Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Comparison of Recurrence-Free Survival Between Hemihepatectomy and Non-hemihepatectomy in Patients with Hepatocellular Carcinoma ≥5 cm: A retrospective study (Orginal article)

Kunyuan Jiang
Kunshan Second People's Hospital
Jingfei Li
the First Affiliated Hospital of the University of Science and Technology of China
Minzi Huan
Kunshan Second People's Hospital
Jun Chang
Kunshan Second People's Hospital
Dongli Zhang
ahmu1609@163.com
Kunshan Second People's Hospital

Research Article

Keywords:

Posted Date: November 18th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9651292/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Comparison of Recurrence-Free Survival Between Hemihepatectomy and Non-hemihepatectomy in Patients with Hepatocellular Carcinoma ≥5 cm: A retrospective study (Orginal article)

Kunyuan Jiang[1†], Jingfei Li[2†], Minzi Huan[1] , Jun Chang[1] , Dongli Zhang[1]

[1] Department of General Surgery, Kunshan Second People's Hospital,

[2]Department of Emergency Surgery, the First Affiliated Hospital of the University of Science and Technology of China

[†]Kunyuan Jiang and Jingfei Li contributed equally to this work and share first authorship.

Corresponding author: Dongli Zhang, Department of General Surgery, Kunshan Second People's Hospital, No. 999 Qianjin Road, Kunshan 215300, Suzhou, China Tel: +86-13451796875. Email:ahmu1609@163.com ORCID: 0000-0001-0288-0924

Ethics Approval Statement and Informed Consent

This study was reviewed and approved by the Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China (ID:2026-RE-166) and Kunshan Second People's Hospital (ID:ksehllsp 2026-003).

Informed consent statement

Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Data sharing statement

Dataset available from the corresponding author at ahmu1609@163.com

Author contributions

Kunyuan Jiang and Jingfei Li designed and conducted the study and wrote the paper; Minzi Huan and Jun Chang provided clinical advice and contributed to the analysis; Dongli Zhang supervised the study.

Disclosure

The authors report no conflicts of interest in this work.

Acknowledgments

None

Funding

None

Abstract

Background

As a standard anatomical liver resection procedure, hemihepatectomy offers the advantages of anatomical resection but also carries the disadvantage of removing more liver parenchyma. This retrospective study primarily evaluates the effect of hemihepatectomy on postoperative recurrence-free survival (RFS) in patients with large hepatocellular carcinoma exceeding 5 cm in diameter.

Methods

Data from dual-centers on HCC patients with solitary HCC ≥5 cm who underwent hepatectomy between January 2019 and December 2022 was analyzed retrospectively. Patients were categorized into hemihepatectomy and non-hemihepatectomy group

based on the surgical approach. The primary endpoint was RFS. Propensity score matching (PSM) was employed to control for potential confounding variables between the two groups.

Results

A total of 266 enrolled patients were categorized into hemihepatectomy (n=86) and non-hemihepatectomy group (n=180). No significant difference in RFS was observed between these two groups either before (median 17.1 vs. 18.1 months, P = 0.984) or after PSM (median 20.6 vs. 18.1 months, P = 0.914). Cox regression identified AFP ≥200 ng/mL (HR = 1.866, 95% CI: 1.390-2.505, P < 0.001) and MVI positivity (HR = 1.882, 95% CI: 1.362-2.600, P < 0.001) as independent risk factors for reduced RFS.

Conclusions

In HCC tumors ≥5 cm, hemihepatectomy showed no significant RFS improvement compared to non-hemihepatectomy overall. Tumor biological characteristics (AFP levels and MVI status) are the primary determinants of postoperative prognosis in HCC patients.

Keywords: Hemihepatectomy, Hepatocellular carcinoma, Recurrence-free survival, Propensity score analysis, Microvascular invasion, Alpha-fetoprotein

Introduction

Hepatocellular carcinoma (HCC) is the fifth most common cancer and the second leading cause of cancer death in China(1). Current international clinical guidelines consistently recommend surgical resection as the primary curative treatment for solitary HCC without major vascular invasion.(2-4). However, the high postoperative

recurrence rate markedly diminishes its therapeutic efficacy, leading to compromised long-term survival outcomes.(5, 6). Particularly in patients with large HCC, the inherently higher malignant potential is associated with significantly elevated postoperative recurrence rates(7, 8).

HCC exhibits highly aggressive biological behavior, with dissemination along the portal venous territory constituting its primary pathological route of spread. This mechanism represents a major contributor to both intrahepatic metastasis and postoperative local recurrence(9). In the 1980s, Professor Makuuchi introduced the concept of completely resecting the tumor-bearing portal territory, known as anatomical liver resection (AR)(10) . AR employs the portal vein-based segments or subsegments defined by the Couinaud classification as fundamental anatomical units. By completely resecting the entire segment, AR removes the tumor along with its portal venous tributaries, thereby eliminating potential micrometastases and dissemination pathways. This approach aims to prevent HCC spread via the portal system and reduce postoperative recurrence(11).

Hemihepatectomy, which typically employs regional hemihepatic inflow occlusion, is considered a hallmark AR procedure due to its reliance on fixed anatomical landmarks. It enables in-situ resection without liver mobilization, minimizing tumor manipulation and adhering to the oncological principle of "no-touch" technique(12). Despite its benefits as an anatomical approach, hemihepatectomy requires substantial parenchymal sacrifice that may impair hepatic function and prognosis(13). This inherent trade-off justifies its selective use for large HCC resection. Current research on

hemihepatectomy predominantly focuses on technical aspects of the procedure and safety, while robust evidence regarding its comparative advantage over other surgical approaches in terms of long-term survival for HCC patients remains limited(14-16). This study aims to compare recurrence-free survival (RFS) between hemihepatectomy and non-hemihepatectomy in patients with HCC ≥5 cm and to evaluate the therapeutic efficacy of hemihepatectomy for large HCC.

Methods

Study design and patient cohort

We conducted a dual-center retrospective cohort study analyzing consecutive patients who underwent curative-intent hepatectomy for HCC between January 2019 and December 2022. Inclusion criteria: (1) aged 18–85 years with treatment-naive HCCs (no prior systemic therapy, transarterial chemoembolization, or ablation). (2) ECOG performance status 0–1 and Child-Pugh class A, with preserved cardiopulmonary, lung and renal function on preoperative evaluation. (3) with no radiological evidence of vascular invasion or extrahepatic tumors before surgery. (4) R0 resection achieved (microscopically negative margins, no macroscopic vascular or biliary thrombi). (5) postoperative pathologic confirmation of solitary HCC ≥ 5cm. (6)complete clinical datasets were available, and patients were actively followed up with full access to their outcome information. Exclusion criteria: (1) had received any antitumor therapy prior to surgery or recurrent tumor after initial resection. (2) not HCC or tumor size < 5cm, or positive resection margins confirmed by pathological results. (3) major postoperative complications (Clavien-Dindo grade ≥III) or 90-day postoperative mortality. (4)

incomplete medical records or lost to follow-up. (5) extended hemihepatectomy or central hepatectomy or other anatomical resection. (Fig 1).

Ultimately, 266 patients were enrolled in this study and categorized into two groups based on surgical approach: the hemihepatectomy group (n=86) and the non-hemihepatectomy group (n=180).

Surgical procedure and definition

All patients underwent standardized preoperative assessment to confirm surgical candidacy. Absolute contraindications (including extrahepatic metastasis, unresectable vascular invasion, or inadequate future liver remnant) were systematically excluded. Curative-intent resection was performed by fellowship-trained hepatobiliary surgeons (minimum 5 years of subspecialty experience). Non-hemihepatectomy was defined as partial hepatic resection involving less than a hemiliver, specifically excluding procedures meeting criteria for anatomical resection. Anatomical resection entails systematic removal of tumor-bearing portal territories. Essential components include: (a) selective inflow control via Glissonean approach, (b) visualization of segmental borders with ICG/IOUS(17).

Outcome endpoints and follow up

All clinical data were prospectively collected. Patients underwent regular follow-up assessments via scheduled outpatient visits and telephone interviews until tumor recurrence or the last contact date. Standardized follow-up protocols documented recurrence status, time-to-recurrence, recurrence patterns (intrahepatic/extrahepatic), and survival outcomes. The primary endpoint was recurrence-free survival (RFS),

defined as the duration from radical resection to the first radiologically confirmed HCC recurrence. Tumor recurrence required definitive imaging evidence from at least one of the following modalities: contrast-enhanced ultrasound (CEUS), multiphase contrast-enhanced computed tomography (CECT), or gadoxetic acid-enhanced magnetic resonance imaging (MRI). All patients were followed for a minimum of 24 months postoperatively or until an endpoint event (recurrence or death).

Statistical analysis

Statistical analyses were performed using SPSS version 26.0 and the R software environment (version 4.1.1; available at https://www.r-project.org/). Continuous variables were expressed as median and interquartile range (IQR). Categorical variables were summarized as frequencies and percentages. Group comparisons employed the Mann-Whitney U test for continuous variables and the χ^2 test for categorical variables. To mitigate selection bias, 1:1 propensity score matching (PSM) was implemented using a nearest-neighbor algorithm with a caliper width of 0.02 to balance baseline characteristics between the hemihepatectomy and the non-hemihepatectomy groups. Matching covariates included age, gender, BMI, AFP level, hepatitis B cirrhosis status, intraoperative transfusion, tumor size, histological differentiation, and MVI. Survival curves were constructed via the Kaplan-Meier method, with between-group differences assessed by log-rank tests. Univariable Cox proportional hazards regression models were fitted to evaluate all candidate prognostic factors for recurrence-free survival (RFS), including: BMI, AFP level, hepatitis B cirrhosis, surgical approach (hemihepatectomy vs. non-hemihepatectomy),

intraoperative transfusion, tumor size, histological differentiation, and MVI status. Variables exhibiting a univariable P value <0.1 were incorporated into the multivariable Cox model to calculate adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). Statistical significance was defined as a two-sided P value <0.05 for all analyses.

Results

Patients and baseline characteristics

Between January 2019 and December 2022, 266 consecutive patients undergoing curative resection for HCC ≥5 cm were enrolled, comprising 224 males (84.2%) and 42 females (15.8%), with a median age of 58 years (range: 26-83). The cohort were stratified into hemihepatectomy (n=86) and non-hemihepatectomy (n=180) groups.

Before PSM, significant differences existed between the two groups. Patients undergoing hemihepatectomy were younger (median 55 vs. 58 years, P=0.023) and had lower albumin levels (39.2 vs. 40.6 g/L, P=0.028). Notably, the hemihepatectomy group exhibited higher rates of aggressive tumor features, including elevated AFP (≥200 ng/mL: 57.0% vs. 37.8%, P=0.003), larger tumor size (≥10 cm: 53.5% vs. 22.2%, P<0.001), and MVI positivity (74.4% vs. 58.9%, P=0.014), collectively indicating tumors with higher malignant potential. Additionally, hemihepatectomy required longer operative time (230 vs. 185 min, P=0.001) and incurred greater blood loss (300 vs. 200 mL, P=0.042), reflecting greater procedural complexity.

After PSM, 138 patients (69 per group) demonstrated balanced baseline characteristics across all covariates (P>0.05), except for persistently longer operative time (230 vs. 180 min, P<0.001) and lower albumin levels (39.0 vs. 41.7 g/L, P=0.025) in the

hemihepatectomy cohort. Blood loss showed a trend toward significance (300 vs. 200 mL, P=0.055). (Table 1)

Survival outcomes before and after PSM

With a median follow-up of 40.7 months among recurrence-free patients, tumor recurrence occurred in 180 cases (67.7%). The median time to recurrence was 9.3 months. No significant difference in RFS was observed between hemihepatectomy and non-hemihepatectomy groups before (median 17.1 vs. 18.1 months, P = 0.984) or after PSM (median 20.6 vs. 18.1 months, P = 0.914). (Fig 2A and 2B) Multivariable Cox regression identified AFP ≥200 ng/mL (HR = 1.866, 95% CI: 1.390-2.505; P<0.001) and MVI positivity (HR = 1.882, 95% CI: 1.362-2.600; P<0.001) as independent risk factors for reduced RFS. In the PSM cohort, multivariable Cox regression yielded similar findings: AFP ≥200 ng/mL (HR=1.842, 95% CI: 1.216–2.790, P=0.004) and MVI positivity (HR=1.858, 95% CI: 1.129–3.060, P=0.015) remained independently associated with reduced RFS. (Table 2)

Subgroup analyses stratified by MVI and AFP status between two groups: MVI-positive: 8.8 vs. 14.5 months (P = 0.623) ; MVI-negative: 50.9 vs. 30.1 months (P = 0.124) (Fig 3C and 3D); AFP ≥200 ng/mL: 7.4 vs. 11.7 months (P = 0.568) ; AFP <200 ng/mL: 50.9 vs. 29.7 months (P = 0.114).(Fig 4E and 4F)

Discussion

Despite significant advances in systemic therapies, curative treatment for HCC still primarily relies on surgical and locoregional approaches, with radical resection being the cornerstone(18, 19). Unlike small HCCs (<5 cm), which offer multiple potentially

curative options (surgical resection, local ablation, liver transplantation) and generally have a more favorable prognosis, large HCCs (≥5 cm) often present with surgical resection as the sole potentially curative modality(20). Besides, these larger HCCs are frequently associated with higher recurrence rates due to their more aggressive biological behavior(8). Consequently, reducing postoperative recurrence is a critical strategy and an urgent clinical need for improving the prognosis of this patient population, representing a major challenge for surgeons.

The mechanisms underlying HCC recurrence after resection are relatively well-established. Based on the timing of recurrence, it is conventionally categorized as early recurrence (within 2 years postoperatively) or late recurrence (beyond 2 years). Compared to late recurrence, early recurrence is generally associated with a significantly worse prognosis(21-23). Early recurrence is currently attributed to the presence and dissemination of microscopic cancer foci that are undetectable by preoperative imaging or intraoperative visual inspection. The development of these micro-metastases is closely linked to the aggressive characteristics of the primary resected HCC. While various studies have identified different risk factors for postoperative recurrence, microvascular invasion (MVI), elevated alpha-fetoprotein (AFP) levels, and large tumor size are widely recognized as significant predictors(7, 24, 25). This aligns with the findings of the present study, which identified MVI positivity and AFP ≥200 ng/mL as independent risk factors for recurrence in large HCC patients. According to the proposed mechanisms of recurrence, eliminating potential residual microscopic disease during or after surgery could theoretically prevent or delay

recurrence. However, previously explored strategies utilizing prophylactic adjuvant therapies – such as transarterial chemoembolization (TACE) or combined immunotherapy and targeted agents – aimed at reducing recurrence, have yielded disappointing results(26-28). Consequently, current guidelines no longer recommend any specific adjuvant therapy regimen(3).

Surgical refinements, particularly anatomic hepatectomy, offer a theoretical advantage by removing potential microscopic spread along the tumor-bearing portal territory. Several clinical studies support this notion; for instance, two meta-analyses analyzing outcomes in overall HCC patients and those with MVI, respectively, concluded that anatomic resection reduces recurrence rate(29, 30). Nevertheless, conflicting evidence exists, with other studies reporting no significant survival benefit associated with anatomic hepatectomy, leaving its impact on HCC prognosis controversial(31, 32). We postulate several potential reasons for these inconsistent findings: (1) Heterogeneity in defining anatomic resection: Despite established definitions, strict adherence to the criteria for anatomic hepatectomy may vary across included studies. (2) Differences in patient populations: The efficacy of anatomic resection may be limited to specific HCC subgroups, and varying patient selection criteria across studies could lead to divergent conclusions. (3) Variability within anatomic resection techniques: Even among procedures classified as anatomic, different extents of resection may yield different outcomes. Therefore, investigating the prognostic impact of specific surgical techniques on well-defined HCC subgroups is essential for drawing more precise conclusions.

This study focused on a specific high-risk population: patients with single, large HCCs (≥5 cm). Furthermore, it evaluated a specific, standardized, and readily reproducible type of anatomic resection: hemihepatectomy. The control group excluded other major anatomic resections, particularly extended hemihepatectomy and central hepatectomy, thereby providing a clearer assessment of hemihepatectomy's impact on long-term outcomes in this cohort. Our key finding was that hemihepatectomy did not confer a significant advantage in recurrence-free survival (RFS) compared to non-hemihepatectomy procedures. Subgroup analysis, however, suggested a potential therapeutic benefit of hemihepatectomy in patients with tumors exhibiting less aggressive biology (AFP <200 ng/mL or MVI negative), compared to those with more aggressive features (AFP ≥200 ng/mL or MVI positive). This may stem from the dual nature of hemihepatectomy: while it offers the theoretical oncological benefit of anatomic resection, it also entails the disadvantage of removing a larger volume of functional liver parenchyma, potentially impacting postoperative liver function and recovery(13, 33-35). This differential effect across subgroups underscores that the intrinsic biological behavior of HCCs may be a more critical determinant of prognosis than the specific surgical approach. However, the limited sample size within these subgroups necessitates caution and further validation of this observation. Given the limited progress in neoadjuvant and adjuvant therapies for HCC, our findings lend support to the emerging concept of precision liver surgery, which aims to optimize the critical balance between radical tumor eradication, maximal parenchymal preservation, and minimal surgical trauma, leveraging advancements in high-resolution imaging and

intraoperative navigation technologies to potentially improve outcomes for HCC patients(34, 36).

This study has several limitations. Firstly, its retrospective design, despite employing strict inclusion/exclusion criteria and propensity score matching, cannot entirely eliminate the influence of confounding factors. Secondly, the important prognostic factor of surgical margin status was regrettably not assessed due to concerns regarding the reliability and consistency of available data(37, 38). Thirdly, the relatively small overall sample size, particularly after subgroup stratification, limits the statistical power and generalizability of the conclusions. Higher-level evidence from prospective studies or larger multi-center analyses is warranted to confirm these findings.

Conclusion

Tumor biological characteristics (AFP levels and MVI status) constitute the primary determinants of postoperative prognosis in HCC patients, outweighing the influence of surgical approach. While hemihepatectomy demonstrated a marginal trend towards improved RFS potentially confined to patients with low-malignancy HCC (AFP<200 ng/mL or MVI-negativity), its impact on RFS in high-malignancy subgroups (AFP≥200 ng/mL or MVI-positive) appeared unaffected.

References

1. Hwang SY, Danpanichkul P, Agopian V, Mehta N, Parikh ND, Abou-Alfa GK, et al. Hepatocellular carcinoma: updates on epidemiology, surveillance, diagnosis and treatment. Clin Mol Hepatol. 2025;31(Suppl):S228-s54.

2. Reig M, Forner A, Rimola J, Ferrer-Fàbrega J, Burrel M, Garcia-Criado Á, et al.

BCLC strategy for prognosis prediction and treatment recommendation: The 2022 update. J Hepatol. 2022;76(3):681-93.

3. Taddei TH, Brown DB, Yarchoan M, Mendiratta-Lala M, Llovet JM. Critical Update: AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. Hepatology. 2025;82(1):272-4.

4. [Guidelines for diagnosis and treatment of primary liver cancer in China (2019 edition)]. Zhonghua Gan Zang Bing Za Zhi. 2020;28(2):112-28.

5. He Y, Luo L, Shan R, Qian J, Cui L, Wu Z, et al. Development and Validation of a Nomogram for Predicting Postoperative Early Relapse and Survival in Hepatocellular Carcinoma. J Natl Compr Canc Netw. 2023;22(1d):e237069.

6. Liu D, Song T. Changes in and challenges regarding the surgical treatment of hepatocellular carcinoma in China. Biosci Trends. 2021;15(3):142-7.

7. Hwang S, Lee YJ, Kim KH, Ahn CS, Moon DB, Ha TY, et al. The Impact of Tumor Size on Long-Term Survival Outcomes After Resection of Solitary Hepatocellular Carcinoma: Single-Institution Experience with 2558 Patients. J Gastrointest Surg. 2015;19(7):1281-90.

8. Liang BY, Gu J, Xiong M, Zhang EL, Zhang ZY, Chen XP, et al. Tumor size may influence the prognosis of solitary hepatocellular carcinoma patients with cirrhosis and without macrovascular invasion after hepatectomy. Sci Rep. 2021;11(1):16343.

9. Sun J, Xia Y, Shen F, Cheng S. Chinese expert consensus on the diagnosis and treatment of hepatocellular carcinoma with microvascular invasion (2024 edition). Hepatobiliary Surg Nutr. 2025;14(2):246-66.

309 10. Takamoto T, Makuuchi M. Precision surgery for primary liver cancer. Cancer Biol
310 Med. 2019;16(3):475-85.
311 11. Shindoh J, Makuuchi M, Matsuyama Y, Mise Y, Arita J, Sakamoto Y, et al.
312 Complete removal of the tumor-bearing portal territory decreases local tumor
313 recurrence and improves disease-specific survival of patients with hepatocellular
314 carcinoma. J Hepatol. 2016;64(3):594-600.
315 12. Vega EA, Salehi O, Panettieri E, Salirrosas O, Brauner E, Mellado S, et al.
316 Subsegmental approaches to S7: anatomic laparoscopic transdiaphragmatic and
317 nonanatomic robotic transthoracic. Surg Endosc. 2023;37(10):8154-5.
318 13. Liang BY, Gu J, Xiong M, Zhang EL, Zhang ZY, Lau WY, et al. Histological
319 Severity of Cirrhosis Influences Surgical Outcomes of Hepatocellular Carcinoma After
320 Curative Hepatectomy. J Hepatocell Carcinoma. 2022;9:633-47.
321 14. Ji J, Hu D, Wang J, Hou Z, Zhang Z, Wang H, et al. Textbook outcome and survival
322 following laparoscopic versus open right hemihepatectomy for hepatocellular
323 carcinoma: A propensity score-matched study. Biosci Trends. 2025;19(4):445-55.
324 15. Cai X. Laparoscopic liver resection: the current status and the future. Hepatobiliary
325 Surg Nutr. 2018;7(2):98-104.
326 16. Gong WF, Zhong JH, Lu Z, Zhang QM, Zhang ZY, Chen CZ, et al. Evaluation of
327 liver regeneration and post-hepatectomy liver failure after hemihepatectomy in patients
328 with hepatocellular carcinoma. Biosci Rep. 2019;39(8).
329 17. Makuuchi M. Surgical treatment for HCC--special reference to anatomical
330 resection. Int J Surg. 2013;11 Suppl 1:S47-9.

18. Brown ZJ, Tsilimigras DI, Ruff SM, Mohseni A, Kamel IR, Cloyd JM, et al. Management of Hepatocellular Carcinoma: A Review. JAMA Surg. 2023;158(4):410-20.

19. Fu Y, Yang Z, Liu S, Guan R, Wang X, Chen J, et al. Comparison of resection, ablation, and stereotactic body radiation therapy in treating solitary hepatocellular carcinoma ≤5 cm: a retrospective, multicenter, cohort study. Int J Surg. 2025;111(1):1535-40.

20. Xie DY, Zhu K, Ren ZG, Zhou J, Fan J, Gao Q. A review of 2022 Chinese clinical guidelines on the management of hepatocellular carcinoma: updates and insights. Hepatobiliary Surg Nutr. 2023;12(2):216-28.

21. Tabrizian P, Jibara G, Shrager B, Schwartz M, Roayaie S. Recurrence of hepatocellular cancer after resection: patterns, treatments, and prognosis. Ann Surg. 2015;261(5):947-55.

22. Nevola R, Ruocco R, Criscuolo L, Villani A, Alfano M, Beccia D, et al. Predictors of early and late hepatocellular carcinoma recurrence. World J Gastroenterol. 2023;29(8):1243-60.

23. Wang MD, Li C, Liang L, Xing H, Sun LY, Quan B, et al. Early and Late Recurrence of Hepatitis B Virus-Associated Hepatocellular Carcinoma. Oncologist. 2020;25(10):e1541-e51.

24. Hu H, Qi S, Zeng S, Zhang P, He L, Wen S, et al. Importance of Microvascular Invasion Risk and Tumor Size on Recurrence and Survival of Hepatocellular Carcinoma After Anatomical Resection and Non-anatomical Resection. Front Oncol.

353 2021;11:621622.
354 25. Norman JS, Li PJ, Kotwani P, Shui AM, Yao F, Mehta N. AFP-L3 and DCP
355 strongly predict early hepatocellular carcinoma recurrence after liver transplantation. J
356 Hepatol. 2023;79(6):1469-77.
357 26. Bruix J, Takayama T, Mazzaferro V, Chau GY, Yang J, Kudo M, et al. Adjuvant
358 sorafenib for hepatocellular carcinoma after resection or ablation (STORM): a phase 3,
359 randomised, double-blind, placebo-controlled trial. Lancet Oncol.
360 2015;16(13):1344-54.
361 27. Ma T, Bai X, Zhang Q, Chen W, Huang K, Qian T, et al. Adjuvant transarterial
362 chemoembolization for hepatocellular carcinoma following curative resection: A
363 randomized, open-label, phase 3 trial. Hepatology. 2025.
364 28. Llovet JM, Pinyol R, Yarchoan M, Singal AG, Marron TU, Schwartz M, et al.
365 Adjuvant and neoadjuvant immunotherapies in hepatocellular carcinoma. Nat Rev Clin
366 Oncol. 2024;21(4):294-311.
367 29. Jiao S, Li G, Zhang D, Xu Y, Liu J, Li G. Anatomic versus non-anatomic resection
368 for hepatocellular carcinoma, do we have an answer? A meta-analysis. Int J Surg.
369 2020;80:243-55.
370 30. Sun Z, Li Z, Shi XL, He XW, Chen J, Song JH. Anatomic versus non-anatomic
371 resection of hepatocellular carcinoma with microvascular invasion: A systematic
372 review and meta-analysis. Asian J Surg. 2021;44(9):1143-50.
373 31. Hidaka M, Eguchi S, Okuda K, Beppu T, Shirabe K, Kondo K, et al. Impact of
374 Anatomical Resection for Hepatocellular Carcinoma With Microportal Invasion (vp1):

A Multi-institutional Study by the Kyushu Study Group of Liver Surgery. Ann Surg. 2020;271(2):339-46.

32. Li SQ, Huang T, Shen SL, Hua YP, Hu WJ, Kuang M, et al. Anatomical versus non-anatomical liver resection for hepatocellular carcinoma exceeding Milan criteria. Br J Surg. 2017;104(1):118-27.

33. Jiang K, Li J, Liu Z, Chen M, Cai W, Liu L, et al. Impact of major hepatectomy on recurrence after resection of hepatocellular carcinoma at CNLC Ib stage: a propensity score matching study. Int J Surg. 2025;111(1):857-64.

34. Magyar CTJ, Rajendran L, Li Z, Banz V, Vogel A, O'Kane GM, et al. Precision surgery for hepatocellular carcinoma. Lancet Gastroenterol Hepatol. 2025;10(4):350-68.

35. Torzilli G, McCormack L, Pawlik T. Parenchyma-sparing liver resections. Int J Surg. 2020;82s:192-7.

36. Tian F, Cao L, Chen J, Zheng S, Li J. 3D laparoscopic anatomical hepatectomy guided by 2D real-time indocyanine green fluorescence imaging for hepatocellular carcinoma. Hepatobiliary Surg Nutr. 2024;13(3):494-9.

37. Zhang XP, Xu S, Lin ZY, Gao QL, Wang K, Chen ZL, et al. Significance of anatomical resection and resection margin status in patients with HBV-related hepatocellular carcinoma and microvascular invasion: a multicenter propensity score-matched study. Int J Surg. 2023;109(4):679-88.

38. Yang S, Ni H, Zhang A, Zhang J, Zang H, Ming Z. Significance of anatomical resection and wide surgical margin for HCC patients with MVI undergoing

397 laparoscopic hepatectomy: A multicenter study. Eur J Surg Oncol. 2025;51(1):109353.

398

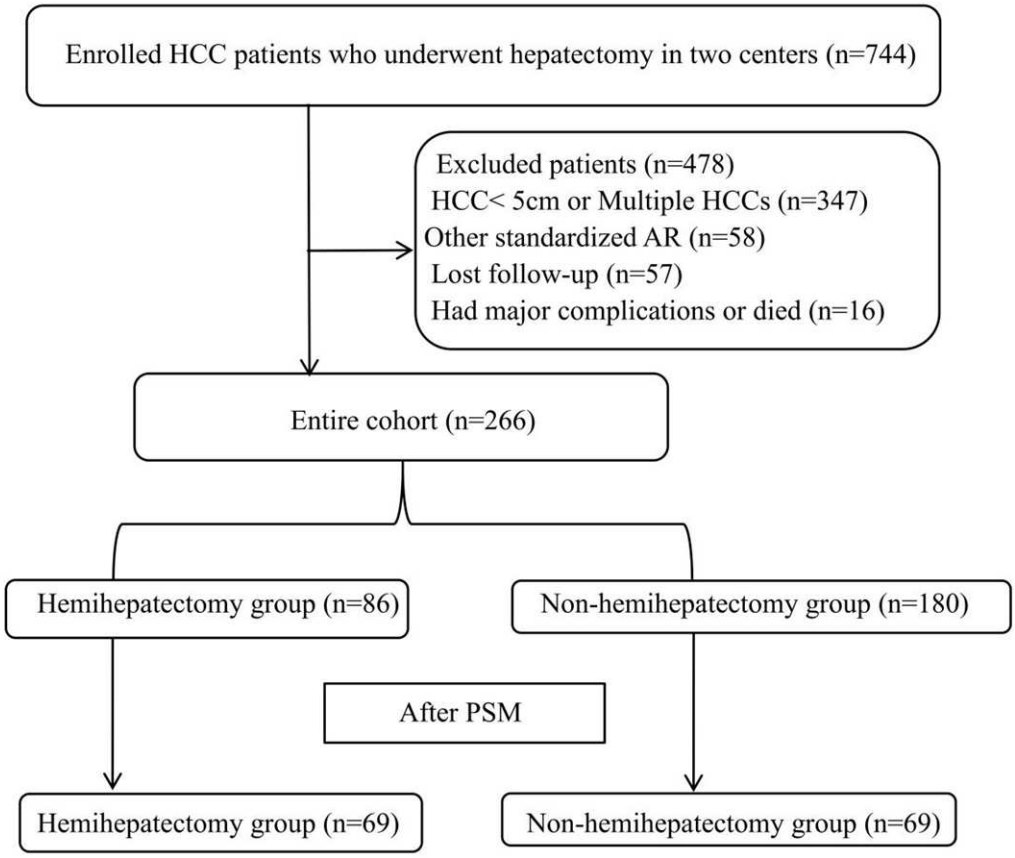


Fig 1 Flowchart of this study.

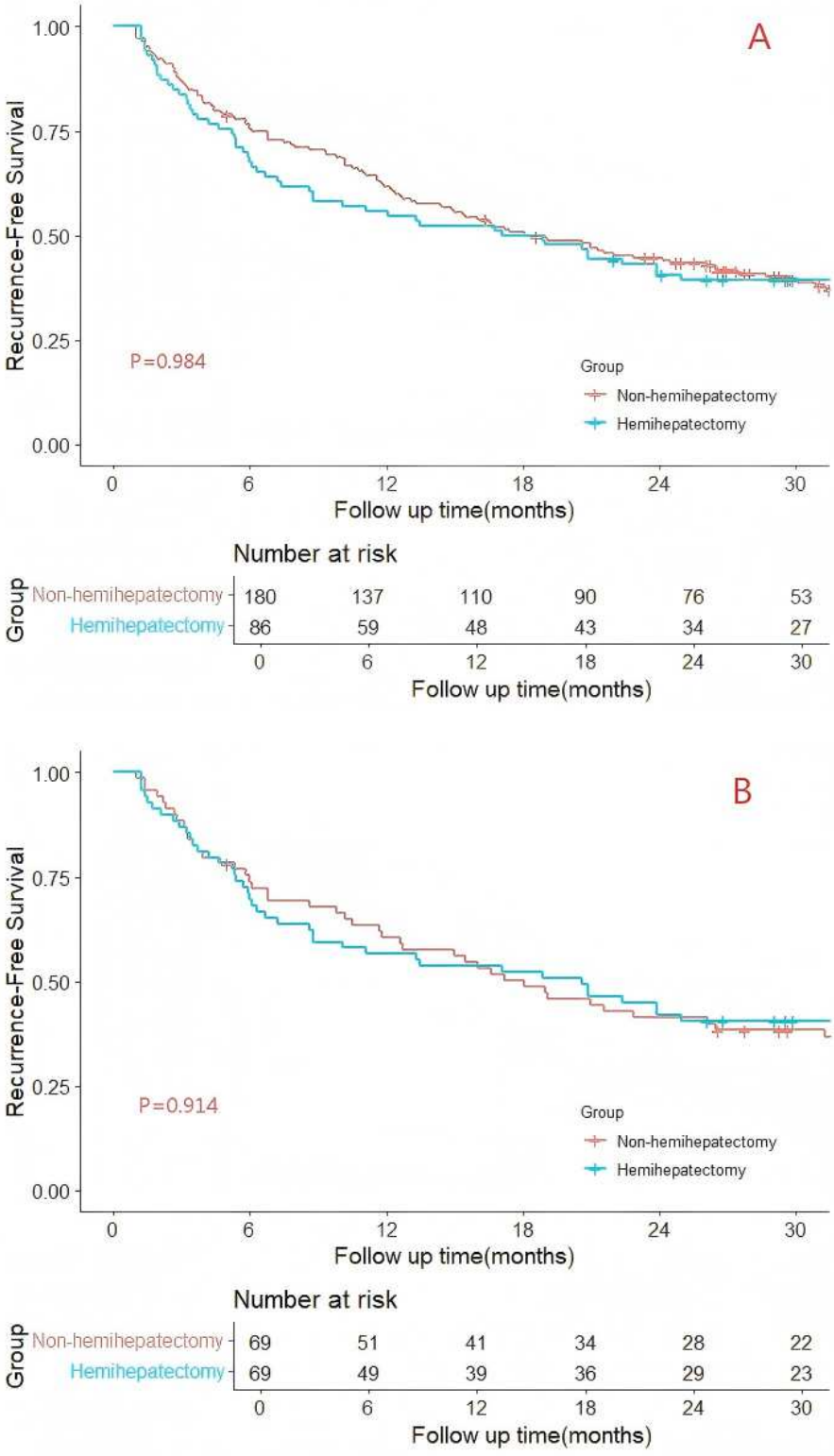


Fig 2 Kaplan-Meier analysis of RFS before(A) and after (B) PSM.

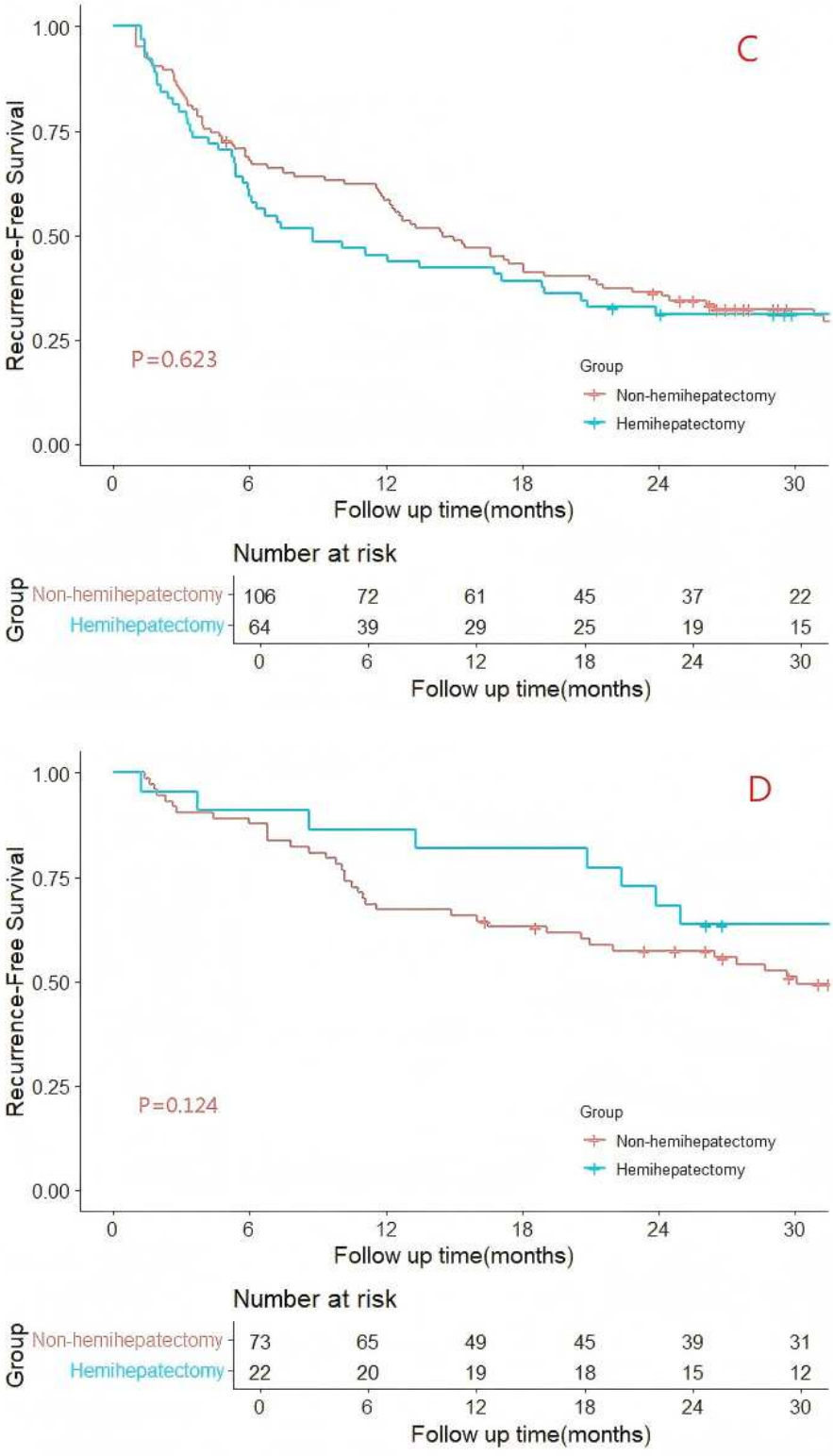


Fig 3 Kaplan-Meier analysis of RFS by MVI Status(C positive; D negative).

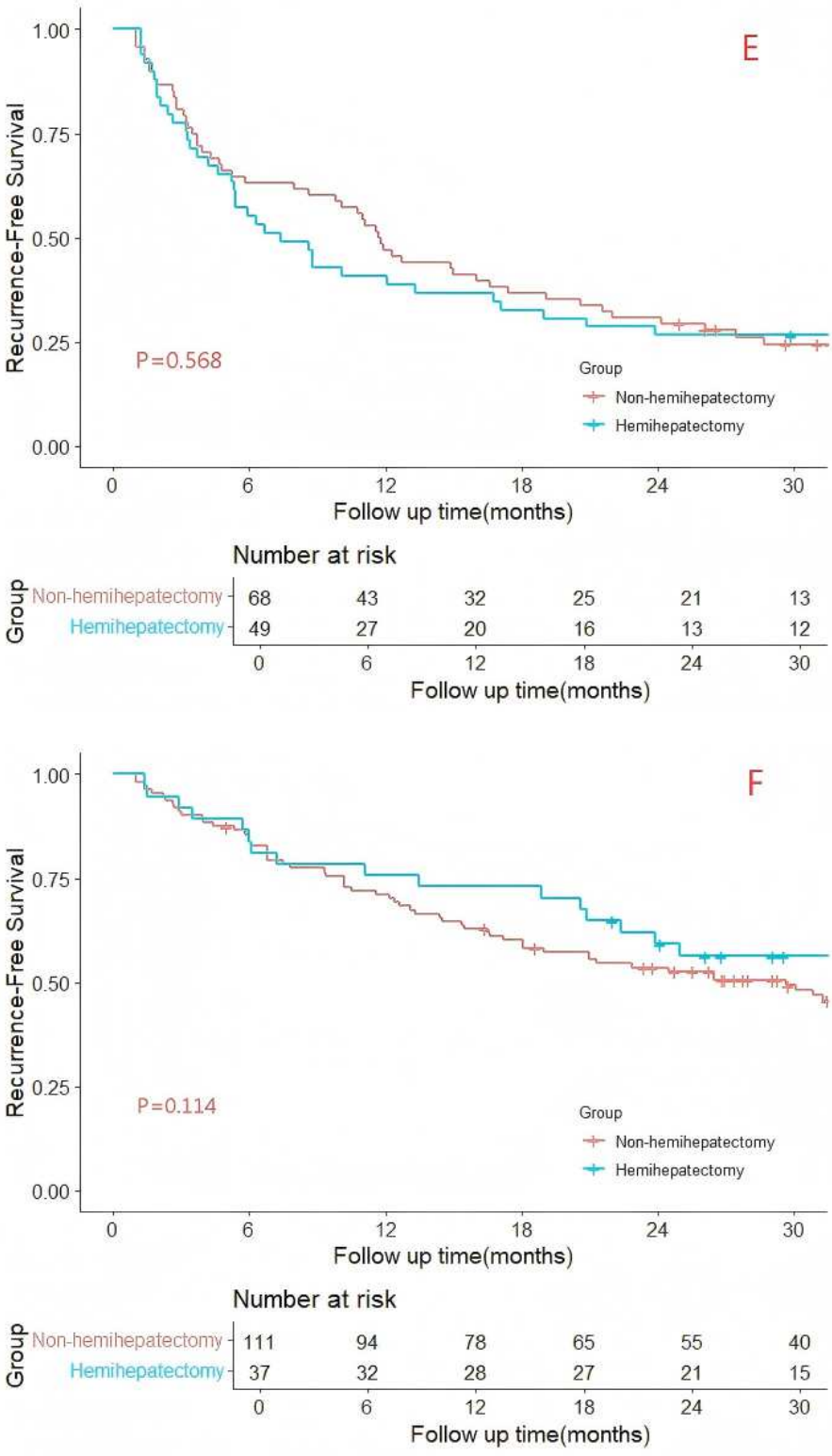


Fig 4 Kaplan-Meier analysis of RFS by AFP Status(E ≥200 ng/mL; D <200 ng/mL).

Table 1 Baseline demographic and disease characteristics before and after PSM

Variable	Before PSM			After PSM		
	Hemihepatectomy (n=86)	Non-hemihepatectomy (n=180)	*P* value	Hemihepatectomy (n=69)	Non-hemihepatectomy (n=69)	*P* value
Age（years）	55（52,58）	58（52,68）	0.023	56（49.0,66.0）	56（50.5,65.5）	0.886
Gender (male,n%)	79.1(68/86)	86.7 (156/180)	0.112	84.1（58/69）	81.2(56/69)	0.653
BMI ≥ 24 kg/m²,n%	47.7(41/86)	42.8 (77/180)	0.452	44.9(31/69)	50.7(35/69)	0.495
WBC count ($\times10^9$/L)	5.27（3.81,6.33）	5.22（4.32,6.43）	0.923	5.2（3.8，6.4）	5.2（4.5,6.6）	0.907
Platelet count ($\times10^9$/L)	168（132,220）	153（121,194）	0.047	168（131,218）	150（122,197）	0.159
Total bilirubin (μmol/L)	14.9（11.1,20.7）	15.7（12.0,21.5）	0.497	15.3（11.3,21.6）	15.1（12.9,21.3）	0.861
Albumin (g/L)	39.2（36.6,42.7）	40.6（37.9,43.7）	0.028	39.0（36.6,42.8）	41.7（38.4,45.1）	0.025
AFP ≥ 200 ng/ml,n（%）	57.0 (49/86)	37.8(68/180)	0.003	50.7(35/69)	46.4(32/69)	0.609
Hepatitis B cirrhosis,n%	61.6 (53/86)	69.4 (125/180)	0.205	65.2(45/69)	60.9(42/69)	0.597
Operation time (min)	230（177,270）	185（145,250）	0.001	230（180,270）	180（134,225）	<0.001
Blood loss (ml)	300（150,500）	200（100,500）	0.042	300（175，500）	200（100,400）	0.055
Intraoperative transfusion,n%	34.9 (30/86)	31.1 (56/180)	0.423	31.9（22/69）	29.0（20/69）	0.711
Tumor size ≥10 cm,n%	53.5 (46/86)	22.2 (40/180)	<0.001	43.5（30/69）	40.6（28/69）	0.730

Poor differentiation, n%	39.5 (34/86)	28.9 (52/180)	0.557	43.5（30/69）	44.9（31/69）	0.864
MVI (+), n(%)	74.4 (64/86)	58.9 (106/180)	0.014	71.0（49/69）	73.9（51/69）	0.703

BMI: Body mass index; WBC: White blood cell; AFP: Alpha-fetoprotein; MVI: Microvascular invasion

Table 2 Univariate and Multivariate Analysis for RFS in Patients with HCC ≥5cm

RFS	Number	Univariate Analysis			Multivariate Analysis		
		HR	**CI**	***P***	**HR**	**CI**	***P***
All patients (n=266)							
BMI(<24/≥24)	148/118	0.792	0.587-1.068	0.126			
AFP(<200/≥200ng/ml)	149/117	1.867	1.391-2.507	<0.001	1.866	1.390-2.505	<0.001
Hepatitis B cirrhosis (negative/positive)	88/178	1.224	0.889-1.685	0.215			
Hemihepatectomy (no/yes)	180/86	1.005	0.733-1.377	0.976			
Intraoperative transfusion(no/yes)	182/84	1.064	0.778-1.457	0.696			
Tumor size (5-10/≥10cm)	185/81	1.147	0.833-1.580	0.401			
Poor differentiation(no/yes)	154/112	1.200	0.892-1.613	0.228			
MVI(negative/positive)	96/170	1.885	1.364-2.604	<0.001	1.882	1.362-2.600	<0.001
Patients after PSM (n=138)							
BMI(<24/≥24)	72/66	0.755	0.498-1.145	0.186			
AFP(<200/≥200ng/ml)	71/67	1.863	1.230-2.822	0.003	1.842	1.216-2.790	0.004
Hepatitis B cirrhosis (negative/positive)	51/87	1.305	0.843-2.022	0.233			
Hemihepatectomy (no/yes)	69/69	0.978	0.648-1.475	0.914			
Intraoperative transfusion(no/yes)	96/42	1.100	0.705-1.719	0.674			
Tumor size (5-10/≥10cm)	80/58	1.145	0.320-0.740	0.523			
Poor differentiation(no/yes)	77/61	1.152	0.762-1.740	0.503			

MVI(negative/positive)	38/100	1.885	1.145-3.105	0.013		1.858	1.129-3.060	0.015