts of all submitted papers was conducted independently by two investigators (CJ and QF). Inclusion criteria were: (1) Participants: patients with HCC; (2) Intervention: LH or RFA; (3) Study type: observational clinical studies, randomized controlled trials (RCTs), case-control studies; (4) at least one interested data has been reported.

Exclusion criteria were: (1) Expert opinions, editorials, abstracts, letters, and case reports ; (2) Studies without available data.

Data extraction and quality assessment

Based on a unified datasheet, two reviewers(CJ, QF) independently extracted data and resolved disagreements by discussion .We extracted the following major data: first author, research design, publication year, country, sample size, age, tumor size, operative times, blood loss, hospitalization, incidence of complications, overall survival (OS) and recurrence-free survival (RFS). In this review, the Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of studies included, with performance scores of 6 being regarded as high. [15]

Statistical analysis

Review Manager 5.3 software was used to analyze dichotomous data using odds ratios (ORs), and weighted mean differences (MDs) and confidence intervals (95% CI) for continuous data. In order to extract OS and RFS data from Kaplan-Meier curves, the Engauge Digitizer v.4.1 software was used [16]. In studies that reported only medians and ranges, Hozo et al.'s original method could be used to estimate the mean and standard deviation [17]. Begg's funnel plot and Egger's test were used to assess publication bias. The X² test with I² was used to quantify heterogeneity. When I2<50%, representing heterogeneity is low or moderate, a fixed-effects model (FEM) was adopted, while I² \geq 50%, (heterogeneity is high) a randomeffects model (REM) was used.

Results

Literature search result and quality assessment

Based on the various electronic databases, 2,834 relevant English publications were identified. The final analysis included 14 retrospective studies comparing LH and RFA in a total of 1,848 patients (810 received LH and 1,038 received RFA, respectively) [18–31]. Six of them are propensity-score matching (PSM) studies which can ensure the baseline data of patients were consistent [21, 22, 27–30]. We only use the data after PSM from six studies to minimize selection bias. Figure 1 summarizes the PRISMA flowchart for study selection. In Table 1, we summarize the general information and the NOS stars of all eligible studies.The results of using the Cochrane risk of bias tool to assess risk of bias is presented in Figure S1. All results of interest outcomes of this meta-analysis are given in Table 2.



Fig. 1 Flow chart of study identification and selection

Operative outcomes

Operative time

There were five studies [19, 23–26] which covered 570 patients (262 underwent LH whereas 308 underwent RFA) reported operative times. It was found that the LH group had a longer operative time (MD: -119.26 min; 95% CI: -163.67 to -74.84; p<0.00001). Heterogeneity of the data was high (I²=94%) and analyzed in REM (Fig. 2A).

Blood loss

As with the surgery time, a total of five literature had reported on the amount of bleeding [19, 23–26]. As shown in Fig. 2B, the pooled data revealed a significant reduction in blood loss in the RFA group(MD: -232.5 ml; 95% CI: -300.55 to -164.45; p<0.00001).

Tumor size

Tumor size data was available in 12 studies [18, 20–26, 28–30]. The meta-analysis suggested tumor size was smaller in RFA group (MD: -0.20; 95% CI: -0. 38 to -0.02; P=0.03).(Fig. 2C).

Postoperative outcomes

Overall complication rates

Ten studies [20-26, 28-30]that encompassed 1,306 patients (538 and 768underwent LH and RFA, respectively) reported the overall complications, and the present analysis shows LH group has lower overall complication rate (OR: 0.50; 95% CI 0.33 to 0.76; *p*=0.001). (Fig. 3A).

Study	Type of study	Research time	Country	Patie	nts	Age(years)		Gender(M/F)	NOS
				RFA	LH	RFA	LH	RFA	LH	
Casaccia-2015	Retrospective	2005-2010	Italy	24	26	61.48±7.75	64.62±9.51	20/4	17/9	8
Song-2015	Retrospective	2007-2013	China	78	78	48	48	70/8	70/8	8
Vitali-2015	Retrospective	1998-2012	France	60	45	67.3(47–83)	61.4(31-84)	52/8	30/15	8
Harada-2016	PSM	2008-2015	Japan	20	20	73±9	74±6	11/9	9/11	7
lto – 2016	PSM	2011-2013	Japan	27	27	69 (66–72)	71 (68–74)	16/11	15/12	8
Lai-2016	Retrospective	2005-2010	China	33	28	62.8 ± 11.3	56.5 ± 12.6	29/4	24/4	7
Yazici-2016	Retrospective	2000-2014	USA	41	41	73.7 ± 5	72.6 ± 6.7	24/17	25/16	8
Yamashita-2018	Retrospective	2000-2016	Japan	62	38	66.5 ± 9.5	66.9 ± 9.1	40/22	25/13	8
Tsukamoto-2019	Retrospective	2000-2017	Japan	94	77	67.4 ± 8.1	65.2 ± 10.2	51/43	53/24	7
Sandro-2019	PSM	2006-2016	Italy	50	50	67 (56, 76)	68 (62, 76)	37/13	33/17	8
Chong-2019	PSM	2014-2016	China	59	59	59.3 ± 11	57.7 ± 10.5	46/13	46/13	7
Pan-2019	PSM	2014-2016	China	236	118	56.00 (45–64)	53.00 (45.2–61)	206/30	101/17	7
Lee-2020	PSM	2014-2016	Korea	118	118	60.5 ± 10.3	59.5 ± 8.7	88/30	91/27	7
Ogiso-2020	Retrospective	2011-2016	Japan	136	85	73 (47–87)	69 (46–88)	98/38	62/23	8

Table 1 Study characteristics

LH laparoscopic hepatectomy, RFA radiofrequency ablation, M/F male/female, PSM propensity-score matching, NOS Newcastle-Ottawa Scale

 Table 2
 Summary results of the meta-analyses

Outcomes of interest	Studies, n	RFA	LH	WMD/OR (95%CI)	P value	Heterog	eneity		
						X2	df	l ² ,%	P value
Opertive outvomes									
Operative time(min)	5	308	262	-199.26(-163.67,-74.84)	< 0.00001	70.33	4	94	< 0.00001
blood loss	5	308	262	-232.5(-300.55,-164.45)	< 0.00001	10.38	4	61	0.03
tumor size	12	910	682	-0.2(-0.38,-0.02)	0.03	140.35	11	92	< 0.00001
Postoperative outcomes									
overall complication rates	10	768	538	0.5(0.33,0.76)	0.001	7.29	9	0	0.61
Length of stay	10	826	596	-3.34(-4.49,-2.18)	< 0.00001	984.54	9	99	< 0.00001
Oncological outcomes									
local recurrence rate	6	316	272	3.9(2.25,6.77)	< 0.00001	5.38	5	7	0.37
1-year overall survival	10	800	572	0.65(0.31,1.35)	0.24	17.51	9	49	0.04
3-year overall survival	11	850	622	0.79(0.48,1.27)	0.33	29.32	10	66	0.001
5-year overall survival	9	581	476	0.68(0.51,0.9)	0.008	11.05	8	28	0.2
1-year recurrence-free survival	11	908	695	0.38(0.27,0.54)	< 0.00001	18.87	10	47	0.04
3-year recurrence-free survival	11	908	695	0.49(0.3,0.8)	0.005	37.6	10	74	< 0.001
5-year recurrence-free survival	9	639	549	0.51(0.23,1.11)	0.09	40.39	8	80	< 0.00001

LH laparoscopic hepatectomy, RFA radiofrequency ablation, MD mean difference, OR odds ratio, CI confidence interval

Hospital stay

Based on eight studies [19, 20, 22–26, 28–30] which included 1,422 HCC patients, the meta-analysis demonstrates that RFA treated HCC had a shorter hospital stay when compared to LH treated HCC. (MD=-3.34; 95% CI – 4.49 to – 2.18; *p*<0.00001), (Fig. 3B).

Oncological outcomes

Local recurrence rate

Nine studies provided data regarding the local recurrence rate [19–21, 23–28]. The results showed that the LH group had a lower local recurrence rate (OR:3.90; 95% CI 2.25–6.77; p<0.00001), with low heterogeneity (I²=7%) as shown in the FEM (Fig. 4).

Overall survival

Ten studies [18–21, 23, 25, 26, 28, 29, 31]assessed 1-year overall survival. The results showed no difference in the 1-year overall survival rate between the two groups(OR: 0.65; 95% CI 0.31 to 1.35; p=0.24), with moderate heterogeneity (I²=49%) in the REM (Fig. 5A). Ten studies [18–21, 23, 25, 26, 28, 29, 31]assessed 3-year overall survival, the result of meta-analysis revealed no difference in 3-year overall survival (OR: 0.79; 95% CI 0.48 to1.27; p=0.33), with high heterogeneity (I²=66%) in the REM (Fig. 5B). Nine studies [18–21, 23, 25, 26, 28, 31] assessed 5-year overall survival. The results showed that the LH group had a higher overall 5-year survival rate (OR: 0.68; 95% CI 0.51 to 0.90; p=0.008), with low heterogeneity (I²=28%) in the FEM (Fig. 5C).

۸		RFA LH Moon SD Total Moon SD Tota							Mean Difference		Mean Differe	ence	
Α.	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI Ye	ear	IV, Random, S	5% CI	
	Song-2015	22.3	4.2	78	195.7	86.9	78	21.1%	-173.40 [-192.71, -154.09] 20	15 -			
	Yazici-2016	116	73	41	214	99	41	19.0%	-98.00 [-135.65, -60.35] 20	16			
	Lai-2016	43.7	8.5	33	120.5	33.2	28	21.6%	-76.80 [-89.43, -64.17] 201	16	-		
	Yamashita-2018	166	130	62	284	105	38	17.7%	-118.00 [-164.49, -71.51] 20	18 -			
	Tsukamoto-2019	188.3	70.3	94	317.3	94	77	20.5%	-129.00 [-154.35, -103.65] 20	19	-		
	Total (95% CI) Heterogeneity: Tau ² = Test for overall effect: 2	2333.79 Z = 5.26	; Chi² : (P < 0	308 = 70.55 0.00001	5, df = 4)	(P < 0	262 .00001	100.0%); l² = 949	-119.26 [-163.67, -74.84] %	-200	-100 0 RFA LH	100	200
	Heterogeneity: Tau ² = Test for overall effect: 2	2333.79 Z = 5.26	; Chi² : (P < 0	= 70.55).00001	-200	-100 0 RFA LH	100	200					



C		RFA				LH			Mean Difference			Mean Di	fference		
C _	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year		IV, Rando	m, 95% C		
	Vitali-2015	2.1	0.23	60	2.3	0.5	45	12.1%	-0.20 [-0.36, -0.04] 2	2015					
	Casaccia-2015	2.63	1.31	24	3.3	1.38	26	4.0%	-0.67 [-1.42, 0.08] 2	2015			-		
	Yazici-2016	2.8	1.1	41	3.8	1.6	41	5.4%	-1.00 [-1.59, -0.41] 2	2016					
	Harada-2016	1.6	0.6	20	1.8	0.6	20	8.5%	-0.20 [-0.57, 0.17] 2	2016			_		
	Lai-2016	2.4	0.9	33	3	1.1	28	6.4%	-0.60 [-1.11, -0.09] 2	2016		<u> </u>			
	Ito -2016	1.7	0.1	27	2	0.13	27	13.2%	-0.30 [-0.36, -0.24] 2	2016		-			
	Yamashita-2018	2	0.6	62	2.4	0.9	38	9.3%	-0.40 [-0.72, -0.08] 2	2018		_			
	Chong-2019	2.3	0.3	59	2	0.3	59	12.7%	0.30 [0.19, 0.41] 2	2019			-		
	Tsukamoto-2019	2.13	6.6	94	2.25	9	77	0.5%	-0.12 [-2.53, 2.29] 2	2019	•				
	Pan-2019	2.55	0.22	236	2.5	0.28	118	13.2%	0.05 [-0.01, 0.11] 2	2019			•		
	Ogiso-2020	1.6	4.16	136	2.1	3.67	85	2.4%	-0.50 [-1.55, 0.55] 2	2020	(<u> </u>				
	Lee-2020	1.87	0.51	118	1.84	0.56	118	12.4%	0.03 [-0.11, 0.17] 2	2020		-	-		
	Total (95% CI)			910			682	100.0%	-0.20 [-0.38, -0.02]			•			
	Heterogeneity: Tau ² =	0.06; Cł	ni² = 14	10.35, c	lf = 11 (P < 0.	00001);	l² = 92%			<u> </u>		,	-	
	Test for overall effect:	7 = 2 21	(P = (03)							-2	-1 (,		2

Fig. 2 Forest plot of comparison of LH versus RFA for operative outcomes. A: Forest plot for Operative time; B: Forest plot for Blood loss; C: Forest plot for Tumor size

Recurrence-free survival

Eleven studies [18, 19, 21, 23, 25–30] that included 1,603 patients (695 who underwent LH and 908 who underwent RFA) assessed 1-year and 3year RFS rate, the result of meta-analysis revealed RFA has higher1-year and 3-year RFS rate (p<0.00001,p=0.005,respectively) (Fig. 6A-B). Nine studies [18, 19, 21, 25–28, 30, 31] assessed 5-year RFS rate, the result of meta-analysis revealed no difference in 5-year RFS rate between LH and RFA (OR: 0.51; 95% CI 0.23 to 1.11; p=0.09), with low heterogeneity (I^2 =80%) in the REM (Fig. 6C).

Publication bias

Using Begg's funnel plot, publication bias was investigated. For overall complications and 5-year survival, all studies lie within 95% CIs, indicating no publication bias. (Figure S2)

Discussion

Minimally invasive surgery and specialization of minimally invasive surgery are the development trend of modern surgery. Due to the rapid development of surgical technology and surgical instruments, as well as the rapid progress of imaging technology, enables surgeons to accurately judge the location, size and whether the surrounding vessels and organs are violated before operation, which greatly promotes the development of minimally invasive surgery of the liver. As Reich et al. performed the first case of LH in 1991, laparoscopic technique gained popularity due to its magnifying effect and

_		RFA		LH			Odds Ratio	00	lds Ratio	
Α	Study or Subgroup	Events T	otal	Events	Total	Weight	M-H, Fixed, 95% CI Year	М-Н, І	-ixed, 95% Cl	
	Vitali-2015	6	60	5	45	8.3%	0.89 [0.25, 3.12] 2015			
	Lai-2016	8	33	7	28	9.2%	0.96 [0.30, 3.09] 2016			
	Yazici-2016	2	41	3	41	4.6%	0.65 [0.10, 4.11] 2016	-	-	
	Harada-2016	4	20	6	20	7.7%	0.58 [0.14, 2.50] 2016			
	Ito -2016	0	27	4	27	7.1%	0.09 [0.00, 1.86] 2016	· ·	<u> </u>	
	Yamashita-2018	6	62	3	38	5.4%	1.25 [0.29, 5.32] 2018			
	Tsukamoto-2019	1	94	3	77	5.2%	0.27 [0.03, 2.60] 2019	· · · ·	<u> </u>	
	Chong-2019	1	59	3	59	4.7%	0.32 [0.03, 3.19] 2019	-	<u> </u>	
	Pan-2019	12	236	14	118	28.5%	0.40 [0.18, 0.89] 2019		-	
	Ogiso-2020	4	136	10	85	19.2%	0.23 [0.07, 0.75] 2020		-	
	Total (95% CI)		768		538	100.0%	0.50 [0.33, 0.76]			
	Total events	44		58						
	Heterogeneity: Chi ² = 7	.29, df = 9 ((P = 0.	.61); l ² =	0%					
	Test for overall effect: 2	Z = 3.28 (P =	= 0.00	1)				0.01 0.1 Ri	FALH	100

n			RFA		14774 (LH			Mean Difference			Mean Di	ifference	:	
Ь.	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	Year		IV, Rando	<u>om, 95%</u>	CI	
_	Vitali-2015	1	2.75	60	6	3.75	45	9.8%	-5.00 [-6.30, -3.70]	2015		_			
	Song-2015	10	0.83	78	15	0.5	78	11.2%	-5.00 [-5.22, -4.78]	2015					
	Ito -2016	7.6	0.15	27	12.6	0.8	27	11.1%	-5.00 [-5.31, -4.69]	2016	-				
	Yazici-2016	2.1	0.7	41	3.4	0.2	41	11.2%	-1.30 [-1.52, -1.08]	2016					
	Lai-2016	6.3	6.9	33	10.4	4.5	28	6.6%	-4.10 [-6.98, -1.22]	2016					
	Yamashita-2018	7	3	62	11	5	38	8.9%	-4.00 [-5.76, -2.24]	2018					
	Chong-2019	2.7	1.3	59	4.6	1.2	59	11.0%	-1.90 [-2.35, -1.45]	2019		-			
	Tsukamoto-2019	16	6	94	16	7	77	8.4%	0.00 [-1.98, 1.98]	2019			<u> </u>		
	Pan-2019	3	0.67	236	5	0.5	118	11.2%	-2.00 [-2.12, -1.88]	2019					
	Ogiso-2020	6	4.33	136	11	3	85	10.4%	-5.00 [-5.97, -4.03]	2020	-	_			
	Total (95% CI)			826			596	100.0%	-3.34 [-4.49, -2.18]			•			
	Heterogeneity: Tau ² =	3.08; Cł	ni² = 98	34.54, 0	lf = 9 (P	< 0.0	0001);	² = 99%			+			<u> </u>	
	Test for overall effect:	Z = 5.67	(P < (0.00001	I) Ì		,.				-10 -5		0	5	10
					,							RFA	LH		

Fig. 3 Forest plot of comparison of LH versus RFA for Postoperative outcomes. A: Forest plot for overall complication rates; B: length of stay

RFA		LH			Odds Ratio				Odds Ratio		
Events 1	Total E	Events	Total	Weight	M-H, Fixed, 95% CI	Year		Μ	-H, Fixed, 95%	CI	
8	22	5	24	21.3%	2.17 [0.58, 8.08]	2015					
17	78	9	78	49.4%	2.14 [0.89, 5.14]	2015			_	_	
8	27	0	27	2.4%	23.97 [1.31, 440.35]	2016					
21	33	7	28	19.3%	5.25 [1.73, 15.95]	2016					
3	62	0	38	4.1%	4.53 [0.23, 90.14]	2018				•	
9	94	0	77	3.5%	17.22 [0.99, 300.84]	2019					
	316		272	100.0%	3.90 [2.25, 6.77]						
66		21									
.38, df = 5 Z = 4.84 (P	(P = 0.3 < 0.000	37); l² = 001)	7%				0.01	0.1	1	10	100
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Fig. 4 Forest plot of comparison of LH versus RFA for local recurrence rate

wider visual field. At present, LH has been proved to be safe and similar long-term oncological outcomes over traditional surgery, but the surgical procedure is difficult and time-consuming [32–34]. The results of previous studies of the outcomes of LH to RFA have been inconsistent. Throughout this meta-analysis, the latest studies from 2015 to 2023 were included to compare the safety and efficacy of LH compared to RFA in the treatment of HCC. Despite the absence of any randomized controlled trials (RCTs), the majority of the studies included were propensity score matching (PSM) studies and demonstrated a relatively high quality based on the NOS assessment, as indicated in Table 1.

In the past few years, radiofrequency ablation and laparoscopic liver resection have been popular choices for the treatment of liver cancer. In order to better understand the effectiveness and advantages and disadvantages of these two methods, we conducted a metaanalysis and conducted a comprehensive evaluation of relevant research. Through collecting and analyzing a large amount of research data, we found that both radiofrequency ablation and laparoscopic liver resection have

٨		RFA	۱	LH			Odds Ratio			Odds	Ratio		
A	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M	-H. Rande	om, 95%		
	Vitali-2015	59	60	44	45	5.3%	1.34 [0.08, 22.03]	2015			•		
	Song-2015	76	78	75	78	9.6%	1.52 [0.25, 9.36]	2015			•		
	Casaccia-2015	18	22	23	24	7.2%	0.20 [0.02, 1.91]	2015	-		_		
	Lai-2016	30	33	27	28	7.0%	0.37 [0.04, 3.78]	2016	-				
	Harada-2016	5	20	17	20	11.2%	0.06 [0.01, 0.29]	2016		-			
	Yamashita-2018	62	62	37	38	4.2%	5.00 [0.20, 125.91]	2018					\rightarrow
	Pan-2019	192	236	107	118	19.4%	0.45 [0.22, 0.90]	2019		-			
	Tsukamoto-2019	92	94	73	77	10.2%	2.52 [0.45, 14.15]	2019			•		
	Chong-2019	57	59	55	59	10.2%	2.07 [0.36, 11.78]	2019				_	
	Ogiso-2020	124	136	80	85	15.6%	0.65 [0.22, 1.90]	2020		-			
	Total (95% CI)		800		572	100.0%	0.65 [0.31, 1.35]						
	Total events	715		538									
	Heterogeneity: Tau ² = 0	0.59; Chi ²	= 17.5	1, df = 9 (P = 0.0)4); l ² = 49	1%						400
	Test for overall effect: 2	Z = 1.16 (P = 0.2	4)		1999-1999 1999-1997			0.01 0.1	RFA	LH	10	100

-		RFA		LH			Odds Ratio			Odds	Ratio		
В	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year		M-H, Rand	om, 95% Cl		
	Vitali-2015	37	60	38	45	9.4%	0.30 [0.11, 0.77]	2015					
	Song-2015	64	78	70	78	9.6%	0.52 [0.21, 1.33]	2015					
	Casaccia-2015	11	22	14	24	8.0%	0.71 [0.22, 2.29]	2015					
	Harada-2016	1	20	6	20	3.6%	0.12 [0.01, 1.14]	2016			-		
	Lai-2016	17	33	24	28	7.4%	0.18 [0.05, 0.62]	2016		-			
	Yamashita-2018	59	62	29	38	6.7%	6.10 [1.54, 24.26]	2018					
	Pan-2019	53	236	17	118	12.2%	1.72 [0.95, 3.13]	2019		1			
	Sandro-2019	17	50	18	50	10.4%	0.92 [0.40, 2.08]	2019					
	Tsukamoto-2019	82	94	67	77	9.9%	1.02 [0.42, 2.51]	2019					
	Chong-2019	40	59	37	59	10.9%	1.25 [0.59, 2.67]	2019		_	-		
	Ogiso-2020	99	136	67	85	11.8%	0.72 [0.38, 1.37]	2020		-	_		
	Total (95% CI)		850		622	100.0%	0.79 [0.48, 1.27]			•	•		
	Total events	480		387									
	Heterogeneity: Tau ² = 0	0.41; Chi ²	= 29.2	2, df = 10	(P = 0)	.001); l ² =	66%						
	Test for overall effect: 2	Z = 0.98 (I	P = 0.3	3)					0.01 0	RFA	LH) 10	0

6		RFA		LH			Odds Ratio			Odds Ratio		
C.	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI Year		M-H	I. Fixed, 95% C	1	
	Song-2015	63	78	68	78	11.4%	0.62 [0.26, 1.47] 2015					
	Casaccia-2015	5	22	9	24	5.8%	0.49 [0.13, 1.79] 2015					
	Vitali-2015	35	60	35	45	14.5%	0.40 [0.17, 0.95] 2015					
	Harada-2016	0	20	3	20	3.0%	0.12 [0.01, 2.53] 2016	←				
	Yamashita-2018	53	62	28	38	4.4%	2.10 [0.77, 5.78] 2018				-	
	Sandro-2019	8	50	5	50	3.7%	1.71 [0.52, 5.66] 2019				-	
	Tsukamoto-2019	71	94	65	77	15.2%	0.57 [0.26, 1.24] 2019					
	Chong-2019	19	59	21	59	12.4%	0.86 [0.40, 1.84] 2019					
	Ogiso-2020	56	136	47	85	29.6%	0.57 [0.33, 0.98] 2020		-	-		
	Total (95% CI)		581		476	100.0%	0.68 [0.51, 0.90]			•		
	Total events	310		281								
	Heterogeneity: Chi ² = 1	1.05, df =	8 (P =	0.20); l ² =	= 28%			L	0.1			
	Test for overall effect: 2	Z = 2.67 (F	P = 0.0	08)				0.02	0.1	RFA LH	10	50

Fig. 5 Forest plot of comparison of LH versus RFA for long-term oncological outcomes A: 1-year overall survival time; B: Forest plot for 3-year survival time; C: Forest plot for 5-year survival time

certain therapeutic effects in the treatment of liver cancer. However, there are differences between these two methods in certain aspects.

Firstly, from the perspective of surgical trauma and recovery, radiofrequency ablation has the advantages of minimally invasive and fast recovery. Through local puncture to destroy liver cancer tissue, radiofrequency ablation has less trauma to patients and faster postoperative recovery. Although laparoscopic liver resection is also a minimally invasive surgery, it requires the establishment of a small incision in the abdomen, which can cause relatively greater trauma to the patient.

۸		RFA		LH			Odds Ratio	Odds Ratio	
Α.	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI Year	M-H, Random, 95% Cl	
	Song-2015	51	78	65	78	10.3%	0.38 [0.18, 0.80] 2015		
	Casaccia-2015	9	22	17	24	5.7%	0.29 [0.08, 0.97] 2015		
	Lai-2016	25	33	24	28	5.0%	0.52 [0.14, 1.96] 2016		
	Harada-2016	5	20	14	20	4.7%	0.14 [0.04, 0.57] 2016		
	Yamashita-2018	48	62	28	38	8.1%	1.22 [0.48, 3.12] 2018		
	Sandro-2019	17	50	36	50	9.1%	0.20 [0.09, 0.47] 2019		
	Tsukamoto-2019	62	94	67	77	9.9%	0.29 [0.13, 0.64] 2019		
	Pan-2019	125	236	90	118	14.5%	0.35 [0.21, 0.57] 2019		
	Chong-2019	35	59	50	59	8.8%	0.26 [0.11, 0.63] 2019		
	Lee-2020	101	118	101	118	10.7%	1.00 [0.48, 2.07] 2020		
	Ogiso-2020	43	136	50	85	13.3%	0.32 [0.18, 0.57] 2020		
	Total (95% CI)		908		695	100.0%	0.38 [0.27, 0.54]	•	
	Total events	521		542					
	Heterogeneity: Tau ² = 0	0.15; Chi ²	= 18.8	7, df = 10	(P = 0.	.04); l ² = 47	7%		
	Test for overall effect: 2	z = 5.53 (I	⊃ < 0.0	0001)				RFA LH	00

D		RFA		LH			Odds Ratio			Odds	Ratio		
D	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	Year		M-H, Rand	om, 95%	CI	
	Song-2015	32	78	52	78	10.9%	0.35 [0.18, 0.67]	2015					
	Casaccia-2015	4	22	6	24	6.3%	0.67 [0.16, 2.77]	2015		-			
	Harada-2016	1	20	4	20	3.4%	0.21 [0.02, 2.08]	2016					
	Lai-2016	9	33	18	28	8.1%	0.21 [0.07, 0.62]	2016		I			
	Yamashita-2018	39	62	26	38	9.6%	0.78 [0.33, 1.84]	2018			_		
	Tsukamoto-2019	29	94	43	77	11.1%	0.35 [0.19, 0.66]	2019					
	Sandro-2019	5	50	13	50	7.9%	0.32 [0.10, 0.97]	2019					
	Pan-2019	28	236	11	118	10.4%	1.31 [0.63, 2.73]	2019		-	•		
	Chong-2019	13	59	27	59	9.9%	0.33 [0.15, 0.75]	2019					
	Ogiso-2020	21	136	35	85	11.0%	0.26 [0.14, 0.49]	2020					
	Lee-2020	39	118	25	118	11.3%	1.84 [1.02, 3.30]	2020			-		
	Total (95% CI)		908		695	100.0%	0.49 [0.30, 0.80]			•			
	Total events	220		260									
	Heterogeneity: Tau ² = 0	0.47; Chi ²	= 37.6	0, df = 10	(P < 0.	.0001); l² =	= 73%					+	
	Test for overall effect: 2	2 = 2.83 (P = 0.0	05)					0.01	RFA	LH	10	100

C		RFA		LH			Odds Ratio		Odds Ratio
	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	r M-H, Random, 95% Cl
	Song-2015	29	78	48	78	14.1%	0.37 [0.19, 0.71]	2015	5
	Casaccia-2015	3	22	2	24	8.2%	1.74 [0.26, 11.51]	2015	5
	Harada-2016	0	20	1	20	4.2%	0.32 [0.01, 8.26]	2016	6
	Yamashita-2018	34	62	22	38	13.4%	0.88 [0.39, 2.00]	2018	8
	Tsukamoto-2019	10	94	35	77	13.5%	0.14 [0.06, 0.32]	2019	9
	Sandro-2019	3	50	2	50	8.4%	1.53 [0.24, 9.59]	2019	9
	Chong-2019	5	59	14	59	12.0%	0.30 [0.10, 0.89]	2019	9
	Lee-2020	26	118	13	118	13.8%	2.28 [1.11, 4.70]	2020	0
	Ogiso-2020	5	136	20	85	12.4%	0.12 [0.04, 0.35]	2020	0
	Total (95% CI)		639		549	100.0%	0.51 [0.23, 1.11]		•
	Total events	115		157					
	Heterogeneity: Tau ² = ²	1.02; Chi ²	= 40.3	9, df = 8 (P < 0.0	00001); l ² =	= 80%		
	Test for overall effect: 2	Z = 1.69 (F	P = 0.0	9)					0.01 0.1 1 10 100 RFA LH

Fig. 6 Forest plot of comparison of LH versus RFA for long-term oncological outcomes. A: Forest plot for 1-year overall survival time; B: Forest plot for 3-year survival time; C: Forest plot for 5-year survival time

Secondly, in terms of tumor control and recurrence rate, laparoscopic liver resection has a wider resection range and lower recurrence rate. For larger liver cancer or multiple liver cancer, laparoscopic liver resection can more thoroughly remove tumor tissue and reduce the risk of recurrence. Radiofrequency ablation is mainly used for the treatment of small liver cancer or unresectable liver cancer, and its efficacy may be limited for larger or multiple liver cancer.

Two previous meta-analyses comparing perioperative and oncologic outcomes of LH to RFA were published. However, the sample size of both studies was relatively small [12, 13]. Jin et al's [8] study only focus on perioperative outcomes between LH and RFA. Seven articles were included in Jin et al's study, and they claim that seven studies are RCTs. After carefully reading these 7 articles, we found that 3 articles were in Chinese and none of them were RCTs. Their results are not credible. Li et al's [13] meta-analysis covered 1,570 HCC participants from 10 retrospective studies and focused on and longterm survival outcomes. They used the data before the PSM to analysis to get a sufficient sample size and 3 of those studies are conference abstracts. They found that LH was associated with longer 1-,3-, and 5-year overall survival time, better 1-year and 3-year DFS rate, lower local recurrence rate and higher complications.

Comparing with their results, our study included some recent studies [28–30], and excluded conference abstracts. The meta-analysis showed LH has a longer hospitalization, more blood loss and longer operative time but a lower local recurrence rate than RFA, which was consistent with the study of Jin et al. The main cause of longer operation time of LH is hemostasis and suture were performed on the liver section.

Local recurrence rate is an important malignancy prognosis factor for HCC [35]. The present meta-analysis revealed that LH has a lower rate of local recurrence than RFA. This difference may be explained by patients with HCC in early stage were selected to perform LH and RFA for larger or irregular tumor may exist three-dimensional leakage phenomenon, resulting in residual lesions, and the scope of thermal ablation is limited. From a clinical point of view, the results of this meta-analysis show that LH has higher 1-and 3- RFS rate, suggesting that LH has better tumor radical effect than RFA.

According to our knowledge, no RCTs have been conducted in patients with HCC that compare long-term survival between LH and RFA. The largest overall survival outcomes data of LH and RFA in the treatment of HCC comes from Korea. Lee et al. reported 566 patients with HCC underwent LH or RFA (251 underwent LH and 315 underwent RFA) and revealed that nonsignificant difference in 1-,2-and 3-year overall survival time in the two groups (100, 99.5, and 97.9% vs. 99.0, 98.3, and 97.2% respectively, p=0.16) [30]. But Pan et al. compared the survival data after PSM of 354 patients with HCC (118 underwent LH and 236 underwent RFA) from China and suggested that LH and RFA can achieved a median overall survival of 25.6 and 23.4 months respectively (p=0.034) and LH has better 1-,2-and 3-year overall survival rate than RFA (97.3, 97.3 and 91.0% vs. 99.5, 87.0 and 79.0%, respectively, p=0.0034) [29]. Although our meta-analysis revealed no significant difference in 1- and 3-year overall survival rate (OR: 0.65; 95% CI 0.31 to 1.35; p=0.24; OR: 0.79; 95% CI 0.48 to1.27; p=0.33, respectively), LH has better 5-year overall survival rate (OR: 0.68; 95% CI 0.51 to 0.90; p=0.008). Based on the pooled data, LH does not appear to be inferior to RFA from an oncological perspective and is actually able to achieve a superior oncologic outcome when compared to RFA in some ways.

In the era of minimally invasive liver resection, robotic surgery is increasingly being explored for its safety and effectiveness in liver resection due to its inherent advantages, including flexible mechanical arms with 360-degree range of motion, strong stability, precision in operation, 3D magnified vision, and improved comfort for the surgeon [36]. Charing et al.'s study found that robot-assisted liver resection has a lower conversion rate to open surgery and reduces postoperative hospital stay compared to laparoscopic liver resection. Once the learning curve is overcome, the conversion rates are similar [37]. Several studies comparing robot-assisted liver resection with traditional open liver resection have found that while the operative time for robot-assisted procedures is longer, the postoperative hospital stay is significantly shorter, and the incidence of severe complications, such as liver failure, is markedly reduced [36, 38]. Nicholas et al. observed a lower 45-day readmission rate for patients undergoing robotic liver resection [39]. Aziz et al. found that the 6-month readmission rate following robotic surgery was lower compared to traditional surgery [40]. It is noteworthy that Zhu et al. found no significant difference in long-term outcomes, including 5-year DFS and OS, among patients with BCLC 0-A stage HCC undergoing robotic-assisted liver resection, laparoscopic liver resection, or traditional open surgery [41].

Despite the significant minimally invasive advantages of radiofrequency ablation (RFA) for liver cancer, there are challenges in safely ablating tumors that are difficult to reach using conventional ultrasound or CT guidance. To further advance the minimally invasive treatment of liver cancer, some researchers are exploring the combination of robotic-assisted navigation systems with RFA [42]. This integration holds promise for enabling RFA of tumors in difficult-to-reach locations under robotic guidance. Additionally, due to the remote control capabilities of robots, this approach could facilitate telemedicine support. Although research in this area is still limited, it is worth exploring as robotic assistance has the potential to revolutionize the future of minimally invasive RFA.

The most advantageous areas for RFA in the treatment of HCC are early HCC (diameter \leq 3.0 cm) and very early hepatocellular carcinoma (diameter \leq 2.0 cm) [43]. A large amount of high-level evidence-based evidence indicates that the curative effect of RFA is not significantly different from that of liver resection and liver transplantation for these two types of HCC, and in most cases, it can be the first choice.

Medium volume HCC (diameter 3.1-5.0 cm) is not a good indication for RFA treatment. Its main pathological feature is that the surrounding microvascular invasion (MVI) is relatively broad, and its pathological volume is much larger than the volume of the main tumor visible on imaging. It is difficult to achieve pathological complete ablation using RFA alone. In principle, the preferred treatment for medium volume HCC is liver resection. For those who cannot or are unwilling to undergo liver resection, RFA can be selectively applied. Generally speaking, the higher the degree of differentiation of HCC, the more complete the capsule, and the better the efficacy of RFA. Microwave ablation, like radiofrequency ablation, is a minimally invasive therapy for liver cancer that was introduced around the same time. The principle is to rapidly and uniformly heat tissues through electromagnetic energy. Initially, people were not clear about the differences between the two, but with clinical applications, multiple studies comparing their efficacy have gradually been published, but the results are slightly different. Most studies indicate no significant difference in disease-free survival (DFS) and overall survival (OS) between the two ablation methods [44, 45]. But a recent meta-analysis showed that microwave ablation can lead to better prognosis and fewer complications [46]. Compared to radiofrequency ablation, microwave ablation has a shorter heating time, a larger ablation area, and a smaller heat sink effect.Consequently, some studies recommend prioritizing microwave ablation for tumors larger than 3 cm or those located adjacent to major blood vessels [47].

In addition, the combination of transcatheter hepatic artery embolization chemotherapy (TACE)/hepatic artery embolization (TAE), with a safety margin of 1.0 cm and consolidation repeat ablation, is an important strategy to improve the ablation efficiency of medium volume HCC and achieve pathological complete ablation.

Solitary large HCC has a huge volume, and single RFA treatment is difficult to achieve complete ablation. The preferred treatment method is liver resection. For patients who cannot be removed, RFA can be considered in combination with TACE/TAE.

Recurrent hepatocellular carcinoma is a good indication for RFA[48]. The compliance of postoperative follow-up in patients with hepatocellular carcinoma is usually good, and recurrent HCC lesions are usually small, making it easy to achieve complete ablation using RFA. Research has shown that there is no significant difference in the efficacy between repeat liver resection and RFA for patients with recurrent HCC. In summary, both radiofrequency ablation and laparoscopic liver resection have certain therapeutic effects in the treatment of liver cancer. However, there are differences between these two methods in terms of surgical trauma, tumor control, recurrence rate, and risk of complications. When selecting treatment methods, comprehensive consideration should be given to factors such as the patient's specific condition, tumor size, location, and the doctor's experience and technical level.

It is important to consider the limitations of the present meta-analysis, even though it includes several PSM studies for a more credible conclusion. First, it is possible that selection bias was caused by the majority of the studies included were retrospective studies and no RCTs was include. Moreover, although all the trials described the distribution of the included cases and the factors affecting the prognosis, it was difficult to achieve the complete matching of the baseline data between the two groups, and the statistical treatment of reducing bias was not used in the statistical analysis stage, and the sample size of some studies was small, so there might be some occurrence bias. It is also important to emphasize that there are insufficient studies reporting long-term survival outcomes. Hence, to further evaluate LH's safety and efficacy in patients with HCC, large-scale and RCT studies with long-term outcomes will be needed .

Conclusions

Overall, our study showed LH was safe, feasible, and technically feasible for HCC patients, providing better 5-year OS and 1-,3-year RFS. Both LH and RFA are the radical minimally invasive treatment for early-stage HCC. Patients with smaller tumor size should choose LH to resect tumor tissue completely to reduce recurrence and obtain longer RFS rate and overall survival. For young patients with HCC, surgical resection should be preferred to achieve better curative effect. However, the older patients can choose the two ways. In view of RFA has advantage of less trauma and shorter operation time, for the elderly and weak patients, or patients with high risk of surgery combined with other diseases, can choose RFA first.

Abbreviations

- LH Laparoscopic hepatectomy
- RFA Radiofrequency ablation
- HCC Hepatocellular carcinoma
- OS Overall survival
- RFS Recurrence-free survival
- HR Hazard ratio
- NOS Newcastle-Ottawa Scale
- OR Odds ratio MD Mean differences
- FFM Fixed-effects model
- REM Random-effects model
- MVI Microvascular invasion
- CI Confidence interval
- ci confidence interval

Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s12957-024-03473-8.

Supplementary Material 2

Acknowledgements

Not applicable.

Author contributions

Study concept and design: CJ, QF; Acquisition of data: CJ, QF; Analysis and interpretation: ZZ, CJ, ZQ; Draft the manuscript and preliminary revise: LX, AD; Analyses and reviewed the manuscript: JL, Study supervision and final approval: JL. All authors read and approved the final manuscript.

Funding

This work was supported by The Project of Guizhou Provincial Department of Science and Technology (Qian Ke He Cheng Guo, LC[2024]109) and Guizhou Provincial Health Commission Science and Technology Fund Project (2025GZWJKJXM1593).

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval

The study was approved by the ethics committee of West China Hospital of Sichuan University.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 21 March 2024 / Accepted: 17 July 2024 Published online: 24 July 2024

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