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ORIGINAL ARTICLE

Efficacy of surgical treatment on different sizes of hepatitis B virus-related hepatocellular carcinoma and prognostic analysis

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Summary

Purpose: *To investigate the efficacy of surgical resection for patients with different sizes of hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC), and to analyze the risk factors influencing the prognosis.*

Methods: *The clinical data of a total of 138 patients with HBV-related HCC admitted to and treated in our hospital from June 2012 to June 2014 were retrospectively analyzed, and the patients were divided into small HCC (SHCC) group (tumor diameter ≤5 cm, n=69) and solitary large HCC (SLHCC) group (tumor diameter >5 cm, n=69) based on the size of tumors. The differences in operative methods, operation time, intraoperative blood loss, number of intraoperative blood transfusion, time of portal triad clamping and incidence of complications, as well as postoperative liver function and alpha fetoprotein (AFP) indexes, tumor recurrence and survival conditions were compared between the two groups.*

Results: *Among the 138 HCC patients who underwent hepatectomy, 54 cases had ≥3 resected hepatic segments, and 84 cases had <3 resected hepatic segments. SHCC group exhibited remarkably shorter operation time and notably smaller intraoperative blood loss than SLHCC group. The 1-, 3- and 5-year overall survival rates were 91.3%, 87.0%, 71.0%, 60.9%, 58.0% and 46.4%, respectively, and the 1-, 3- and 5-year disease-free survival rates were 71.0%, 63.8%, 47.8%, 44.9%, 37.7% and 30.4%, respectively, in the two groups. The log-rank test showed that the overall survival rate in SHCC group was distinctly higher than that in SLHCC group (p=0.041), and no statistically significant difference in the disease-free survival rate was detected. According to multivariate analysis, HBV deoxyribonucleic acid (DNA) load ≥10^4 U/mL, tumor diameter >5 cm and positive microvascular invasion were independent risk factors for the patient's prognosis (p<0.05).*

Conclusions: *SLHCC has a similar disease-free survival rate to SHCC but a lower overall survival rate than SHCC. HBV DNA load ≥10^4 U/mL, tumor diameter >5 cm and positive microvascular invasion are independent risk factors for the patient's prognosis.*

Key words: *hepatocellular carcinoma, hepatectomy, hepatitis B virus, prognosis*

Introduction

Hepatocellular carcinoma (HCC) is not only a prevalent malignant tumor in the world but also the second most common cause of cancer-related death [1,2]. Currently, surgery is still the major therapeutic method for HCC, but the postoperative recurrence rate in the HCC patients is relatively high, with a 3-year recurrence rate of about 50% and 5-year recurrence rate >70% [3]. The long-term survival after surgical operation is unsatisfactory, and tumor diameter is an important risk factor for postoperative survival and recurrence. The long-term postoperative survival of large HCC (LHCC) (tumor diameter >5 cm) is poorer than that of small HCC (SHCC) (tumor diameter ≤5 cm) [4-6]. Some authors

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argued that there is a special type of LHCC with a tumor diameter >5 cm, expansive growth and intact capsule, named solitary LHCC (SLHCC), which has similar clinical features, postoperative overall survival rate and disease-free survival rate to SHCC, but this viewpoint is still under controversy [7-9].

Viral hepatitis B is the major reason of HCC onset in China, and the replication of hepatitis B virus (HBV) deoxyribonucleic acid (DNA) in liver cells will cause persistent damage to the liver cells, thus inducing hepatic fibrosis and then triggering liver carcinogenesis [10,11]. In this research, the clinical and pathological data of 138 patients with HBV-related HCC admitted to and treated in our hospital from June 2016 to June 2018 were retrospectively reviewed, so as to investigate the efficacy of surgical resection for patients with different sizes of HBV-related HCC and analyze the risk factors influencing their prognosis.

Methods

General data

Retrospective case-control research methods were applied, the clinical and pathological data of 138 HBV-related HCC patients were collected, and all the patients underwent hepatectomy. The patients with a tumor diameter ≤5 cm were assigned into SHCC group (n=69), while those with a tumor diameter >5 cm, solitary and expansive growth and complete capsule according to the diagnostic criteria in literature [7] were enrolled into the SLHCC group (n=69). There were 106 males and 32 females aged 27-81 years old, with a median age of 52.8 years. Inclusion criteria: 1) patients with positive hepatitis B virus surface antigen (HBsAg); 2) those with a liver function Child-Pugh class A or B before operation; 3) those without lymph node or distant metastasis; 4) those who did not receive other non-operative anti-tumor therapies before operation and were not complicated with macroscopic cancer thrombi in the bile duct or blood

Table 1. Demographics and general clinical data of all studied patients

Parameters	*SHCC group n=69*	*SLHCC group n=69*	*p value*
Gender (Male/Female)	51/18	55/14	0.546
Age (years)	51.34±10.71	53.68±10.82	0.204
HBeAg, n (%)			0.473
+	21 (30.4)	26 (37.7)	
-	48 (69.6)	43 (62.3)	
HBV DNA level (U/mL), n (%)			0.610
$<10^4$	32 (46.4)	36 (52.2)	
$\geq10^4$	37 (53.6)	33 (47.8)	
Tumor diameter (cm)	3.3±1.4	8.8±3.2	0.001
Cirrhosis, n (%)	43 (62.3)	35 (50.7)	0.229
Child-Pugh class, n (%)			0.300
A	58 (84.1)	63 (91.3)	
B	11 (15.9)	6 (8.7)	
Microvascular invasion, n (%)			0.166
+	13 (18.8)	21 (30.4)	
-	56 (81.2)	48 (69.6)	
AFP (μg/L), n (%)			0.603
>20	39 (56.5)	43 (62.3)	
≤20	30 (43.5)	26 (37.7)	
Alb (g/L), n (%)			0.532
≥35	65 (94.2)	62 (89.9)	
<35	4 (5.8)	7 (10.1)	
TBIL (μmol/L), n (%)			0.276
<17.1	59 (85.5)	53 (76.8)	
≥17.1	10 (14.5)	16 (23.2)	
Edmondson-Steiner Grade			0.584
I-II	24 (34.8)	20 (29.0)	
III-IV	45 (65.2)	49 (71.0)	

SHCC: Small hepatocellular carcinoma; SLHCC: Solitary large hepatocellular carcinoma; HBeAg: Hepatitis B antigen; HBV: Hepatitis B virus; DNA: Deoxyribonucleic acid; AFP: Alpha fetoprotein; Alb: Albumin; TBIL: Total bilirubin vessel; and 5) those who were definitely diagnosed with HCC via postoperative histopathology. Exclusion criteria: 1) patients with negative HBsAg; 2) those undergoing other anti-tumor therapies before operation; 3) those complicated with macroscopic cancer thrombi in the bile duct or blood vessel; 4) those complicated with severe heart, lung or kidney diseases or serious coagulation disorders; or 5) those complicated with other types of viral hepatitis, alcoholic cirrhosis, autoimmune hepatitis or other primary malignant tumors. The comparisons of general clinical data between the two groups of patients are shown in Table 1. There were no statistically significant differences in HBsAg, HBV DNA load, liver function Child-Pugh classification, complication with liver cirrhosis, microvascular invasion, levels of alpha fetoprotein (AFP), albumin (ALB) and total bilirubin (TBiL) and pathological grade between the two groups before operation (p>0.05). The *Declaration of Helsinki* was followed, the duty of disclosure was performed, and all the patients enrolled signed the informed consent form.

Preoperative evaluation

Blood routine, hepatic and renal functions, tumor markers [AFP, carcinoembryonic antigen (CEA), carbohydrate antigen (CA) 19-9, etc.], 5 markers of hepatitis B, HCV and HBV DNA load were assessed in all the patients before operation. Major imaging examinations such as abdominal B-ultrasound, chest anteroposterior X-ray, contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) were employed. Besides, conventional gastroscopy was conducted to evaluate the conditions of the esophagus, stomach and duodenum before operation. Preoperative diagnosis was performed in accordance with the criteria recommended by the American Association for the Study of Liver Diseases: 1) lesion diameter of 1-2 cm: Enhancement in arterial phase and contrast medium evacuation in venous phase are displayed on two imaging examinations (contrast-enhanced ultrasound and dynamic CT or MRI examination), and 2) lesion diameter >2 cm: Enhancement in arterial phase and contrast medium evaluation in venous phase are detected by 1 kind of imaging examination.

Preoperative antiviral therapy

Targeted antiviral therapy was adopted for hepatitis B before operation as per the stages in 2005 *Guideline of Prevention and Treatment for Chronic Hepatitis B*. INF-α or nucleoside analogues such as lamivudine, adefovir dipivoxil and entecavir were selected as the medicines based on the drug resistance and progression of disease.

Operative treatment

Pringle's maneuver was adopted to temporarily occlude human hepatic blood flow in the hepatic artery and portal vein, traditional clamping method was used for hepatectomy, and argon beam coagulator was employed for liver surface hemostasis. Anatomical hepatectomy was generally utilized as the operative method, where 1 hepatic segment and the dominant regions of subordinate portal vein branches together with the arteries were resected systematically along the portal vein, including the hepatic lobe, hepatic segment and hepatic subsegment, with surgical margins at least 0.5 cm away from the tumor edges. Besides, non-anatomical hepatectomy would be performed if anatomical hepatectomy was not possible. Major hepatectomy was defined as ≥3 hepatic segments resected. Postoperative pathological examinations of the excised hepatic tissues were performed by 3 experienced pathologists, and Edmondson-Steiner grade was used for pathological grading of tumor cells.

Observation indexes

Perioperative indexes: operative method, operation time (from the start of skin incision to the end of skin suture), intraoperative blood loss (suction amount in suction bottle - amount of flushing liquid during operation), number of cases with intraoperative blood transfusion and time of portal triad clamping.

The patients were reexamined once every 3 months within 2 years after operation and once every 6 months later for tumor markers (AFP, CEA, CA19-9, etc.), hepatic function, HBV DNA load and abdominal B-ultrasound. CT or MRI were performed once every 6 months or in the case of suspected tumor recurrence or metastasis, and typical HCC signs discovered in the two imaging examinations indicated intrahepatic recurrence or metastasis. PET/CT was applied to confirm the diagnosis if necessary. The follow-up was terminated in June 2019. The overall survival (from the time of operation to the death or the last follow-up of the patients) and disease-free survival (from the time of operation to the time of tumor recurrence) of the patients were recorded during the follow-up.

The factors that probably affected the prognosis of the patients were subjected to univariate analysis, and then the indexes that exhibited statistical differences were included into Cox's proportional hazards regression model for multivariate analysis.

Statistics

SPSS 22.0 (IBM, Armonk, NY, USA) was utilized for statistical analyses. The normally distributed measurement data were expressed as (x±s), and t-test or Mann-Whitney U test were used for continuous variables. The measurement data in skewed distribution were presented as M (range). Categorical variables were expressed by count (percentage), and x^2 test or corrected x^2 test was employed for inter-group comparison. Survival curves were plotted by Kaplan-Meier method, log-rank test was utilized for survival analysis, and prognostic factors were analyzed by means of the Cox's proportional hazards regression model. P<0.05 suggested that the difference was statistically significant.

Results

Comparison of surgical treatment between the two groups of patients

Among the 138 HCC patients who underwent hepatectomy, 54 cases had ≥3 resected hepatic segments, and 84 cases had <3 resected hepatic segments. The SHCC group had remarkably shorter operation time than the SLHCC group [(92±29) min *vs.* (109±33) min], with a statistically significant difference (p=0.002). There was no statistically significant difference in the time of portal triad clamping during operation between the two groups [(19±14) mL *vs.* (21±17) mL, p=0.452]. The intraoperative blood loss in the SHCC group was notably smaller than that in the SLHCC group [(203.3±38.9) mL *vs.* (297.2±46.9) mL, p<0.001]. The number of cases of intraoperative blood transfusion was 5 and 12 in the two groups, respectively, displaying no statistically significant difference (p=0.118). The postoperative complication rate was 13.0% and 21.7%, respectively, and the difference was not statistically significant between the two groups of

Table 2. Comparison of parameters related to surgery

Parameters	*SHCC group n=69*	*SLHCC group n=69*	*p value*
Operation time (min)	92±29	109±33	0.002
Hepatic inflow occlusion time (min)	19±14	21±17	0.452
Blood loss (mL)	203.3±38.9	297.2±46.9	0.001
Blood transfusion, n (%)	5 (7.2)	12 (17.4)	0.118
Complication, n (%)	9 (13.0)	15 (21.7)	0.261
Incision infection	2 (2.9)	1 (1.4)	
Pulmonary infection	3 (4.3)	2 (2.9)	
Abdominal infection	1 (1.4)	1 (1.4)	
Ascites	0 (0)	2 (2.9)	
Ileus	2 (2.9)	5 (7.2)	
Hepatic failure	1 (1.4)	4 (5.8)	

SHCC: Small hepatocellular carcinoma; SLHCC: Solitary large hepatocellular carcinoma

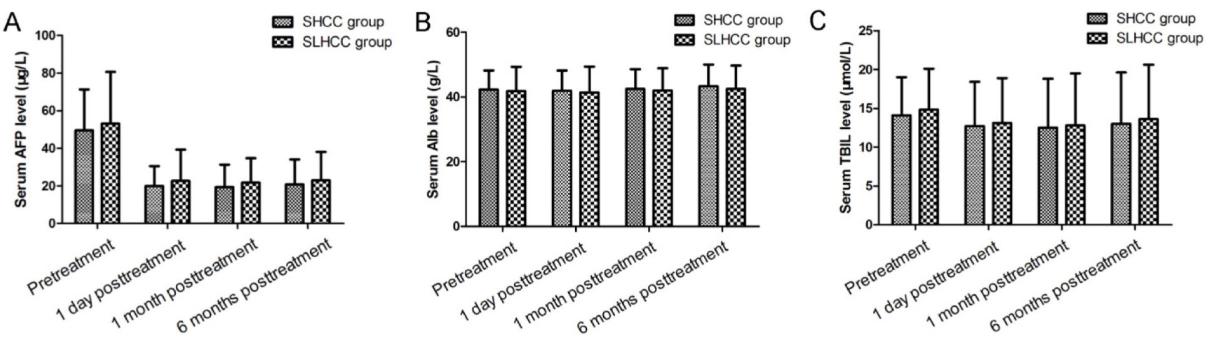

Figure 1. Comparison of pretreatment and posttreatment liver function indexes and serum tumor markers of the patients in the two groups. The differences of serum AFP **(A)**, Alb **(B)**, TBIL **(C)** level (pretreatment and day 1, 1 month, 6 months posttreatment) of patients between SHCC group and SLHCC group had no statistical significance (p>0.05).

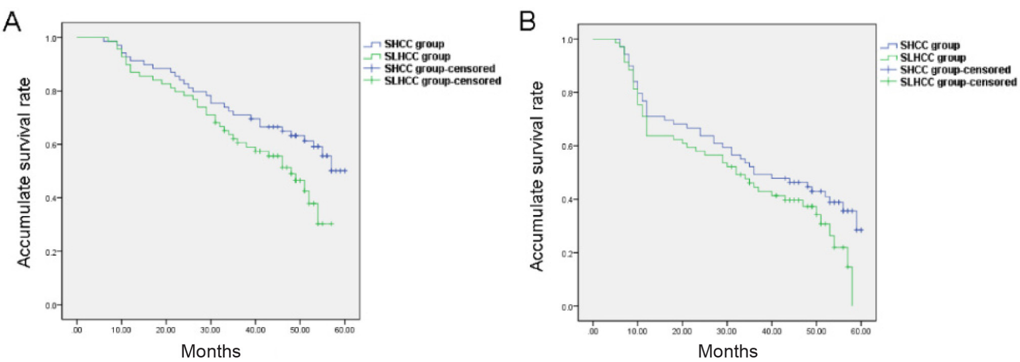

Figure 2. Kaplan-Meier survival curves of patients in the SHCC group and SLHCC group. **A:** The overall survival rate of patients in the SHCC group was significantly higher than that of SLHCC group (p=0.041). **B:** The difference between tumor-free survival rate of patients in the two groups had no statistical significance (p=0.120).

patients (p=0.261). After operation, there were 2 (2.9%) and 1 (1.4%) cases of incision infection in the two groups, respectively. Three (4.3%) and 2 (2.9%) patients were complicated with pulmonary infection. There were 0 (0%) and 2 (2.9%) patients complicated with ascites. Complicated abdominal infection emerged in 1 (1.4%) patient in each group. Two (2.9%) and 5 (7.2%) patients developed ileus. Besides, 1 (1.4%) and 4 (5.8%) patients were complicated with hepatic failure (Table 2).

Recovery of test indexes after operation

The serum AFP levels were 19.9±10.6 μg/L *vs.* 22.6±16.7 μg/L (p=0.259), 19.4±11.9 μg/L *vs.* 21.7±13.1μg/L (p=0.282) and 20.8±13.3 μg/L *vs.* 22.9±15.2 μg/L (p=0.389) on day 1, 1 month and 6 months after operation, respectively, in the two groups, and SHCC group manifested lower levels than the SLHCC group, but the differences were not statistically significant. The serum ALB levels

Table 3. Univariate analysis of predictors for 5-year overall survival rate in patients with hepatitis B virus-related hepatocellular carcinoma

Parameters	*Cases*	*5-year overall survival rate %*	*p value*
Gender			0.851
Male	106	54.7	
Female	32	43.8	
Age (years)			0.805
≤65	119	52.9	
>65	19	47.4	
HBeAg			0.376
+	47	46.8	
-	91	54.9	
HBV DNA level (U/mL)			0.027
$<10^4$	68	60.3	
$\geq10^4$	70	44.3	
Tumor diameter (cm)			0.040
≤5	69	58.0	
>5	69	42.0	
Cirrhosis			0.606
Yes	78	51.3	
No	60	56.6	
Child-Pugh class			0.797
A	121	52.9	
B	17	47.1	
Microvascular invasion			0.003
+	34	29.4	
-	104	59.6	
AFP (μg/L)			0.387
>20	82	48.8	
≤20	56	57.1	
Alb (g/L)			0.757
≥35	127	52.8	
<35	11	45.5	
TBIL (μmol/L)			0.521
≥17.1	26	46.2	
<17.1	112	53.6	
Edmondson-Steiner Grade			0.464
I-II	44	59.1	
III-IV	94	51.1	

HBeAg: Hepatitis Be antigen; HBV: Hepatitis B virus; DNA: Deoxyribonucleic acid; AFP: Alpha fetoprotein; Alb: Albumin; TBIL: Total bilirubin

Table 4. Univariate analysis of predictors for 5-year tumor-free survival rate in patients with hepatitis B virus-related hepatocellular carcinoma

Parameters	*Cases*	*5-year Tumor-free survival rate %*	*p value*
Gender			0.092
Male	106	30.2	
Female	32	46.9	
Age (years)			0.604
≤65	119	35.3	
>65	19	26.3	
HBeAg			0.570
+	47	29.8	
-	91	36.3	
HBV DNA level (U/mL)			0.036
$<10^4$	68	41.2	
$\geq10^4$	70	27.1	
Tumor diameter (cm)			0.029
≤5	69	42.0	
>5	69	26.1	
Cirrhosis			0.371
Yes	78	30.8	
No	60	38.3	
Child-Pugh class			0.789
A	121	34.7	
B	17	29.4	
Microvascular invasion			0.041
+	34	23.5	
-	104	37.5	
AFP (μg/L)			0.855
>20	82	32.9	
≤20	56	35.7	
Alb (g/L)			0.749
≥35	127	34.6	
<35	11	27.3	
TBIL (μmol/L)			0.820
≥17.1	26	30.8	
<17.1	112	34.8	
Edmondson-Steiner Grade			0.704
I-II	44	36.4	
III-IV	94	33.0	

HBeAg: Hepatitis Be antigen; HBV: Hepatitis B virus; DNA: Deoxyribonucleic acid; AFP: Alpha fetoprotein; Alb: Albumin; TBIL: Total bilirubin

Table 5. Multivariate Cox regression analysis of predictors for hepatitis B virus-related hepatocellular carcinoma patients

Parameters	*HR value*	*95% CI*	*p value*
5-year overall survival rate			
HBV DNA level (U/mL)	2.31	1.79-4.50	0.016
Tumor diameter (cm)	1.92	1.55-2.76	0.011
Microvascular invasion	1.95	1.19-3.14	0.009
5-year tumor-free survival rate			
HBV DNA level (U/mL)	2.42	1.81-3.43	0.019
Tumor diameter (cm)	1.88	1.65-3.71	0.011
Microvascular invasion	1.79	1.29-2.89	0.007

HR: Hazard ratio; CI: Confidence interval; HBV: Hepatitis B virus; DNA: Deoxyribonucleic acid in the SHCC group were elevated compared with those in the SLHCC group on day 1, 1 month and 6 months after operation, without statistically significant differences 41.9±3.6 g/L *vs.* 41.4±8.0 g/L (p=0.684), 42.5±6.1 g/L *vs.* 42.0±6.9 g/L p=0.653 and 43.3±6.7 g/L *vs.* 42.5±7.2 g/L p=0.491. On day 1, 1 month and 6 months after operation, the serum TBiL levels declined in SHCC group in comparison with those in SLHCC group, while there were no statistically significant differences 12.7±5.7 μmol/L *vs.* 13.1±5.8 μmol/L (p=0.684), 12.5±6.3 μmol/L *vs.* 12.8±6.7 μmol/L (p=0.787) and 13.0±6.6 μmol/L *vs.* 13.6±7.0 μmol/L (p=0.605)] (Figure 1).

Follow-up results of patient survival

After 60 months of follow-up, 2 patients were lost to follow-up in the SHCC group at 31 and 41 months after operation, respectively, and 3 patients were lost to follow-up in the SLHCC group at 25, 37 and 49 months after operation, respectively. The 1-, 3- and 5-year overall survival rates were 91.3%, 87.0%, 71.0%, 60.9%, 58.0% and 46.4%, respectively, and the 1-, 3- and 5-year disease-free survival rates were 71.0%, 63.8%, 47.8%, 44.9%, 37.7% and 30.4%, respectively, in the two groups. According to the postoperative Kaplan-Meier survival curves in the SHCC group and the SLHCC group (Figure 2), the overall survival rate after log-rank test was obviously better in the SHCC group than in the SLHCC group (p=0.041). The log-rank test revealed that the difference in the disease-free survival rate was not statistically significant between the two groups (p=0.120).

Analysis of prognostic factors for HBV-related HCC patients

The gender, age, HBeAg, HBV DNA load, tumor size, complication with liver cirrhosis, Child-Pugh liver function classification, microvascular invasion, preoperative AFP level, ALB concentration, TBiL level and Edmondson-Steiner grade were included into the univariate analysis. The results indicated that BV DNA load, tumor diameter and microvascular invasion were risk factors for the 5-year overall survival rate (p=0.027, p=0.040, p=0.003) (Table 3) and the 5-year disease-free survival rate (p=0.036, p=0.029, p=0.041) (Table 4) after operation. After the factors with statistical differences in the univariate analysis were enrolled into the Cox's proportional hazards regression model, it was shown in the multivariate analysis results that HBV DNA load $\geq 10^4$ U/mL, tumor diameter >5 cm and positive microvascular invasion were independent risk factors influencing the patient's 5-year overall survival rate and 5-year disease-free survival rate after operation (p<0.05) (Table 5).

Discussion

LHCC is classified as Barcelona stage B or C, so it is not proposed as an indication of hepatectomy, while transcatheter arterial chemoembolization, sorafenib and other combined treatments are recommended, which cannot prominently prolong the survival of the patients either [12]. Long-term clinical practices have discovered that although SLHCC belong to Barcelona stage B or C (hepatectomy not recommended), a similar long-term survival outcome to that of SHCC can be obtained through hepatectomy [7, 8]. In this research, the 5-year overall survival rate after operation was 46.4% in the SLHCC group, higher than that (38.2%) reported by Yang et al [7] but lower than 47.0% reported by Zhou et al [12]. The results also indicated that both SLHCC and SHCC had a similar disease-free survival rate, but the overall survival rate of the SLHCC was lower than in SHCC, which is consistent with the findings of Zhou et al [12] but inconsistent with those of Yang et al [7]. The reason of such a difference may be attributable to the HBV-related HCC patients enrolled in this research.

Previous research results argued that the clinicopathologic characteristics of SLHCC resemble to those of SHCC [7]. In this research, it was shown that there were no statistically significant differences in the majority of the clinical and pathological features between SLHCC and SHCC, such as gender, age, Child-Pugh liver function classification, HBsAg, HBV DNA load, ALB, TBiL, AFP and Edmondson-Steiner grade, which is in line with previous reports. All the patients included into this research were subjected to hepatectomy, and the operation time and intraoperative blood loss were evidently reduced in the SHCC group compared with those in the SLHCC group, while no statistically significant differences in the time of portal triad clamping, amount of intraoperative blood transfusion and incidence of complications were observed.

The multivariate analysis results of Zhou et al [12] demonstrated that Edmondson-Steiner grade is an independent risk factor for the prognosis of SLHCC. According to the results in this research, HBV DNA load $\geq 10^4$ U/mL, tumor diameter >5cm and positive microvascular invasion were independent risk factors for the prognosis of the patients. Vascular spread of tumor cells in the early stage is a crucial mechanism of intrahepatic metastasis of HCC, while microvascular invasion is a vital feature of early dissemination of HCC [13,14]. Zhou et al [12] found that the HCC patients with positive microvascular invasion had a 5-year disease-free survival rate of 11.7% after hepatectomy, lower than 18.8%

in patients with negative microvascular invasion. Microvascular invasion can emerge in the early stage of HCC, but it cannot be diagnosed by conventional imaging examinations before operation, so its role in the survival and prognosis of HCC has been paid increasingly more attention to in recent years [15,16]. In the study of Sumie et al [17] in which 110 HCC patients treated with hepatectomy were retrospectively analyzed, the subgroup with microvascular invasion had poorer postoperative recurrence and survival outcome than those without microvascular invasion, which is consistent with the findings in this research, suggesting that microvascular invasion has an important effect on poor prognosis. Lei et al [18] revealed that nomogram can predict the occurrence of microvascular invasion after operation for HBV-related HCC meeting the Milan criteria in a favorable manner. Therefore, it is feasible to predict the occurrence of microvascular invasion after operation for SLHCC patients by plotting the nomogram, which can guide clinical practices preferably.

Chen et al [19] reported that the overexpression of HBV adaptor protein in HCC cells enhances the invasive and metastatic ability of HCC cells. The findings of Yang et al [20] revealed that HBV infection makes the TGF-β-miR-34a-CCL22 pathway more active, which is able to induce vascular invasion of HCC cells more easily by destroying the immune microenvironment in human body. Lei et al [18] also indicated through predicting postoperative microvascular invasion via nomogram that the high HBV DNA load is an independent risk factor for the occurrence of microvascular invasion. The above arguments are also supported by the results of this research that the raised incidence rate of microvascular invasion in HCC patients with a high HBV DNA load might be an important reason of relatively poor prognosis.

There were still limitations in this research. Firstly, it was a single-center retrospective study, with few patients enrolled. Secondly, the prognostic factors were distributed unevenly in the medical records. Therefore, the conclusion obtained in this research should be verified by multi-center large-sample, randomized prospective studies in the future.

Conclusions

SLHCC has a similar disease-free survival rate to SHCC but a lower overall survival rate than SHCC. HBV DNA load $\geq 10^4$ U/mL, tumor diameter >5 cm and positive microvascular invasion are independent risk factors for the patient's prognosis.

Conflict of interests

The authors declare no conflict of interests.

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