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AIMS AND SCOPE

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ORIGINAL ARTICLE

Retrospective Study

Postoperative outcomes and recurrence patterns of intermediate-stage hepatocellular carcinoma dictated by the sum of tumor size and number

Xin-Sheng Hu, Hui-Yuan Yang, Chao Leng, Zhi-Wei Zhang

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Xin-Sheng Hu, Hui-Yuan Yang, Chao Leng, Zhi-Wei Zhang, Hepatic Surgery Center, Tongji Hospital, Tongji Medical College of Huazhong University of Science and Technology, Wuhan 430030, Hubei Province, China

Corresponding author: Chao Leng, PhD, Doctor, Hepatic Surgery Center, Tongji Hospital, Tongji Medical College of Huazhong University of Science and Technology, No. 1095 Jiefang Avenue, Wuhan 430030, Hubei Province, China. lengchaojdld@163.com

Abstract

BACKGROUND

The selection criteria for Barcelona Clinic Liver Cancer (BCLC) intermediate-stage hepatocellular carcinoma (HCC) patients who would truly benefit from liver resection (LR) remain undefined.

AIM

To identify BCLC-B HCC patients more suitable for LR.

METHODS

We included patients undergoing curative LR for BCLC stage A or B multinodular HCC (MNHCC) and stratified BCLC-B patients by the sum of tumor size and number (N + S). Overall survival (OS), recurrence-free survival (RFS), recurrence-to-death survival (RTDS), recurrence patterns, and treatments after recurrence in BCLC-B patients in each subgroup were compared with those in BCLC-A patients.

RESULTS

In total, 143 patients who underwent curative LR for MNHCC with BCLC-A (n = 25) or BCLC-B (n = 118) were retrospectively analyzed. According to the N + S, patients with BCLC-B HCC were divided into two subgroups: BCLC-B1 (N + S ≤ 10, n = 83) and BCLC-B2 (N + S > 10, n = 35). Compared with BCLC-B2 patients, those with BCLC-B1 had a better OS (5-year OS rate: 67.4% *vs* 33.6%; P < 0.001), which was comparable to that in BCLC-A patients (5-year OS rate: 67.4% *vs* 74.1%; P = 0.250), and a better RFS (median RFS: 19 mo *vs* 7 mo; P < 0.001), which was worse than that in BCLC-A patients (median RFS: 19 mo *vs* 48 mo; P = 0.022). Further analysis of patients who developed recurrence showed that both BCLC-B1 and BCLC-A patients had better RTDS (median RTDS: Not reached *vs* 49 mo; P =

0.599), while the RTDS in BCLC-B2 patients was worse (median RTDS: 16 mo *vs* not reached, $P < 0.001$; 16 mo *vs* 49 mo, $P = 0.042$). The recurrence patterns were similar between BCLC-B1 and BCLC-A patients, but BCLC-B2 patients had a shorter recurrence time and a higher proportion of patients had recurrence with macrovascular invasion and/or extrahepatic metastasis, both of which were independent risk factors for RTDS.

CONCLUSION

BCLC-B HCC patients undergoing hepatectomy with N + S ≤ 10 had mild recurrence patterns and excellent OS similar to those in BCLC-A MNHCC patients, and LR should be considered in these patients.

Key Words: Hepatocellular carcinoma; Multinodular; Intermediate-stage; Liver resection; Recurrence pattern; Prognosis

Core Tip: Subgroups of Barcelona Clinic Liver Cancer (BCLC) intermediate-stage hepatocellular carcinoma (HCC) patients who would truly benefit from liver resection (LR) remain undefined. We demonstrated that the sum of tumor size and number (N + S) can predict not only prognosis in BCLC-B patients undergoing LR, but also the recurrence patterns and recurrence-to-death survival (RTDS) in these patients. In addition, we indicated that BCLC-B patients undergoing hepatectomy with N + S ≤ 10 had mild recurrence patterns, good RTDS and excellent overall survival similar to those in BCLC-A multinodular HCC patients. The results of this study are helpful in selecting BCLC-B patients more suitable for LR.

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INTRODUCTION

As the sixth most common cancer globally, primary liver cancer accounted for 906,000 newly confirmed cancer cases and 830,000 cancer-related deaths worldwide in 2020, of which 75%-85% were hepatocellular carcinoma (HCC)[1].

Barcelona Clinic Liver Cancer (BCLC) staging system, which was proposed in 1999, has been widely used to guide treatment decisions in patients with HCC[2,3]. The 2022 version of the BCLC strategy recommends liver transplantation (LT), transarterial chemoembolization (TACE), and systemic therapy, respectively, for BCLC intermediate-stage HCC patients based on their expected survival time[4].

In addition, emerging studies have suggested that liver resection (LR) may also be a good treatment option for BCLC-B HCC patients[5,6]. Nevertheless, the subgroups of BCLC-B HCC patients who would truly benefit from LR have yet to be defined. Several previous studies found that some BCLC-B HCC patients undergoing LR had favorable long-term overall survival (OS) rates (5-year OS rates: 50%-75%); however, these selected patients still had high postoperative recurrence rates (2-year recurrence rate: ≥ 50%), which means that many of these patients had good recurrence-to-death survival (RTDS)[7,8]. Both recurrence patterns and treatments after recurrence can affect the RTDS of HCC patients who develop recurrence after LR[9-11]. However, previous studies did not analyze the main reasons why these selected patients had good RTDS, which may affect the judgment of the role of LR in these patients[7,8].

In this study, we retrospectively included patients undergoing curative LR for BCLC stage A or B multinodular HCC (MNHCC) and stratified the BCLC-B patients by the sum of tumor size and number (N + S), which combines the two main prognostic factors of BCLC-B patients into a continuous variable [7,8]. BCLC-B patients more suitable for LR were identified by comparing the outcomes, recurrence patterns, and treatments after recurrence in BCLC-B patients in each subgroup with those in BCLC-A patients.

MATERIALS AND METHODS

Patients

We enrolled BCLC stage A or B MNHCC patients who underwent curative LR in Tongji Hospital from January 2010 to May 2018. The inclusion criteria were: (1) MNHCC pathologically diagnosed with two or more nodules, in which lesions less than 1 cm in diameter and less than 2 cm away from the main nodule were defined as satellite nodules[12]; (2) Curative resection, defined as complete macroscopic removal of all tumors with negative histologic resection margins for the tumors (R0 resection)[13,14]; and (3) No preoperative anticancer treatment other than TACE. The exclusion criteria were: (1) Recurrent HCC or combined HCC and cholangiocarcinoma; and (2) Complicated with other malignancies.

Data collection

Patient data at the time of initial hepatectomy including sex, age, body mass index, hepatitis B antigen status, liver function, tumor characteristics, surgical procedure, and preoperative treatment were recorded. Liver function in this study was classified by the albumin-bilirubin score[15]. Maximum tumor size was defined as the maximum diameter of the largest tumor. Microvascular invasion was defined as tumor within a vascular space lined by endothelium that was visible only on microscopy[16].

In addition, the recurrence patterns, which consisted of recurrence time and tumor characteristics at the time of recurrence, and treatments after recurrence in those patients who developed recurrence during follow-up were also recorded. Recurrence time was defined as the time between initial LR and the first recurrence.

Initial hepatectomy

In our center, we routinely estimated the residual liver volume in MNHCC patients before hepatectomy, and only patients with residual liver volume of more than 40% of the standard liver volume (for patients with liver cirrhosis) or more than 30% (for patients without liver cirrhosis) would receive LR [17,18]. The decision to perform anatomical or non-anatomical hepatectomy depended largely on the tumor distribution, and major resection was defined as the resection of three or more Couinaud liver segments[19]. Intraoperative ultrasound was routinely used to locate the tumor and screen the nodules. All nodules were completely resected intraoperatively and negative margin was determined according to postoperative pathology.

Follow-up

Patients were followed every month with measurement of serum alpha-fetoprotein (AFP), chest radiography and ultrasound or computed tomography (CT) or magnetic resonance imaging (MRI) in the first 6 mo after discharge from hospital, and every 3-6 mo thereafter. When HCC recurrence was confirmed by CT or MRI, patients were treated with repeated hepatectomy, ablation, TACE or systemic therapy. Follow-up was terminated on May 15, 2022.

Recurrence-free survival (RFS) was calculated from the date of hepatectomy until recurrence or last follow-up. OS was defined as the time from LR to death or last follow-up, and RTDS was defined as the time from recurrence to death or last follow-up.

Statistical analysis

Continuous variables were presented as mean ± SD or median (interquartile range; IQR). Categorical variables were described by frequency and percentage. In the comparison of different subgroups, continuous variables were compared using the Student's t or Mann-Whitney U test, and categorical variables using the χ^2 or Fisher's exact test, as appropriate. Survival was analyzed by the Kaplan-Meier method, and survival curves were compared by the log-rank test. Univariate and multivariate analyses were based on the Cox proportional analysis. Variables with P values less than 0.1 identified by the univariate analysis were included in multivariate analysis. The cutoff value of N + S was determined by X-tile, a bioinformatics tool produced by Camp and colleagues[20]. The area under receiver operating characteristic (ROC) curve (AUC) was compared using DeLong test[21]. $P < 0.05$ was considered to indicate statistical significance. Both SPSS (version 23.0, SPSS, Inc., Chicago, IL, United States) and MedCalc software (version 20.115, MedCalc Software, Ostend, Belgium) were used for the analysis.

RESULTS

Variables and outcomes of the entire cohort

A total of 143 patients who underwent curative LR for BCLC stage A or B MNHCC were enrolled. Their mean age was 52.1 years and most patients were male (n = 134, 93.7%) and were hepatitis B surface antigen positive (n = 131, 91.6%). Median maximum tumor size in the entire cohort was 5.6 cm (IQR: 3.4–7.6) and tumor number in the vast majority of patients was ≤ 3 (n = 136, 95.1%). Overall, 17.5% (n = 25) of patients had BCLC-A MNHCC, and 82.5% (n = 118) had BCLC-B MNHCC (Table 1).

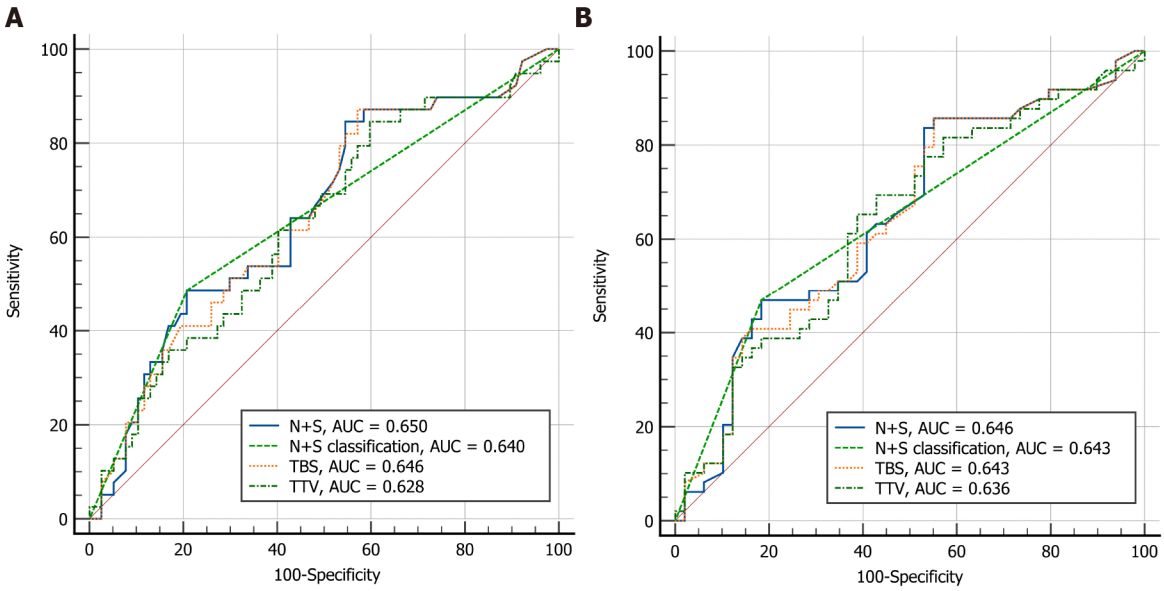

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Figure 1 The receiver operating characteristic analysis of the sum of tumor size and number, the classification of the sum of tumor size and number, tumor burden score and total tumor volume in intermediate-stage hepatocellular carcinoma patients. A: 3-year overall survival (OS); B: 5-year OS. N + S: The sum of tumor size and number; TBS: Tumor burden score; TTV: Total tumor volume; AUC: Area under receiver operating characteristic curve.

After a median follow-up of 54 mo (IQR 27–79), 5-year OS and RFS after R0 resection in all patients were 60.2% and 23.2%, respectively. Of note, BCLC-B patients had worse 5-year OS (57.2% *vs* 74.1%, P = 0.028, Supplementary Figure 1A) and RFS (19.4% *vs* 41.6%, P = 0.002, Supplementary Figure 1B).

Stratification of BCLC-B patients based on N + S

Among patients undergoing LR for BCLC-B HCC, the median maximum tumor size was 6.2 cm (IQR: 4.1–8.4) and tumor number in 111 (94.1%) patients was ≤ 3. Of note, 43.2% (n = 51) of patients had bilateral disease and 14.4% (n = 17) of patients underwent TACE before initial LR (Table 1).

Using the X-tile program[20], patients with BCLC-B HCC were divided into two groups by N + S: BCLC-B1 (≤ 10, n = 83, 70.3%), BCLC-B2 (> 10, n = 35, 29.7%) (Supplementary Figure 2).

The prognostic ability of N + S and the rationality of the cut-off value of 10 were then verified by time-dependent ROC curves and Cox-regression analysis. The AUCs for 3-year and 5-year OS in BCLC-B patients were 0.650 and 0.646, respectively, for N + S, and 0.640 and 0.643, respectively, for stratification according to N + S (Figure 1). Multivariate analysis showed that N + S > 10 was an independent risk factor for OS [hazard ratio (HR) 2.996, 1.779 to 5.045; P < 0.001] (Table 2) and RFS (HR 1.657, 1.057 to 2.596; P = 0.028) (Table 3) in BCLC-B patients.

In addition, we compared the predictive accuracy of N + S with those of tumor burden score (TBS) and total tumor volume (TTV), both of which were previous prognostic models based on tumor size and number of HCC patients[22,23]. The results showed that the AUCs of N + S at 3 and 5 years were both similar to those of TBS (3-year AUC, 0.650 *vs* 0.646, P = 0.552; 5-year AUC, 0.646 *vs* 0.643, P = 0.762) and TTV (3-year AUC, 0.650 *vs* 0.628, P = 0.171; 5-year AUC, 0.646 *vs* 0.636, P = 0.535) (Figure 1).

Comparison of the clinical characteristics, OS, and RFS among BCLC-A, BCLC-B1 and BCLC-B2 patients

Clinical characteristics, OS and RFS of patients with BCLC-B1, BCLC-B2, and BCLC-A were compared (Figure 2, Supplementary Table 1). The results showed that BCLC-B2 patients had a higher serum AFP level and a larger proportion of bilateral tumor distribution, compared to patients with BCLC-A and BCLC-B1. With an increase in N + S, the maximum tumor size gradually increased, and a larger proportion of patients underwent major resection (Supplementary Table 1).

Both BCLC-A patients and BCLC-B1 patients had good 5-year OS (74.1% *vs* 67.4%, P = 0.250), which was better than that in BCLC-B2 patients (74.1% *vs* 33.6%, P < 0.001; 67.4% *vs* 33.6%, P < 0.001) (Figure 2A). Compared with BCLC-A patients, BCLC-B1 patients had a worse RFS (median RFS: 19 mo *vs* 48 mo; P = 0.022), which was better than that in BCLC-B2 patients (median RFS: 19 mo *vs* 7 mo; P < 0.001) (Figure 2B).

Table 1 Characteristics of patients with Barcelona Clinic Liver Cancer stage A or B multinodular hepatocellular carcinoma, *n* (%)

Variables	Total (*n* = 143)	BCLC-A (*n* = 25)	BCLC-B (*n* = 118)	*P* value
Male gender	134 (93.7)	25 (100)	109 (92.4)	0.330
Age (yr)	52.1 ± 12.7	50.5 ± 14.5	52.4 ± 12.4	0.490
BMI	22.97 ± 3.15	23.05 ± 3.35	22.96 ± 3.12	0.895
HBs-Ag positive	131 (91.6)	24 (96)	107 (90.7)	0.635
Albumin (g/L)	38.89 ± 4.51	39.95 ± 5.15	38.65 ± 4.34	0.194
Bilirubin (μmol/L)	13.8 (9.9, 18)	12.9 (10.2, 20.9)	13.9 (9.7, 17.8)	0.568
ALBI grade				0.680
1	69 (48.3)	13 (52)	56 (47.5)	
2/3	74 (51.7)	12/0 (48/0)	62/0 (52.5/0)	
AFP (μg/L)	239 (13, 2338)	74 (6, 390)	483 (16, 2944)	0.011
Maximum tumor size (cm)	5.6 (3.4, 7.6)	2.5 (2.1, 2.9)	6.2 (4.1, 8.4)	< 0.001
Tumor number				0.460
≤ 3	136 (95.1)	25 (100)	111 (94.1)	
> 3	7 (4.9)	0	7 (5.9)	
Tumor distribution				0.506
Unilateral	83 (58)	16 (64)	67 (56.8)	
Bilateral	60 (42)	9 (36)	51 (43.2)	
Presence of microvascular invasion	15 (10.5)	1 (4)	14 (11.9)	0.420
Edmondson-Steiner grade				0.337
I-II	85 (59.4)	17 (68)	68 (57.6)	
III-IV	58 (40.6)	8 (32)	50 (42.4)	
Major resection	64 (44.8)	4 (16)	60 (50.8)	0.001
Anatomical hepatectomy	22 (15.4)	4 (16)	18 (15.3)	1.000
Preoperative TACE				0.690
No	121 (84.6)	20 (80)	101 (85.6)	
Yes	22 (15.4)	5 (20)	17 (14.4)	

BMI: Body mass index; HBs-Ag: Hepatitis B surface antigen; ALBI: Albumin-bilirubin; AFP: Alpha-fetoprotein; IQR: Interquartile range; TACE: Transarterial chemoembolization.

Comparison of recurrence patterns, treatments after recurrence, and RTDS in BCLC-A, BCLC-B1 and BCLC-B2 patients

During follow-up, 14 (56%) BCLC-A, 66 (79.5%) BCLC-B1 and 34 (97.1%) BCLC-B2 patients developed recurrences ($P < 0.001$). Nine BCLC-B1 and 4 BCLC-B2 patients who lacked information on tumor characteristics at the time of recurrence and treatments after recurrence were excluded from the analysis. Ultimately, 14 BCLC-A, 57 BCLC-B1 and 30 BCLC-B2 patients with recurrence were included in the analysis. The recurrence patterns and treatments after recurrence in these patients are summarized in Supplementary Table 2.

Compared with BCLC-A and BCLC-B1 patients, BCLC-B2 patients had a shorter recurrence time and a higher proportion of recurrence with macrovascular invasion and/or extrahepatic metastasis. However, there were no significant statistical differences in recurrence patterns and treatment after recurrence between BCLC-B1 and BCLC-A patients. Fewer BCLC-B2 patients underwent curative treatments after recurrence than BCLC-A patients, but the treatment after recurrence was similar between BCLC-B2 patients and BCLC-B1 patients (Supplementary Table 2).

Both BCLC-B1 and BCLC-A patients had good RTDS (median RTDS: Not reached, *vs* 49 mo for BCLC-B1 and BCLC-A patients, respectively; $P = 0.599$), while BCLC-B2 patients had a worse RTDS (16 mo *vs* not reached, $P < 0.001$; 16 mo *vs* 49 mo, $P = 0.042$) (Figure 3).

Table 2 Univariate and multivariate analysis of overall survival in patients with Barcelona Clinic Liver Cancer stage B hepatocellular carcinoma

Variables	Univariate analysis		Multivariate analysis	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value
Gender (male)	1.128 (0.409-3.117)	0.816		
Age (> 65 yr)	0.668 (0.285-1.562)	0.352		
BMI > 25	0.954 (0.513-1.772)	0.880		
HBs-Ag positive	1.084 (0.466-2.525)	0.851		
ALBI grade				
1	1.00 (Reference)		1.00 (Reference)	
2	1.891 (1.112-3.217)	0.019	2.279 (1.236-4.201)	0.008
AFP > 400 ng/mL	1.969 (1.165-3.327)	0.011		
Maximum tumor size > 5 cm	2.510 (1.354-4.651)	0.003		
Tumor number > 3	3.806 (1.716-8.444)	0.001	5.519 (2.207-13.803)	< 0.001
N + S > 10	3.403 (2.031-5.702)	< 0.001	2.996 (1.779-5.045)	< 0.001
Bilateral tumor distribution	2.201 (1.312-3.694)	0.003		
Presence of MVI	1.816 (0.855-3.858)	0.120		
Edmondson-Steiner III-IV	2.084 (1.248-3.480)	0.005	2.051 (1.219-3.449)	0.007
Major resection	1.886 (1.115-3.191)	0.018		
NAH	0.905 (0.458-1.788)	0.775		
Preoperative TACE				
No	1.00 (Reference)			
Yes	0.494 (0.198-1.238)	0.132		

BMI: Body mass index; HBs-Ag: Hepatitis B surface antigen; ALBI: Albumin-bilirubin; AFP: Alpha-fetoprotein; N + S: The sum of tumor size and number; MVI: Microvascular invasion; NAH: Non-anatomical hepatectomy; TACE: Transarterial chemoembolization.

Independent risk factors for RTDS

We further conducted a multivariate analysis of the factors affecting RTDS of BCLC stage A or B MNHCC patients undergoing LR. Multivariate analysis showed that initial tumor with BCLC-B2 (N + S > 10) (HR 2.696, 1.468 to 4.953; $P = 0.001$), recurrence within 2-year (HR 4.353, 1.024 to 18.503; $P = 0.046$), recurrent tumor number > 3 (HR 3.247, 1.629 to 6.474; $P = 0.001$), recurrence with macrovascular invasion and/or extrahepatic spread (HR 2.894, 1.458 to 5.746; $P = 0.002$) and noncurative treatments after recurrence (HR 2.423, 1.209 to 4.854; $P = 0.013$) were independent risk factors for RTDS (Supplementary Table 3).

DISCUSSION

The role of LR in BCLC-B HCC patients is unclear. Although the latest BCLC staging system still does not recommend LR for BCLC-B patients, the results of emerging studies have indicated that LR resulted in a good 5-year OS for BCLC-B HCC patients[4-6]. In this study, patients who underwent LR for BCLC-B HCC had an overall 5-year OS rate of 57.2%, which demonstrated that LR was a good treatment option in these patients.

To select BCLC-B patients more suitable for LR, we stratified these patients according to N + S, which has been used to select HCC patients who are more suitable for LT and for TACE[24,25]. In fact, Matsukuma *et al*[26] suggested that N + S was a good prognostic factor for BCLC-B HCC patients undergoing hepatectomy. The present study increased the cutoff point of N + S from 8 to 10, which may be related to different study cohorts and different calculation methods used for the cutoff value[26]. Nevertheless, the results of this study and in the study by Matsukuma *et al*[26] demonstrated that N + S could predict the recurrence and OS of BCLC-B HCC patients undergoing hepatectomy. In addition, the present study showed that N + S had a predictive accuracy similar to TBS and TTV in predicting OS in

Table 3 Univariate and multivariate analysis of recurrence-free survival in patients with Barcelona Clinic Liver Cancer stage B hepatocellular carcinoma

Variables	Univariate analysis		Multivariate analysis	
	HR (95%CI)	P value	HR (95%CI)	P value
Gender (male)	1.135 (0.526-2.450)	0.747		
Age (> 65 yr)	0.881 (0.514-1.511)	0.646		
BMI > 25	1.157 (0.729-1.836)	0.536		
HBs-Ag positive	1.109 (0.558-2.202)	0.769		
ALBI grade				
1	1.00 (Reference)			
2	1.474 (0.988-2.198)	0.057		
AFP > 400 ng/mL	1.458 (0.984-2.162)	0.060		
Maximum tumor size > 5 cm	1.253 (0.830-1.891)	0.283		
Tumor number > 3	2.449 (1.123-5.343)	0.024		
N + S > 10	2.113 (1.385-3.224)	0.001	1.657 (1.057-2.596)	0.028
Bilateral tumor distribution	2.104 (1.409-3.140)	< 0.001	1.820 (1.187-2.791)	0.006
Presence of MVI	1.757 (0.973-3.171)	0.062		
Edmondson-Steiner III-IV	1.709 (1.151-2.539)	0.008	1.676 (1.127-2.493)	0.011
Major resection	1.285 (0.867-1.904)	0.211		
NAH	1.126 (0.650-1.950)	0.673		
Preoperative TACE				
No	1.00 (Reference)			
Yes	0.784 (0.437-1.405)	0.414		

BMI: Body mass index; HBs-Ag: Hepatitis B surface antigen; ALBI: Albumin-bilirubin; AFP: Alpha-fetoprotein; N + S: The sum of tumor size and number; MVI: Microvascular invasion; NAH: Non-anatomical hepatectomy; TACE: Transarterial chemoembolization.

BCLC-B patients. However, compared with the complicated calculation of TBS and TTV, the calculation of N + S is simpler and more suitable for clinical application.

Previous studies have focused on the OS when selecting BCLC-B patients for LR, and ignored that those selected patients still had a high postoperative recurrence rate[7,8]. In order to demonstrate that the selected BCLC-B HCC patients truly benefit from LR rather than remedial treatments after recurrence, and to better understand the tumor characteristics of the selected patients, we compared not only the OS and RFS, but also the RTDS, recurrence patterns, and treatments after recurrence.

In the present study, BCLC-B1 (BCLC-B with N + S ≤ 10) HCC patients were considered as BCLC-B HCC patients who likely benefitted most from LR. Although BCLC-B1 HCC patients were still more likely to develop recurrence after LR than BCLC-A MNHCC patients, these BCLC-B1 patients had mild recurrence pattern, good RTDS and excellent OS similar to BCLC-A MNHCC patients.

However, BCLC-B2 (BCLC-B with N + S > 10) HCC patients not only had a high postoperative recurrence rate, but also an aggressive recurrence pattern. Although the treatment after recurrence was similar between BCLC-B2 patients and BCLC-B1 patients, the BCLC-B2 patients still had a worse RTDS. The long-term OS of BCLC-B2 patients undergoing LR is not satisfactory.

To the best of our knowledge, this study is the first to demonstrate that N + S could predict not only prognosis in BCLC-B HCC patients, but also the recurrence patterns and RTDS in these patients.

In addition, it is interesting to note that patients with BCLC-B1 HCC had worse RFS but comparable OS than patients with BCLC-A MNHCC in this study. In fact, previous studies comparing LT *vs* LR in HCC patients found a similar phenomenon. These studies showed that although patients receiving LR had a higher rate of postoperative recurrence, the 5-year OS between LR and LT was comparable[27,28]. Previous studies have suggested that the reasons for this phenomenon may be related to noncancerous death in the LT group and treatment after recurrence in the LR group, and our results suggest that it may also be related to the recurrence patterns after LR.

As a single-center retrospective study, the present study has some limitations. Firstly, the sample size was small, which may have affected the accuracy of the results. Secondly, there was a lack of

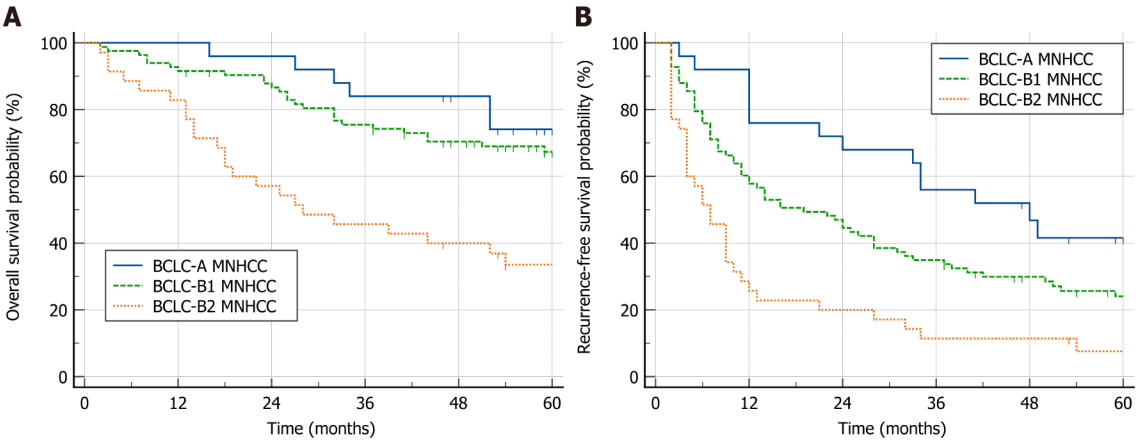

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Figure 2 Comparison of overall survival and recurrence-free survival in multinodular hepatocellular carcinoma patients with Barcelona Clinic Liver Cancer stage A, B1 and B2. A: overall survival; B: recurrence-free survival. BCLC: Barcelona Clinic Liver Cancer; MNHCC: Multinodular hepatocellular carcinoma.

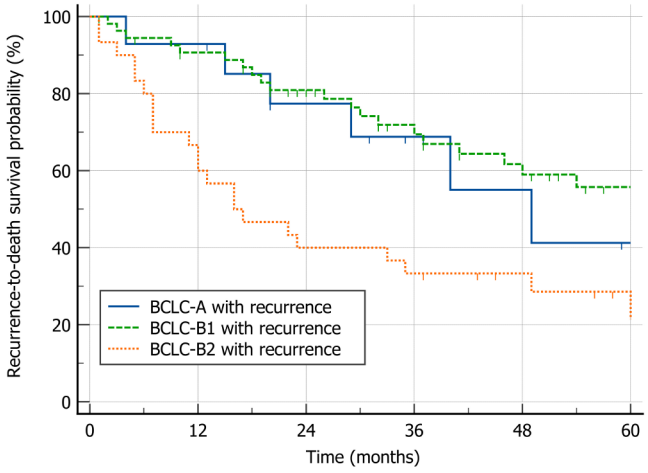

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Figure 3 Comparison of recurrence-to-death survival in Barcelona Clinic Liver Cancer stage A, B1 and B2 multinodular hepatocellular carcinoma patients with recurrence. BCLC: Barcelona Clinic Liver Cancer.

comparison of treatment options other than LR. Some patients with BCLC-B HCC and N + S ≤ 10 would meet the 'Extended Liver Transplant criteria', and the best treatment option for these patients remains to be explored[29]. Finally, the results of this study need to be verified by an external cohort.

CONCLUSION

N + S is a good measure that could predict the OS, RFS, RTDS and recurrence patterns in BCLC-B HCC patients undergoing LR. In particular, BCLC-B patients with N + S ≤ 10 had survivals similar to those of BCLC-A MNHCC patients. Given the computational simplicity of N + S, it is worth exploring the application of N + S to guide decision-making in the treatment of BCLC-B patients.

ARTICLE HIGHLIGHTS

Research background

Emerging studies have shown that Barcelona Clinic Liver Cancer (BCLC) intermediate-stage hepatocellular carcinoma (HCC) patients had a good prognosis after liver resection (LR), but the subgroups of BCLC-B patients more suitable for LR have yet to be defined.

Research motivation

There is a lack of studies on whether the sum of tumor size and number (N + S) can be used to select BCLC-B patients who are more suitable for LR. The effect of recurrence patterns on long-term survival in BCLC-B patients undergoing LR is also poorly explored.

Research objectives

The present study aimed to identify BCLC-B patients more suitable for LR and to further analyze the reasons why these patients could benefit from LR.

Research methods

BCLC stage A or B multinodular HCC (MNHCC) patients undergoing curative hepatectomy were enrolled. Overall survival (OS), recurrence-free survival (RFS), recurrence-to-death survival (RTDS), recurrence patterns, and treatments after recurrence in BCLC-B patients in each subgroup according to N + S were compared with those in BCLC-A patients.

Research results

N + S could predict not only the OS and RFS in BCLC-B HCC patients undergoing hepatectomy, but also the recurrence patterns and RTDS in these patients. BCLC-B patients with N + S ≤ 10 had mild recurrence patterns, good RTDS and excellent OS similar to those in BCLC-A MNHCC patients.

Research conclusions

N + S can be used to select BCLC-B HCC patients who are more suitable for LR, and LR should be considered in BCLC-B patients with N + S ≤ 10.

Research perspectives

As a measure that can be easily obtained and calculated in clinical practice, N + S can help with the clinical decision-making in the treatment of BCLC-B HCC patients.

FOOTNOTES

Author contributions: Hu XS performed the research and wrote the paper; Yang HY performed the follow-up; Leng C designed the research and supervised the report; Zhang ZW provided clinical advice and supervised the report; and all authors read and approved the final version.

Institutional review board statement: This study was reviewed and approved by the Ethics Committee of the Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology (Approval No. TJ-IRB20210918).

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.

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Country/Territory of origin: China

ORCID number: Xin-Sheng Hu 0000-0002-0863-7909; Hui-Yuan Yang 0000-0003-0877-656X; Chao Leng 0000-0002-5391-651X; Zhi-Wei Zhang 0000-0002-4679-2598.

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