Am J Transl Res 2026;18(4):3097-3107
www.ajtr.org /ISSN:1943-8141/AJTR0170765

Original Article

Significance of surgical margin width versus anatomical resection for hepatocellular carcinoma

Ping Liu[1*], Ting Zhao[2,3*], Yang Shi[2*], Ning Yang[2], Jing-Ni Zhu[1]

[1]Department of Medical Oncology, The Affiliated Cancer Hospital of Nanjing Medical University, Jiangsu Cancer Hospital, Jiangsu Institute of Cancer Research, No. 42 Baiziting, Xuanwu District, Nanjing 210000, Jiangsu, China; [2]Department V of Hepatic Surgery, Eastern Hepatobiliary Surgery Hospital, Naval Medical University, Shanghai 201800, China; [3]Department of General Surgery, Suzhou Xiangcheng People's Hospital, Suzhou 215133, Jiangsu, China. [*]Equal contributors.

Received December 15, 2025; Accepted March 11, 2026; Epub April 15, 2026; Published April 30, 2026

Abstract: Objectives: Extensive research has examined the survival benefits of anatomical resection versus wide surgical margins in hepatocellular carcinoma (HCC). Yet how to choose between them in practice remains unsettled. We therefore investigated whether tumor size could inform this surgical decision. Methods: We retrospectively analyzed 302 patients with HCC who underwent curative liver resection at three centers between December 2009 and December 2010. Patients were divided into two groups according to tumor diameter: ≤3 cm (n=104) and >3 cm (n=198). Baseline clinicopathologic characteristics and longterm oncologic outcomes were compared between the two groups. We also assessed how surgical margin width (≥1 cm vs. <1 cm) and anatomical resection influenced overall survival (OS) and recurrencefree survival (RFS) in each subgroup. All statistical analyses were performed using SPSS 25.0 (IBM Corp., Armonk, NY). Results: The effect of surgical margin width on prognosis differed based on tumor size. Among patients with tumors >3 cm, a margin ≥1 cm was associated with better OS and RFS ($P<0.05$) and lower rates of early recurrence. For tumors ≤3 cm, survival correlated with multiple factors-including Hepatitis B Virus Deoxyribonucleic Acid (HBV-DNA) level, serum Alpha-fetoprotein (AFP), tumor number, Tumor-Node-Metastasis (TNM) stage, tumor capsule, microvascular invasion, and vascular thrombus but not with surgical margin width. Conclusion: Tumor diameter influences the choice of surgical strategy for HCC. Anatomical and nonanatomical resection yielded comparable prognosis for tumors ≤3 cm. For lesions larger than 3 cm, however, wide-margin resection offered better survival than anatomical resection alone.

Keywords: Hepatocellular carcinoma, margin, anatomical hepatectomy, tumor size, prognosis

Introduction

Hepatocellular carcinoma (HCC) is the sixth most common cancer and the third biggest cause of cancer-related deaths in the world [1]. Tumor size is widely accepted as a key factor for predicting outcome in HCC [1], but doctors still disagree on the best tumor diameter to use when making clinical decisions. The American Joint Committee on Cancer (AJCC) staging system was based on western patient groups, and it used a 5 cm cutoff for tumor (T) staging [2-4]. Chinese clinical guidelines, though, use a 3 cm cutoff [5]. These different standards made us think that HCCs of different sizes might act differently biologically - which is why we did this subgroup analysis.

Surgical resection offers potentially curative treatment for suitable HCC patients, but the 5-year recurrence rate remains up to 70% even with current surgical approaches [2-6]. Advances in laparoscopic surgery and a deeper understanding of liver anatomy have made anatomical resection more common. Still, surgeons disagree - does this approach truly outperform simple wide-margin resection?

Some studies have shown that a 1 cm surgical margin might improve oncologic outcomes [7-9], but other research cannot consistently confirm this [10-13]. We analyzed 302 HCC patients, splitting them into groups based on the 3 cm tumor threshold, to sort out these conflicting results. We focused specifically on

https://doi.org/10.62347/MNLC1449

whether the width of the surgical margin matters more for prognosis in small tumors (≤3 cm) compared to larger ones. Our goal was to give surgeons practical guidance when choosing between anatomical resection and wide-margin excision in day-to-day practice.

Materials and methods

Patients

This study enrolled 302 patients from three Chinese hospitals, all of whom underwent curative-intent liver resection for HCC during the period from December 2009 to December 2010. We included patients in this study only if they met all three criteria. First, they had histologically confirmed HCC. Second, curative resection. Third, we had complete data on surgical margin width, the type of resection (anatomical or non-anatomical), and follow-up information related to tumor recurrence and survival. We excluded patients who met any of the following criteria: (1) pathological diagnosis of a primary liver malignancy other than HCC; (2) incomplete or missing data on surgical margins, resection type, or follow-up outcomes; and (3) presence of other malignancies - either concurrent or previous - outside the liver. We extracted demographic and clinical data from each patient's electronic medical records, including age, sex, Tumor-Node-Metastasis (TNM) stage, serum Alpha-fetoprotein (AFP) level, Hepatitis B Virus Deoxyribonucleic Acid (HBV-DNA) level, number of tumors, and maximum tumor diameter. Pathologic features - such as thrombus, capsule status, microvascular invasion (MVI), and surgical margin width - were determined from histopathology reports. Operative records were also reviewed to confirm whether anatomical resection was performed. In this study, early postoperative recurrence was defined as the detection of new intra- or extrahepatic lesions within one year after curative resection. To minimize inter-institutional heterogeneity in surgical and perioperative management among the three participating centers, standardized criteria were applied throughout the treatment process. Preoperatively, liver function was required to be Child-Pugh class A or good Child-Pugh class B (score ≤7). For patients with evident cirrhotic nodules on preoperative imaging, an indocyanine green retention rate at 15 minutes of less than 10% was mandated. Anatomical resection was defined as complete removal of the tumor-bearing hepatic segment or lobe along with its corresponding portal pedicle and draining hepatic vein. Curative resection required complete tumor excision with negative microscopic margins on pathologic examination, along with no evidence of residual disease on both tumor marker assessment and imaging studies performed one month after surgery. In addition, for potentially complex hepatectomies, a multidisciplinary team (MDT) conducted a thorough preoperative evaluation and formulated the surgical plan through collective discussion. Before the study was launched, ethical approval was obtained from the Ethics Committee of our affiliated hospital. All patients provided written informed consent to allow their clinical data to be used for this research. For patients unable to consent personally, approval was obtained from their legal guardians.

Follow-up

After surgery, patients were followed up every 3 months in the first 2 years and every 6 months thereafter until July 2019. During surveillance, we evaluated liver function, serum AFP and HBV-DNA levels, and performed abdominal imaging including ultrasound, contrast-enhanced Computed Tomography (CT), or Magnetic Resonance Imaging (MRI). Recurrence-free survival (RFS) was defined from the date of surgery to tumor recurrence, and overall survival (OS) from surgery to death. Patients were censored at their last followup if no endpoint was reached.

Statistical analysis

Statistical analyses were performed using Statistical Product and Service Solutions (SPSS) software version 25.0. Categorical variables were reported as counts and percentages. Group comparisons were made using the chi-square test or Fisher exact test when indicated. Cox proportional hazards regression models were used for univariate and multivariate analyses. Variables that reached significance ($P<0.05$) in univariate testing were further included in the multivariate model to recognize independent prognostic factors. Kaplan-Meier methods were used to plot RFS and OS curves, and differences were examined with the log-rank test. P<0.05 was considered significant.

Results

Baseline characteristics stratified by tumor size

In **Table 1**, we present the baseline clinicopathologic features of the 302 HCC patients, categorized by tumor size using a 3-cm cutoff. Among them, 104 individuals (34.4%) had tumors measuring ≤3 cm in diameter, while the remaining 198 (65.6%) presented with lesions exceeding 3 cm. The overall mean age was 51 years (range: 27-76), with a male predominance (86.4%). HBV-DNA >1000 copies/mL was present in 63.2% of patients, and 79.5% had a solitary tumor. Preoperative AFP levels were distributed as follows: >400 ng/mL in 33.0% of patients, 20-400 ng/mL in 28.1%, and <20 ng/mL in 31.8%. According to the TNM staging system, 50.7% were stage I, 27.2% stage II, 20.5% stage III, and 1.7% stage IV. Pathologically, a fibrous capsule was identified in 74.2% of patients, MVI in 39.8%, and thrombus in 14.6%. Between-group comparisons revealed that patients with HCC >3 cm were more likely to present with elevated serum AFP levels, advanced TNM stage, and a higher incidence of MVI and tumor thrombus formation.

Prognostic analysis stratified by tumor size

Among the 302 patients, 236 (78.1%) experienced recurrence. The median RFS and OS for the entire cohort were 16.4 and 68.2 months, respectively.

In the ≤3 cm tumor cohort, univariate analysis showed no significant difference in RFS between anatomical and non-anatomical resection, or between a resection margin ≥1 cm and <1 cm (**Table 2**; **Figure 1A**, **1B**). However, Kaplan-Meier analysis revealed a significantly higher 5-year RFS rate in the wide-margin (≥1 cm) group compared to the narrow-margin (<1 cm) group in the >3 cm tumor cohort (P=0.036; **Table 2**; **Figure 2A**).

In the >3 cm cohort, a wide surgical margin (≥1 cm) was associated with a markedly superior 5-year OS rate (82.7%) compared to a narrow margin (38.6%) (P=0.001; **Table 3**; **Figure 2C**). In patients with HCC >3 cm, anatomical resection was not superior to non-anatomical resection regarding RFS or OS (**Figure 2B**, **2D**). Univariate analysis within this cohort identified high HBV-DNA (P=0.041), high AFP, multiple tumors, advanced TNM stage, absence of capsule, presence of MVI, and thrombus formation (all P<0.001) as factors associated with worse OS (**Table 3**). Subsequent multivariate Cox regression analysis confirmed AFP level (P=0.010), TNM stage (P<0.001), and thrombus formation (P=0.015) as independent prognostic factors for OS (**Table 4**). In contrast, no independent prognostic factor for OS was identified in the ≤3 cm cohort upon multivariate analysis (**Table 4**). We hypothesized that surgical margin width might affect the completeness of resection and thus influence early postoperative recurrence of HCC. Therefore, we further compared early recurrence rates between wide and narrow margin groups stratified by tumor size. As shown in **Figure 3A** and **3B**, in patients with tumors <3 cm in maximum diameter, margin width did not significantly affect early recurrence. In contrast, among those with tumors >3 cm, wide-margin resection was associated with a significantly lower incidence of early postoperative recurrence.

Discussion

Modern imaging techniques have become increasingly sensitive, allowing HCC to be identified at earlier stages and with smaller tumor diameters. In response to this trend, the Chinese guidelines for primary liver cancer have revised the definition of small HCC, adopting a 3-cm cutoff in place of the earlier 5-cm criterion. Clinicians already agree on this [14], and new evidence also points to a biological reason for the 3-cm threshold. Our analysis revealed that tumors larger than 3 cm tend to exhibit more aggressive behavior and distinct molecular pathological features relative to smaller HCCs [15]. Since then, several clinical studies have supported these observations and confirmed the 3 cm threshold has prognostic value [16, 17]. Thus, we split our patient group using a 3 cm tumor diameter cutoff in this study. Our results demonstrated that tumor size was significantly associated with AFP level, TNM stage, tumor number, vascular invasion, MVI, and postoperative recurrence. These results are consistent with those reported in previous literature [3, 15]. A possible explanation is that the accumulation of genetic chang-

Table 1. Comparison of clinicopathologic features of hepatocellular carcinoma, stratified by tumor size

Characteristic	n (302)	Tumor size		χ^2	*P* value
		≤3 cm (n, %)	>3 cm (n, %)		
Age					0.581
≤51	156	56 (53.8)	100 (50.5)	0.305	
>51	146	48 (46.2)	98 (49.5)		
Gender					0.506
Male	261	88 (84.6)	173 (87.4)	0.442	
Female	41	16 (15.4)	25 (12.6)		
AFP					<0.001*
≤20	96	45 (43.3)	51 (25.8)	21.694	
20-400	85	36 (34.6)	49 (24.7)		
>400	121	23 (22.1)	98 (49.5)		
HBV-DNA					0.230
≤1000	111	43 (41.3)	68 (34.3)	1.438	
>1000	191	61 (58.7)	130 (65.7)		
TNM					<0.001*
I	153	83 (79.8)	70 (35.4)	60.584	
II	82	19 (18.3)	63 (31.8)		
III	62	2 (1.9)	60 (30.3)		
IV	5	0 (0)	5 (2.5)		
Tumor number					<0.001*
1	240	97 (93.3)	143 (72.2)	18.513	
2	62	7 (6.7)	55 (27.8)		
Capsule					0.089
YES	224	71 (68.3)	153 (77.3)	2.885	
NO	78	33 (31.7)	45 (22.7)		
MVI					<0.001*
Negative	182	88 (84.6)	94 (47.5)	39.278	
Positive	120	16 (15.4)	104 (52.5)		
Recurring					0.001*
YES	236	70 (67.3)	166 (83.8)	10.910	
NO	66	34 (32.7)	32 (16.2)		
Thrombus					<0.001*
YES	44	2 (1.9)	42 (21.2)	20.382	
NO	258	102 (98.1)	156 (78.8)		
Occlusion					0.100
YES	268	88 (84.6)	180 (90.9)	2.703	
NO	34	16 (15.4)	18 (9.1)		

Note: AFP: Alpha-fetoprotein; HBV DNA: Hepatitis B Virus Deoxyribonucleic Acid; TNM: Tumor-Node-Metastasis; MVI: microvascular invasion; * indicates P<0.05.

es during tumor growth may lead to a more malignant phenotype once tumor diameter surpasses 3 cm [18, 19]. The higher rate of MVI in larger tumors may also account for the greater prevalence of satellite lesions, since MVI is known to promote the formation of these nodules and facilitate intrahepatic metastasis [16].

Improvements in surgical methods and a better understanding of hepatic anatomy and tumor biology have increased the popularity of anatomical liver resection. Anatomical resection refers to the removal of one or more functionally independent hepatic segments as defined by Couinaud's classification, guided by surface landmarks and intraoperative ultrasound [20].

Table 2. Univariate analysis of factors affecting recurrence-free survival based on tumor size

Characteristic	≤3 cm		>3 cm	
	five-year recurrence-free survival rate	P	five-year recurrence-free survival rate	P
Age		0.199		0.647
≤51	48.2%		25.6%	
>51	44.8%		25.3%	
Gender		0.897		0.048*
Male	46.3%		23.5%	
Female	50.0%		39.3%	
AFP		0.354		0.004*
≤20	37.8%		35.8%	
20-400	57.8%		30.5%	
>400	47.1%		17.7%	
HBV-DNA		0.891		0.224
≤1000	50.7%		27.4%	
>1000	44.0%		24.5%	
TNM		0.016*		<0.001*
I	48.9%		47.8%	
II	36.8%		25.8%	
III	50%		1.7%	
IV	-		0	
Tumor number		0.173		<0.001*
1	47.0%		32.6%	
2	42.9%		7.4%	
Capsule		0.119		0.004*
YES	53.3%		41.7%	
NO	43.7%		20.7%	
MVI		0.541		<0.001*
Negative	47.3%		82.0%	
Positive	43.8%		38.0%	
Thrombus		0.842		<0.001*
YES	50.0%		0	
NO	46.7%		32.4%	
Occlusion		0.855		0.488
YES	47.3%		25.3%	
NO	43.8%		26.7%	
Anatomical surgery		0.684		0.882
YES	40.8%		28.2%	
NO	47.5%		24.8%	
Margin width		0.438		0.036*
≥1 cm	38.5%		44.0%	
<1 cm	49.6%		23.4%	

Note: AFP: Alpha-fetoprotein; HBV DNA: Hepatitis B Virus Deoxyribonucleic Acid; TNM: Tumor-Node-Metastasis; MVI: microvascular invasion; * indicates P<0.05.

Some studies have reported that anatomical resection is associated with a lower 1-year recurrence rate than non-anatomical resection [21-23]. However, other investigations found no obvious advantages in RFS or 1-, 3-, or 5-year OS between the two approaches [24, 25]. We split patients into anatomical and non-anatomical resection groups to work out this inconsis-

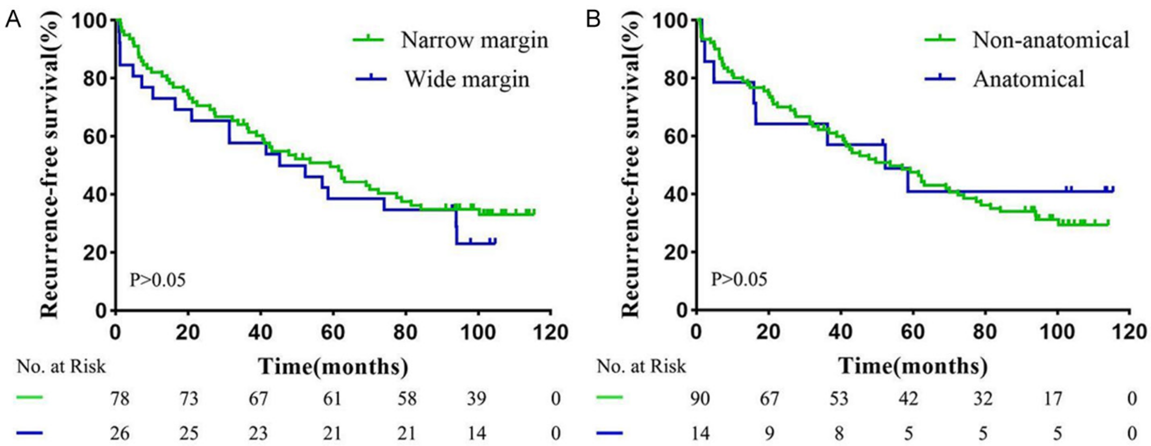

Figure 1. Recurrence-free survival according to margin width (A) and surgical procedure (anatomical vs. non-anatomical) (B) in hepatocellular carcinoma patients with tumor size ≤3 cm.

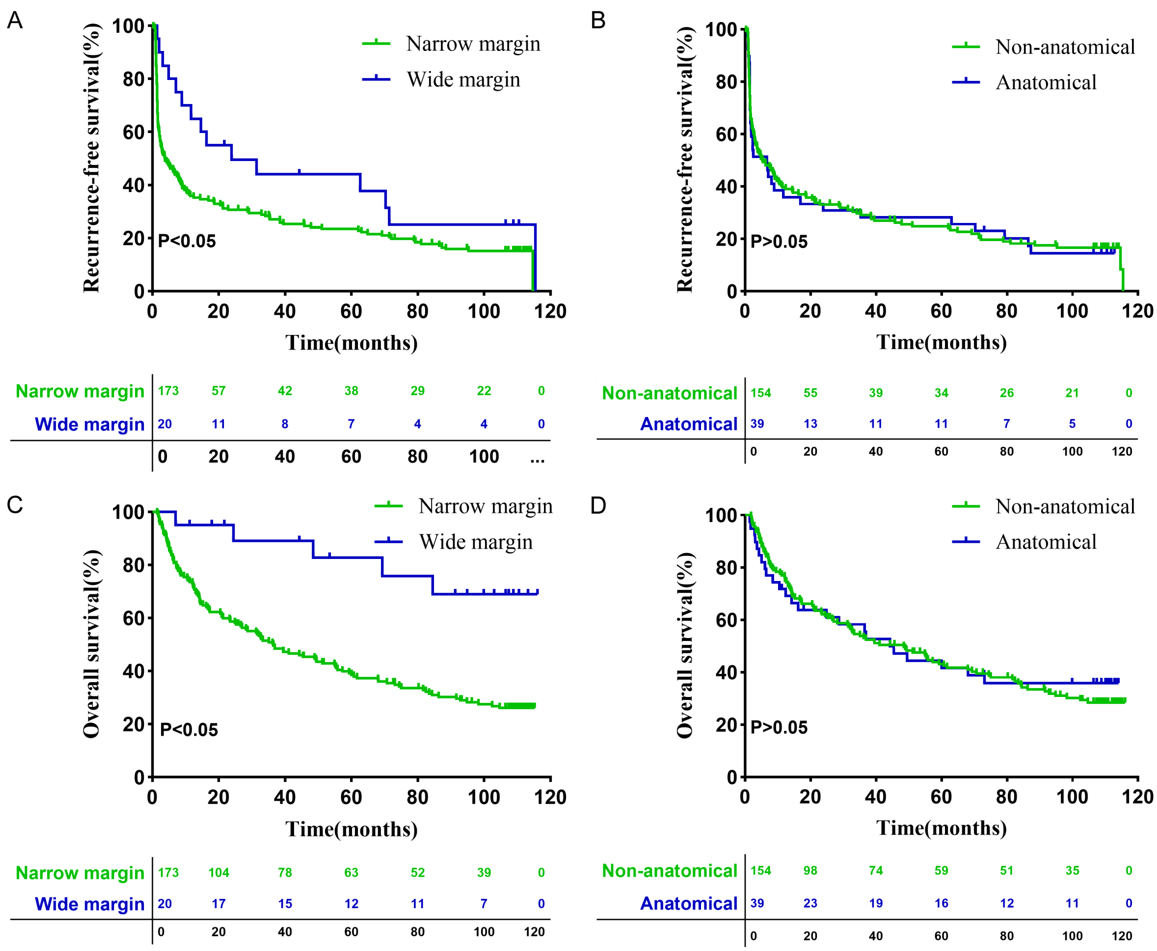

Figure 2. Recurrence-free survival (A, B) and overall survival (C, D) according to margin width (A, C) and surgical procedure (anatomical vs. non-anatomical) (B, D) in hepatocellular carcinoma patients with tumors >3 cm.

tency. We set out to determine whether some subgroups might benefit more from one procedure than the other. There was no significant survival advantage for anatomical resection in either small or large tumor subgroups. Given the lack of a clear benefit, more studies are

Table 3. Univariate analysis of prognostic factors for overall survival, stratified by tumor size

Characteristic	≤3 cm		>3 cm	
	five-year survival rate	P	five-year survival rate	P
Age		0.830		0.877
≤51	81.9%		40.6%	
>51	84.7%		45.1%	
Gender		0.110		0.339
Male	84.8%		40.4%	
Female	75.0%		62.0%	
AFP		0.145		<0.001*
≤20	86.3%		65.0%	
20-400	82.6%		51.8%	
>400	78.0%		26.4%	
HBV-DNA		0.063		0.041*
≤1000	90.5%		53.7%	
>1000	78.0%		36.9%	
TNM		0.078		<0.001*
I	87.5%		72.4%	
II	68.4%		39.9%	
III	50%		13.5%	
IV	-		0	
Tumor number		0.094		<0.001*
1	85.1%		51.9%	
2	57.1%		19.6%	
Capsule		0.562		<0.001*
YES	83.7%		72.7%	
NO	82.8%		34.2%	
MVI		0.680		<0.001*
Negative	84.8%		64.9%	
Positive	74.5%		23.0%	
Thrombus		0.168		<0.001*
YES	50.0%		5.2%	
NO	83.9%		52.0%	
Occlusion		0.385		0.480
YES	84.8%		42.8%	
NO	75.0%		50.0%	
Anatomical surgery		0.024*		0.761
YES	63.5%		41.6%	
NO	86.2%		43.2%	
Margin width		0.356		0.001*
≥1 cm	84.0%		82.7%	
<1 cm	83.0%		38.6%	

Note: AFP: Alpha-fetoprotein; HBV DNA: Hepatitis B Virus Deoxyribonucleic Acid; TNM: Tumor-Node-Metastasis; MVI: microvascular invasion; * indicates P<0.05.

needed - ones that focus on more precisely defined patient groups - to work out which patients benefit most from anatomical hepatectomy.

Beyond the type of resection, surgeons still disagree on the best width for the surgical margin. Recent evidence has also raised doubts about whether a wide surgical margin is even

Table 4. Multivariate analysis of prognostic factors for overall survival, stratified by tumor size

	≤3 cm		>3 cm	
	HR (95% CI)	P	HR (95% CI)	P
AFP	1.345 (0.774-2.336)	0.218	1.359 (1.077-1.717)	0.010*
TNM	1.621 (0.503-5.218)	0.197	1.762 (1.363-2.276)	<.001*
Tumor number	1.468 (0.253-8.525)	0.169	1.126 (0.733-1.729)	0.629
Capsule	0.902 (0.331-2.455)	0.630	0.860 (0.498-1.485)	0.601
Thrombus	0.373 (0.020-6.911)	0.643	1.796 (1.119-2.884)	0.015*
Anatomical surgery	2.805 (1.104-7.129)	0.030*	0.858 (0.549-1.342)	0.512
Margin width	0.509 (0.166-1.558)	0.319	0.416 (0.167-1.033)	0.059

Note: HR: hazard ratio; CI: confidence interval; AFP: Alpha-fetoprotein; HBV DNA: Hepatitis B Virus Deoxyribonucleic Acid; TNM: Tumor-Node-Metastasis; MVI: microvascular invasion; * indicates P<0.05.

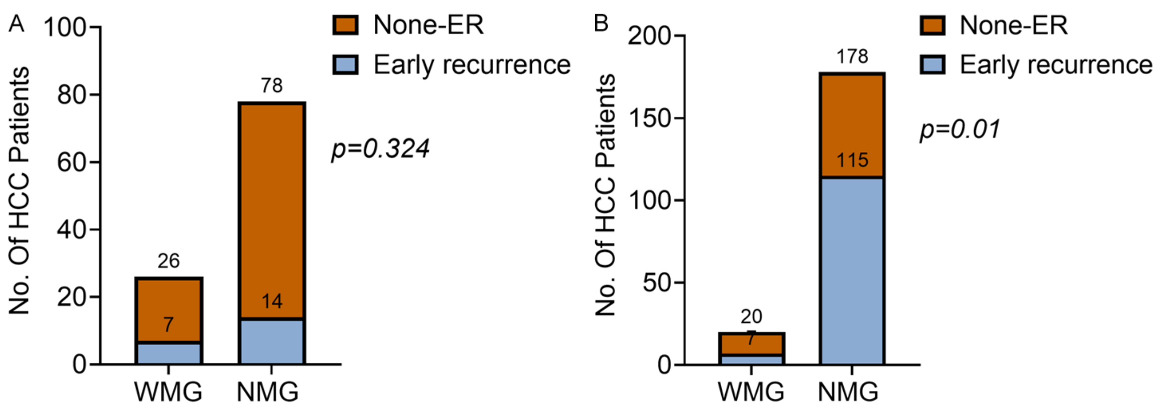

Figure 3. Differential effect of surgical margin status on early recurrence (ER) in patients with hepatocellular carcinoma (HCC) >3 cm vs. ≤3 cm. A. Rates of early postoperative recurrence in patients with HCC ≤3 cm, stratified by surgical margin width (wide margin group *vs.* narrow margin group, *p=0.324*). B. Rates of early postoperative recurrence in patients with HCC >3 cm, stratified by surgical margin width (wide margin group *vs.* narrow margin group, *p=0.010*). WMG: wide margin group; NWG: narrow margin group; ER: early recurrence; None-ER: none early recurrence.

necessary for HCC. Negative margins are still critical for curative intent, but studies show that margins narrower than 1 mm can still remove the tumor entirely. This narrower margin does not appear to significantly increase local recurrence rates or compromise OS [15-17]. As small HCCs typically exhibit less aggressive tumor biology [3, 4], they are generally associated with a better prognosis than larger tumors. From a practical standpoint, a narrow but still negative margin can be therapeutically beneficial, especially in cirrhotic livers where parenchymal sparing is essential for minimizing postoperative hepatic decompensation. Furthermore, this approach facilitates the feasibility of repeat hepatectomy in the event of intrahepatic recurrence, potentially contributing to improved OS. Large-scale studies have reported that a surgical margin of ≥1 cm is associated with significantly improved 1-, 3-, and 5-year RFS [10, 26]. Our study demonstrated that a resection margin ≥1 cm was associated with superior RFS and OS in patients with tumors >3 cm, compared to a narrower margin. Correspondingly, a margin width of ≥1 cm is recommended for this subgroup. Wide-margin resection did not emerge as an independent predictor of RFS in the multivariate Cox model (Supplementary Table 1). One possible interpretation is that its prognostic value is mediated through its association with tumor biology. Given that tumors >3 cm were more frequently accompanied by MVI and other adverse features, wide-margin resection may improve outcomes by enabling more complete clearance of such biologically aggressive lesions. Accordingly, its effect on survival may be indirect, reflecting its role in mitigating the negative impact of MVI rather than conferring an independent survival benefit. Conversely, in patients with HCC ≤3 cm, achieving a wide margin seems to confer no clear prognostic advantage. Hence, surgical planning should be guided by a comprehensive assessment that integrates tumor diameter with key pathological and hepatic reserve factors-most notably MVI status and the degree of cirrhosis.

Beyond surgical approach, we analyzed additional clinicopathologic prognostic factors stratified by tumor size. In patients with tumors ≤3 cm, TNM stage was the only factor with a significant link to OS (P=0.016; **Table 2**). This aligns with what we already know about small HCCs - they usually have lower rates of MVI and satellite lesions, and are also less likely to recur or form vascular thrombi [4]. In patients with tumors larger than 3 cm, we did a univariate analysis and found several factors linked to poor prognosis - high HBV DNA load, elevated AFP levels, multinodular tumors, advanced TNM stage, no tumor capsule, and confirmed MVI or vascular thrombus. Each of these factors was strongly correlated with worse OS. These findings point to two key clinical takeaways. First, early detection is crucial - we need to catch tumors before they reach this point where they become more biologically aggressive. Second, patients with larger HCCs need more frequent follow-up and adjuvant therapy for them. We believe that such personalized, risk-stratified treatment approaches hold the potential to improve survival outcomes and reduce recurrence rates in this specific patient group.

Several limitations of the present study merit consideration. First, as a retrospective study, it inherently carries the risk of selection bias and residual confounding factors - this is a common constraint of such study designs. Second, even though our data were collected from multiple centers, the sample size is still relatively small and may not fully reflect the clinical outcomes seen in current practice. Third, while we observed that HCCs larger than 3 cm behave more aggressively, we did not support this conclusion with basic experimental or genomic analyses, which limits the depth of our findings. Another limitation is the relatively long recruitment period, which began in 2009; this means our data may not fully align with current standards in HCC surgical management. To address these limitations, we are currently collecting post-2020 data from the same multicenter network. Our goal is to validate the prognostic model and surgical recommendations presented in this study. Moving forward, future research will focus on confirming these findings using larger, more recent datasets, combined with basic laboratory studies to strengthen the evidence base.

Conclusion

Tumor diameter influences the choice of surgical strategy for HCC. Anatomical and nonanatomical resection yielded comparable prognosis for tumors ≤3 cm. For lesions larger than 3 cm, however, wide-margin resection offered better survival than anatomical resection alone.

Acknowledgements

This study was supported by the Research Project of Jiangsu Cancer Hospital (No. ZM-202023).

Disclosure of conflict of interest

None.

Address correspondence to: Jing-Ni Zhu, Department of Medical Oncology, The Affiliated Cancer Hospital of Nanjing Medical University, Jiangsu Cancer Hospital, Jiangsu Institute of Cancer Research, No. 42 Baiziting, Xuanwu District, Nanjing 210000, Jiangsu, China. Tel: +86-025-83283595; E-mail: zhujingni@njmu.edu.cn; Ning Yang, Department V of Hepatic Surgery, Eastern Hepatobiliary Surgery Hospital, Naval Medical University, Shanghai 201805, China. Tel: +86-021-81887593; E-mail: Lancet00@163.com

References

[1] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A and 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] Ikai I, Kudo M, Arii S, Omata M, Kojiro M, Sakamoto M, Takayasu K, Hayashi N, Makuuchi M, Matsuyama Y and Monden M. Report of the 18th follow-up survey of primary liver cancer in Japan. Hepatol Res 2010; 40: 1043-1059.

[3] Poon RT, Fan ST, Lo CM, Liu CL and Wong J. Long-term survival and pattern of recurrence

after resection of small hepatocellular carcinoma in patients with preserved liver function: implications for a strategy of salvage transplantation. Ann Surg 2002; 235: 373-382.
[4] Wu CC, Cheng SB, Ho WM, Chen JT, Liu TJ and P'Eng FK. Liver resection for hepatocellular carcinoma in patients with cirrhosis. Br J Surg 2005; 92: 348-355.
[5] Sakon M, Nagano H, Nakamori S, Dono K, Umeshita K, Murakami T, Nakamura H and Monden M. Intrahepatic recurrences of hepatocellular carcinoma after hepatectomy: analysis based on tumor hemodynamics. Arch Surg 2002; 137: 94-99.
[6] Kumar AM, Fredman ET, Coppa C, El-Gazzaz G, Aucejo FN and Abdel-Wahab M. Patterns of cancer recurrence in localized resected hepatocellular carcinoma. Hepatobiliary Pancreat Dis Int 2015; 14: 269-275.
[7] Chau GY, Lui WY, Tsay SH, King KL, Loong CC, Chiu JH, Wu CW and P'Eng FK. Prognostic significance of surgical margin in hepatocellular carcinoma resection: an analysis of 165 Childs' A patients. J Surg Oncol 1997; 66: 122-126.
[8] Lise M, Bacchetti S, Da Pian P, Nitti D, Pilati PL and Pigato P. Prognostic factors affecting long term outcome after liver resection for hepatocellular carcinoma: results in a series of 100 Italian patients. Cancer 1998; 82: 1028-1036.
[9] Arii S, Tanaka J, Yamazoe Y, Minematsu S, Morino T, Fujita K, Maetani S and Tobe T. Predictive factors for intrahepatic recurrence of hepatocellular carcinoma after partial hepatectomy. Cancer 1992; 69: 913-919.
[10] Tsilimigras DI, Sahara K, Moris D, Hyer JM, Paredes AZ, Bagante F, Merath K, Farooq AS, Ratti F, Marques HP, Soubrane O, Azoulay D, Lam V, Poultsides GA, Popescu I, Alexandrescu S, Martel G, Guglielmi A, Hugh T, Aldrighetti L, Endo I and Pawlik TM. Effect of surgical margin width on patterns of recurrence among patients undergoing R0 hepatectomy for T1 hepatocellular carcinoma: an international multi-institutional analysis. J Gastrointest Surg 2020; 24: 1552-1560.
[11] Torzilli G, Montorsi M, Del Fabbro D, Palmisano A, Donadon M and Makuuchi M. Ultrasonographically guided surgical approach to liver tumours involving the hepatic veins close to the caval confluence. Br J Surg 2006; 93: 1238-1246.
[12] Poon RT, Fan ST, Ng IO and Wong J. Significance of resection margin in hepatectomy for hepatocellular carcinoma: a critical reappraisal. Ann Surg 2000; 231: 544-551.
[13] Nara S, Shimada K, Sakamoto Y, Esaki M, Kishi Y, Kosuge T and Ojima H. Prognostic impact of marginal resection for patients with solitary hepatocellular carcinoma: evidence from 570 hepatectomies. Surgery 2012; 151: 526-536.
[14] Xie DY, Ren ZG, Zhou J, Fan J and Gao Q. Critical appraisal of Chinese 2017 guideline on the management of hepatocellular carcinoma. Hepatobiliary Surg Nutr 2017; 6: 387-396.
[15] Liu PH, Hsu CY, Hsia CY, Lee YH, Su CW, Huang YH, Lee FY, Lin HC and Huo TI. Prognosis of hepatocellular carcinoma: assessment of eleven staging systems. J Hepatol 2016; 64: 601-608.
[16] Feng LH, Dong H, Lau WY, Yu H, Zhu YY, Zhao Y, Lin YX, Chen J, Wu MC and Cong WM. Novel microvascular invasion-based prognostic nomograms to predict survival outcomes in patients after R0 resection for hepatocellular carcinoma. J Cancer Res Clin Oncol 2017; 143: 293-303.
[17] Xie DY, Ren ZG, Zhou J, Fan J and Gao Q. 2019 Chinese clinical guidelines for the management of hepatocellular carcinoma: updates and insights. Hepatobiliary Surg Nutr 2020; 9: 452-463.
[18] Groeschl RT, Gamblin TC and Turaga KK. Ablation for hepatocellular carcinoma: validating the 3-cm breakpoint. Ann Surg Oncol 2013; 20: 3591-3595.
[19] Lu XY, Xi T, Lau WY, Dong H, Xian ZH, Yu H, Zhu Z, Shen F, Wu MC and Cong WM. Pathobiological features of small hepatocellular carcinoma: correlation between tumor size and biological behavior. J Cancer Res Clin Oncol 2011; 137: 567-575.
[20] Figueroa R, Laurenzi A, Laurent A and Cherqui D. Perihilar Glissonian approach for anatomical parenchymal sparing liver resections: technical aspects: the taping game. Ann Surg 2018; 267: 537-543.
[21] Su CM, Chou CC, Yang TH and Lin YJ. Comparison of anatomic and non-anatomic resections for very early-stage hepatocellular carcinoma: the importance of surgical resection margin width in non-anatomic resection. Surg Oncol 2021; 36: 15-22.
[22] Ju M and Yopp AC. The utility of anatomical liver resection in hepatocellular carcinoma: associated with improved outcomes or lack of supportive evidence? Cancers (Basel) 2019; 11: 1441.
[23] Hidaka M, Eguchi S, Okuda K, Beppu T, Shirabe K, Kondo K, Takami Y, Ohta M, Shiraishi M, Ueno S, Nanashima A, Noritomi T, Kitahara K and Fujioka H. Impact of 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: 339-346.
[24] Nanashima A, Sumida Y, Abo T, Nagasaki T, Tobinaga S, Fukuoka H, Takeshita H, Hidaka S,

Tanaka K, Sawai T, Yasutake T and Nagayasu T. Comparison of survival between anatomic and non-anatomic liver resection in patients with hepatocellular carcinoma: significance of surgical margin in non-anatomic resection. Acta Chir Belg 2008; 108: 532-537.
[25] Marubashi S, Gotoh K, Akita H, Takahashi H, Ito Y, Yano M, Ishikawa O and Sakon M. Anatomical versus non-anatomical resection for hepatocellular carcinoma. Br J Surg 2015; 102: 776-784.
[26] Zhong FP, Zhang YJ, Liu Y and Zou SB. Prognostic impact of surgical margin in patients with hepatocellular carcinoma: a meta-analysis. Medicine (Baltimore) 2017; 96: e8043.

Supplementary Table 1. Multivariate analysis of prognostic factors for recurrence-free survival, stratified by tumor size

	≤3 cm		>3 cm	
	HR (95% CI)	P	HR (95% CI)	P
Gender			0.538 (0.322-0.897)	0.018*
TNM	2.258 (1.293-3.944)	0.004*	1.702 (1.237-2.341)	0.001*
AFP			1.018 (0.826-1.254)	0.868
Margin width	1.075 (0.621-1.861)	0.796	0.811 (0.459-1.433)	0.470
Capsule			1.353 (0.853-2.146)	0.199
Tumor number			1.212 (0.814-1.805)	0.344
MVI	1.023 (0.536-1.953)	0.944	1.453 (0.927-2.276)	0.103
Thrombus	0.190 (0.021-1.763)	0.144	2.696 (1.717-4.233)	<0.001*

Note: HR: hazard ratio; CI: confidence interval; AFP: Alpha-fetoprotein; HBV DNA: Hepatitis B Virus Deoxyribonucleic Acid; TNM: Tumor-Node-Metastasis; MVI: microvascular invasion; * indicates P<0.05.