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Surgery for postoperative intrahepatic recurrence after curative resection for hepatocellular carcinoma: Repeat hepatectomy versus salvage liver transplantation

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Abstract: Liver resection (LR) remains a cornerstone curative option for patients with hepatocellular carcinoma (HCC), and yet the high rate of postoperative intrahepatic recurrence poses a significant clinical challenge. Despite numerous attempts, no adjuvant therapy has shown definitive efficacy in preventing recurrence. In this context, salvage liver transplantation (SLT) and repeat hepatectomy (RH) have emerged as key curative strategies for recurrent disease. While SLT is associated with the most favorable survival outcomes, limited donor availability, particularly in Eastern countries, often necessitates the use of RH, which can also offer promising results. These evolving treatment strategies underscore the urgent need for improved risk stratification, optimized surgical decision-making, and innovative approaches to managing recurrent HCC.

***Keywords*:** hepatocellular carcinoma, salvage liver transplantation, repeat hepatectomy

1. Introduction

Hepatocellular carcinoma (HCC) is rated as the sixth most common cancer and the third leading cause of cancer-related deaths worldwide (*1*). The widely accepted and recommended first-line curative treatments for HCC are liver resection (LR), liver transplantation (LT), and local ablation (*e.g*., radiofrequency ablation (RFA) and microwave ablation) (*2*). However, the recurrence rate after curative LR remains high. The curative treatment modalities for intrahepatic recurrent HCC include salvage liver transplantation (SLT), repeat hepatectomy (RH), and RFA (*3*). The surgeries recommended for postoperative intrahepatic recurrence include RH and SLT (*4*). However, the choice of surgery to treat intrahepatic recurrence of HCC needs to be further investigated.

The current review covers recent studies dealing with surgery to treat postoperative intrahepatic recurrence of HCC.

2. Salvage liver transplantation and salvage living donor liver transplantation

Starzl *et al*. reported the first LT in 1963 (*5*). Since then, improvements in surgical techniques and perioperative patient care for LT have resulted in LT becoming a common and routine surgery. A study by Mazzaferro *et al*. resulted in LT becoming a standard treatment for HCC (*6*). Over the past few years, salvage liver transplantation (SLT) has been recommended for treating recurrent HCC following primary LR to improve the survival rates of patients with HCC. SLT was initially proposed by Majno *et al*. (*7*) and involves the curative resection or ablation of the primary tumor, followed by transplantation in the event of recurrence.

With advances in surgical technology, SLT has become widespread because of its effectiveness (*8,9*). SLT is thought to be comparable to primary liver transplantation and is associated with a decent long-term survival rate (*10*). The long-term survival rate for SLT is superior compared to RH or other salvage therapies for HCC recurrence (*11-13*).

The indications for SLT differ among studies, particularly with regard to the acceptable extent of recurrent HCC lesions (*14-16*). The definition of "transplantability criteria in SLT," referring to the standards identifying those patients who would get the maximum benefit from transplantation for HCC recurrence following hepatectomy, remains controversial (*17*). Most of the studies agree that the Milan criteria are suitable for deciding the transplantability criteria in SLT (*18*).

The scarcity of cadaveric donors has prompted Eastern countries to opt for living donor liver

Table 1. Summary of studies comparing salvage liver transplantation and repeat hepatectomy for treating hepatocellular carcinoma patients with postoperative intrahepatic recurrence

First author	Year	Country/region	Number of patients	Type of treatment	5-year survival *3-year survival ** 5-year disease-specific survival
Yamashita Y (*20*)	2015	Japan	*n* = 13	SLDLT	75%
			n = 146	RH	61%
Ali MA (*31*)	2016	Taiwan	*n* = 25	SLT	80%
			n = 31	RH	60%
Lim C (*32*)	2017	Japan and France	*n* = 77	SLT	71%
			n = 314	RH	71%
Fang JZ (*33*)	2020	China	*n* = 46	SLT	77%
			n = 78	RH	56%
Kim JM (*34*)	2020	South Korea	*n* = 21	SLDLT	81%*
			n = 45	RH	60%*
Yoon YI (*35*)	2022	South Korea	*n* = 84	sLDLT	87%**
			n = 163	RH	56%**
Yang L (*36*)	2025	China	*n* = 77	SLT	76%
			n = 401	RH	58%

Abbreviations: SLT: salvage liver transplantation; SLDLT: salvage living donor liver transplantation; RH: repeat hepatectomy.

transplantation (LDLT) (*19*). Reports on salvage LDLT (sLDLT) for recurrent HCC are scarce. Yamashita *et al*. (*20*) reported 13 patients undergoing sLDLT for recurrence and concluded that in patients with grade B liver damage, sLDLT is superior to RH.

3. Repeat hepatectomy

Several treatment centers currently recommend RH as the first line of therapy for recurrent HCC because it is safe and has survival rates that are comparable to the first hepatectomy (*21*). Currently, there are no uniform guidelines on the indications for RH; however, according to the Japanese HCC guidelines, the basic principles are similar to those in primary cases (*22*).

A study by Nagasue *et al*. in 1986 was the first to report on the performance of RH for recurrent HCC in nine patients (*23*). That study indicated that RH is a possible and meaningful therapeutic approach for treating patients with recurrent HCC in the remnant liver. Later, several studies reported the technical feasibility of RH for treating intrahepatic HCC recurrence (*24-27*). Mise *et al*. (*28*) reported that RH was successful even in patients who had had recurrence three or more times. However, the surgical procedure for repeat LR is challenging and is associated with complications. The more times that a hepatectomy is performed, the more challenging the resection becomes.

Laparoscopic or robotic hepatectomy is being increasingly preferred as it is a minimally invasive method of treating HCC. Compared to open LR, minimally invasive liver surgery is associated with lesser intraoperative bleeding and a shorter hospital stay (*29*). RH is more feasible after laparoscopic resection because of the minimal adhesions (*30*). Therefore, the number of patients undergoing RH is expected to increase considering the increase in the number of patients with primary HCC undergoing minimally invasive hepatectomy.

Currently, there is no consensus on whether RH is superior to other methods used to treat recurrent HCC. The prognosis for RH compared to other treatments might not be valid due to selection bias. Patients for whom RH is not recommended might have poor liver function, or tumor recurrence might be too severe. Prospective randomized studies that prove the superiority of RH over other alternative treatments for recurrent HCC need to be conducted.

4. Comparative study of SLT and RH

Table 1 shows previous studies recommending SLT and RH for intrahepatic recurrent HCC (*20,31-36*). Most of the studies are from Eastern countries, where RH is a commonly performed procedure. The 5-year survival rates have been reported in most studies, and the 5-year survival rates for patients undergoing SLT or SLDLT (71–87%) are generally superior to those for patients undergoing RH (56–71%). Although the postoperative complication rate was not considered, SLT is considered to be the best treatment for intrahepatic recurrent HCC. Of course, one needs to understood that the condition of the patients in the two groups differs; that said, the disease-free survival associated with SLT is better even after propensity score matching (*32,35,36*).

In conclusion, the current article conducted an overview of the reported surgeries for treatment of postoperative intrahepatic recurrence of HCC. Results indicated that SLT yields the best survival outcomes when the tumor conditions are reasonable and the donor pool is sufficient. RH is frequently performed as the second-best treatment option in Eastern countries and is associated with an acceptable survival outcome.

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References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021; 71:209-249.
2. Vogel A, Meyer T, Sapisochin G, Salem R, Saborowski A. Hepatocellular carcinoma. Lancet. 2022; 400:1345-1362.
3. Zhang X, Li C, Wen T, Peng W, Yan L, Yang J. Treatment for intrahepatic recurrence after curative resection of hepatocellular carcinoma: Salvage liver transplantation or re-resection/radiofrequency ablation? A retrospective cohort study. Int J Surg. 2017; 46:178-185.
4. Liu J, Zhang G, Yang L, Yan D, Yu J, Wei S, Li J, Yi P. Salvage liver transplantation versus curative treatment for patients with recurrent hepatocellular carcinoma: A systematic review and meta-analysis. Eur J Surg Oncol. 2024; 50:108427.
5. Starzl TE, Marchioro TL, Vonkaulla KN, Hermann G, Brittain RS, Waddell WR. Homotransplantation of the liver in humans. Surg Gynecol Obstet. 1963; 117:659-676.
6. Mazzaferro V, Regalia E, Doci R, Andreola S, Pulvirenti A, Bozzetti F, Montalto F, Ammatuna M, Morabito A, Gennari L. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. N Engl J Med. 1996; 334:693-699.
7. Majno PE, Sarasin FP, Mentha G, Hadengue A. Primary liver resection and salvage transplantation or primary liver transplantation in patients with single, small hepatocellular carcinoma and preserved liver function: An outcome-oriented decision analysis. Hepatology. 2000; 31:899-906.
8. Vennarecci G, Ettorre GM, Antonini M, Santoro R, Maritti M, Tacconi G, Spoletini D, Tessitore L, Perracchio L, Visco G, Puoti C, Santoro E. First-line liver resection and salvage liver transplantation are increasing therapeutic strategies for patients with hepatocellular carcinoma and Child A cirrhosis. Transplant Proc. 2007; 39:1857-1860.
9. Kim BW, Park YK, Kim YB, Wang HJ, Kim MW. Salvage liver transplantation for recurrent hepatocellular carcinoma after liver resection: Feasibility of the Milan criteria and operative risk. Transplant Proc. 2008; 40:3558-3561.
10. Bhangui P, Allard MA, Vibert E, Cherqui D, Pelletier G, Cunha AS, Guettier C, Vallee JC, Saliba F, Bismuth H, Samuel D, Castaing D, Adam R. Salvage versus primary liver transplantation for early hepatocellular carcinoma: Do both strategies yield similar outcomes? Ann Surg. 2016; 264:155-163.
11. Lu WP, Dong JH. Hepatectomy for hepatocellular carcinoma in the era of liver transplantation. World J Gastroenterol. 2014; 20:9237-9244.
12. Yong CC, Tsai MC, Lin CC, Wang CC, Lu SN, Hung CH, Hu TH, Chen CL. Comparison of salvage living donor liver transplantation and local regional therapy for recurrent hepatocellular carcinoma. World J Surg. 2016; 40:2472-2480.
13. Yang L, Huang Y, Deng D, Liu J, Xu L, Yi P. Efficacy and prognostic impact of preoperative risk factors for salvage liver transplantation and repeat hepatectomy in patients with early-stage recurrent hepatocellular carcinoma: a propensity score-matched analysis. Front Oncol. 2025; 15:1547054.
14. Belghiti J, Cortes A, Abdalla EK, Régimbeau JM, Prakash K, Durand F, Sommacale D, Dondero F, Lesurtel M, Sauvanet A, Farges O, Kianmanesh R. Resection prior to liver transplantation for hepatocellular carcinoma. Ann Surg. 2003; 238:885-892; discussion 892-893.
15. Rhu J, Kim JM, Choi GS, Kwon CHD, Joh JW. Continuing five or more locoregional therapies before living donor salvage liver transplantation for hepatocellular carcinoma is related to poor recurrence-free survival. Ann Surg Treat Res. 2018; 95:152-160.
16. Lee S, Hyuck David Kwon C, Man Kim J, Joh JW, Woon Paik S, Kim BW, Wang HJ, Lee KW, Suh KS, Lee SK. Time of hepatocellular carcinoma recurrence after liver resection and alpha-fetoprotein are important prognostic factors for salvage liver transplantation. Liver Transpl. 2014; 20:1057-1063.
17. Lee SG. Salvage living-donor liver transplantation to previously hepatectomized hepatocellular carcinoma patients: Is it a reasonable strategy? Hepatobiliary Pancreat Dis Int. 2013; 12:10-11.
18. Fuks D, Dokmak S, Paradis V, Diouf M, Durand F, Belghiti J. Benefit of initial resection of hepatocellular carcinoma followed by transplantation in case of recurrence: An intention-to-treat analysis. Hepatology 2012; 55:132-140.
19. Sugawara Y, Hibi T. Recent trends and new developments in liver transplantation. Biosci Trends. 2024; 18:206-211.
20. Yamashita Y, Yoshida Y, Kurihara T, Itoh S, Harimoto N, Ikegami T, Yoshizumi T, Uchiyama H, Shirabe K, Maehara Y. Surgical results for recurrent hepatocellular carcinoma after curative hepatectomy: Repeat hepatectomy versus salvage living donor liver transplantation. Liver Transpl. 2015 ;21:961-968.
21. Tung-Ping Poon R, Fan ST, Wong J. Risk factors, prevention, and management of postoperative recurrence after resection of hepatocellular carcinoma. Ann Surg. 2000; 232:10-24.
22 Kudo M, Kawamura Y, Hasegawa K, *et al*. Management of hepatocellular carcinoma in Japan: JSH consensus statements and recommendations 2021 update. Liver Cancer. 2021; 10:181-223.
23. Nagasue N, Yukaya H, Ogawa Y, Sasaki Y, Chang YC, Niimi K. Second hepatic resection for recurrent hepatocellular carcinoma. Br J Surg. 1986; 73:434-438.
24. Itamoto T, Nakahara H, Amano H, Kohashi T, Ohdan H, Tashiro H, Asahara T. Repeat hepatectomy for recurrent hepatocellular carcinoma. Surgery 2007; 141:589-597.
25. Kakazu T, Makuuchi M, Kawasaki S, Miyagawa S, Hashikura Y, Kosuge T, Takayama T, Yamamoto J. Repeat hepatic resection for recurrent hepatocellular carcinoma. Hepatogastroenterology. 1993; 40:337-341.
26. Matsuda M, Fujii H, Kono H, Matsumoto Y. Surgical treatment of recurrent hepatocellular carcinoma based on the mode of recurrence: Repeat hepatic resection or ablation are good choices for patients with recurrent multicentric cancer. J Hepatobiliary Pancreat Surg. 2001; 8:353-359.
27. Wu CC, Cheng SB, Yeh DC, Wang J, P'eng FK. Second and third hepatectomies for recurrent hepatocellular carcinoma are justified. Br J Surg. 2009; 96:1049-1057.
28. Mise Y, Hasegawa K, Shindoh J, Ishizawa T, Aoki T, Sakamoto Y, Sugawara Y, Makuuchi M, Kokudo N. The feasibility of third or more repeat hepatectomy for

recurrent hepatocellular carcinoma. Ann Surg. 2015; 262:347-357.
29. Kokudo T, Takemura N, Inagaki F, Yoshizaki Y, Mihara F, Edamoto Y, Yamada K, Kokudo N. Laparoscopic minor liver resection for hepatocellular carcinoma. Jpn J Clin Oncol. 2023; 53:1087-1090.
30. Morise Z. Perspective of laparoscopic liver resection for hepatocellular carcinoma. World J Gastrointest Surg. 2015; 7:102-106.
31. Ali MA, Li WF, Wang JH, Lin CC, Chen YJ, Lin TL, Lin TS, Lu SN, Wang CC, Chen CL. Impact of pathological features of primary hepatocellular carcinoma on the outcomes of intrahepatic recurrence management: Single center experience from Southern Taiwan. HPB (Oxford). 2016; 18:851-860.
32. Lim C, Shinkawa H, Hasegawa K, Bhangui P, Salloum C, Gomez Gavara C, Lahat E, Omichi K, Arita J, Sakamoto Y, Compagnon P, Feray C, Kokudo N, Azoulay D. Salvage liver transplantation or repeat hepatectomy for recurrent hepatocellular carcinoma: An intent-to-treat analysis. Liver Transpl. 2017; 23:1553-1563.
33. Fang JZ, Xiang L, Hu YK, Yang Y, Zhu HD, Lu CD. Options for the treatment of intrahepatic recurrent hepatocellular carcinoma: Salvage liver transplantation or rehepatectomy? Clin Transplant. 2020; 34:e13831.
34. Kim JM, Joh JW, Yi NJ, Choi GS, Kwon CHD, Lee KW, Suh KS. 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.
35. Yoon YI, Song GW, Lee S, Moon D, Hwang S, Kang WH, Cho HD, Ha SM, Kim MJ, Kim SH, Na BG, Yang G, Min Kim S, Hyun Shim J, Park JI. Salvage living donor liver transplantation versus repeat liver resection for patients with recurrent hepatocellular carcinoma and Child-Pugh class A liver cirrhosis: A propensity score-matched comparison. Am J Transplant. 2022; 22:165-176.
36. Yang L, Huang Y, Deng D, Liu J, Xu L, Yi P. Efficacy and prognostic impact of preoperative risk factors for salvage liver transplantation and repeat hepatectomy in patients with early-stage recurrent hepatocellular carcinoma: A propensity score-matched analysis. Front Oncol. 2025; 15:1547054.

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