Global Health & Medicine. 2025; 7(6):414-415.

EDITORIAL

DOI: 10.35772/ghm.2025.01133

Surgical treatments for early-stage hepatocellular carcinoma: Resection versus transplantation

Takashi Kokudo[1,*], Takamune Yamaguchi[2], Nermin Halkic[3], Norihiro Kokudo[1]

[1] National Center for Global Health and Medicine, Japan Institute for Health Security, Tokyo, Japan;
[2] Department of Surgery, Tokyo Metropolitan Bokutoh Hospital, Tokyo, Japan;
[3] Clinique Cecil, Lausanne, Switzerland.

Abstract: Liver resection (LR) and liver transplantation (LT) are the two principal curative options for early-stage hepatocellular carcinoma (HCC), but the optimal choice for individual patients remains uncertain. Recent meta-analyses suggest that LT confers superior long-term survival compared with LR, particularly when tumor burden meets transplant criteria and donor availability is sufficient. Although LT requires lifelong immunosuppressive therapy, patient-reported quality of life appears comparable between LT and LR. Overall, current evidence indicates that LT may offer improved survival without compromising quality of life in appropriately selected patients.

***Keywords*:** hepatocellular carcinoma, liver transplantation, liver resection, quality of life

Hepatocellular carcinoma (HCC) is the sixth most common cancer and the third leading cause of cancer-related death worldwide (*1*). Liver resection (LR) and liver transplantation (LT) are the recommended first-line surgical treatments for HCC (*2*). A recent systematic review has demonstrated that LT offers better survival than LR (*3*). In this editorial, we focus on recent evidence comparing LT and LR for early-stage HCC and examine postoperative quality of life (QOL).

LT and living donor liver transplantation (LDLT)

Starzl *et al*. reported the first LT in 1963 (*4*). Since then, improvements in surgical techniques and perioperative patient care for LT have made LT a common, routine surgery. Mazzaferro *et al*. considered LT a standard treatment for HCC (*5*).

In Eastern countries, the scarcity of cadaveric donors prompts LDLT (*6*). Nonetheless, in both LDLT and deceased donor liver transplantation, the Milan criteria are mainly used as the indication for LT (*7*). The Milan criteria are the best-known criteria for LT (*5*). The criteria comprise a tumor ≤ 5 cm in diameter in patients with a single HCC and < 3 tumor nodules, each ≤ 3 cm in diameter in patients with multiple tumors.

The Milan criteria depend on morphological parameters and consider only 30% of the patients with HCC suitable for LT. Nevertheless, patients with tumors beyond the Milan criteria can have favorable outcomes after LT (*8*).

LR

LR is another curative surgical treatment for patients with HCC, resulting in long-term survival; however, LR is only applicable to a minority of patients. According to the Barcelona Clinic Liver Cancer staging and treatment guidelines, LR is recommended for patients with a single tumor without portal hypertension (*9*). However, these guidelines are not universally adopted, and Eastern guidelines, such as the Asian Pacific Association for the Study of the Liver guidelines (*10*), have radically different recommendations. There is growing evidence indicating that the prognosis after LR is comparable for 2–3 tumors (*11*). Therefore, the treatment most beneficial for patients with HCC up to three tumors remains unclear.

Comparing survival after LT and LR

Numerous studies have compared LT *vs*. LR in patients with early-stage HCC (*12*). Most studies reported superior long-term survival with LT compared with LR. As earlier meta-analyses have shown that LT results in better long-term survival, recent evaluations of treatment benefits now place increasing importance on patients' QOL, considering it just as crucial as the actual

therapy provided (*12*). As such, the focus is not only on achieving long-term survival but also on how patients live in relation to their disease and treatment (*13*).

One of the biggest differences between transplantation and resection is the low immune status caused by immunosuppressive agents in transplanted patients (*14*). Theoretically, a low immune status may increase the risk for infections, which may lower QOL scores. However, a previous study found no significant differences in QOL (*15*). In addition, daily treatment with immunosuppressants did not affect the recipients' physical QOL and psychological outcomes when compared with patients who underwent resection.

In conclusion, we highlight key considerations in the surgical management of early-stage HCC. The present evidence indicates that LT offers better survival outcomes in patients with acceptable tumor burden, provided that donor availability is sufficient. In addition, QOL after LT is comparable to that following LR, despite the requirement for lifelong immunosuppressive therapy.

Funding: This work was supported by the Japan Grant-in-Aid for Scientific Research (23K06739).

Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024; 74:229-263.
2. Vogel A, Meyer T, Sapisochin G, Salem R, Saborowski A. Hepatocellular carcinoma. Lancet. 2022; 400:1345-1362.
3. Rehman M, Shah M, Gul M, Shamoon V, Tariq MM, Bibi K, Ishola AO, Manoharan M, Anika NN, Bilal A. Long-term survival and recurrence after liver transplantation versus resection in cirrhotic hepatocellular carcinoma: A systematic review. Cureus. 2025; 17:e83418.
4. 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.
5. 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.
6. Sugawara Y, Hibi T. Recent trends and new developments in liver transplantation. Biosci Trends. 2024; 18:206-211.
7. Sequeira LM, Ozturk NB, Sierra L, Gurakar M, Toruner MD, Zheng M, Simsek C, Gurakar A, Kim AK. Hepatocellular carcinoma and the role of liver transplantation: An update and review. J Clin Transl Hepatol. 2025; 13:327-338.
8. Kokudo T, Kokudo N. Evolving indications for liver transplantation for hepatocellular carcinoma following the Milan criteria. Cancers (Basel). 2025; 17:507.
9. Reig M, Forner A, Rimola J, *et al*. BCLC strategy for prognosis prediction and treatment recommendation: The 2022 update. J Hepatol. 2022; 76:681-693.
10. Lau G, Obi S, Zhou J, *et al*. APASL clinical practice guidelines on systemic therapy for hepatocellular carcinoma–2024. Hepatol Int. 2024; 18:1661-1683.
11. Kokudo T, Ishizawa T, Nagata R, Ichida A, Mihara Y, Kawaguchi Y, Akamatsu N, Kaneko J, Arita J, Kokudo N, Hasegawa K. Optimal tumor numbers in surgical candidates for multiple hepatocellular carcinomas. Surgery. 2022; 172:1174-1178.
12. Beumer BR, de Wilde RF, Metselaar HJ, de Man RA, Polak WG, Ijzermans JNM. The treatment effect of liver transplantation versus liver resection for HCC: A review and future perspectives. Cancers (Basel). 2021; 13:3730.
13. Toro A, Pulvirenti E, Palermo F, Di Carlo I. Health-related quality of life in patients with hepatocellular carcinoma after hepatic resection, transcatheter arterial chemoembolization, radiofrequency ablation or not treatment. Surg Oncol. 2012; 21:e23-e30.
14. Gabrielli F, Bernasconi E, Toscano A, Avossa A, Cavicchioli A, Andreone P, Gitto S. Side Effects of Immunosuppressant Drugs After Liver Transplant. Pharmaceuticals (Basel). 2025; 18:342.
15. Lei JY, Yan LN, Wang WT, Zhu JQ, Li DJ. Health-related quality of life and psychological distress in patients with early-stage hepatocellular carcinoma after hepatic resection or transplantation. Transplant Proc. 2016; 48:2107-2111.

Received December 5, 2025; Revised December 11, 2025; Accepted December 15, 2025.

Released online in J-STAGE as advance publication December 18, 2025.

**Address correspondence to*:
Takashi Kokudo, National Center for Global Health and Medicine, Japan Institute for Health Security, 1-21-1 Toyama, Shinjuku-ku, Tokyo 162-8655, Japan.
E-mail: kokudo-tky@umin.ac.jp