Correlation of postoperative splenic volume increase with prognosis of hepatocellular carcinoma after curative hepatectomy

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Background: Previous studies have reported a close connection between the spleen and hepatic tumours. We investigated the prognostic value of postoperative splenic volume increase (PSVI) in patients with hepatocellular carcinoma after curative hepatectomy.

Methods: This was a retrospective study of adult patients with hepatocellular carcinoma who underwent hepatectomy between January 2007 and May 2013. We categorized patients into 2 groups according to the cut-off value of the receiver operating characteristic curve: group A (PSVI < 19.0%) and group B (PSVI ≥ 19.0%). We compared the clinicopathological data, overall survival and disease-free survival between the 2 groups. We performed univariate and multivariate analyses to identify factors associated with disease-free and overall survival.

Results: There were 275 patients in group A and 196 patients in group B. The 1-, 3- and 5-year overall survival rates were 98.9%, 74.9% and 63.6%, respectively, for patients in group A, and 97.4%, 65.3% and 49.8%, respectively, for patients in group B ($p = 0.004$). The corresponding disease-free survival rates were 69.5%, 48.0% and 40.3%, and 58.1%, 36.5%, and 29.8% ($p = 0.01$). On multivariate analysis, PSVI was an independent predictor of overall ($p = 0.01$) and disease-free ($p = 0.03$) survival.

Conclusion: Postoperative splenic volume increase correlates with poor prognosis of patients with hepatocellular carcinoma after curative hepatectomy.

Contexte : Des études antérieures faisaient état d'un lien étroit entre la rate et les tumeurs hépatiques. Nous avons étudié la valeur pronostique de l'augmentation postopératoire du volume de la rate (APVR) chez les patients ayant subi une hépatectomie curative en raison d'un carcinome hépatocellulaire.

Méthodes : Il s'agit d'une étude rétrospective portant sur des adultes qui ont subi une hépatectomie entre janvier 2007 et mai 2013 pour cause de carcinome hépatocellulaire. Nous avons classé les patients en 2 groupes, selon un seuil sur la courbe ROC : le groupe A (APVR : < 19,0 %) et le groupe B (APVR : ≥ 19,0 %). Nous avons ensuite comparé les données clinicopathologiques, le taux de survie globale et le taux de survie sans récidive des 2 groupes, et avons effectué des analyses univariées et multivariées pour repérer les facteurs associés à la survie sans récidive et à la survie globale.

Résultats : Le groupe A comptait 275 patients, tandis que le groupe B en comptait 196. Les taux de survie globale à 1 an, à 3 ans et à 5 ans étaient de 98,9 %, de 74,9 % et de 63,6 %, respectivement, dans le groupe A, et de 97,4 %, de 65,3 % et de 49,8 %, respectivement, dans le groupe B ($p = 0{,}004$). Les taux de survie sans récidive à 1 an, à 3 ans et à 5 ans étaient de 69,5 %, de 48,0 % et de 40,3 %, respectivement, dans le groupe A, et de 58,1 %, de 36,5 % et de 29,8 %, respectivement, dans le groupe B ($p = 0{,}01$). Selon l'analyse multivariée, l'APVR était un prédicteur indépendant de survie globale ($p = 0{,}01$) et de survie sans récidive ($p = 0{,}03$).

Conclusion : L'augmentation postopératoire du volume de la rate est corrélée à un mauvais pronostic chez les patients ayant subi une hépatectomie curative en raison d'un carcinome hépatocellulaire.

Hepatocellular carcinoma remains a major public health concern and is one of the leading causes of cancer-related deaths.[1] Hepatectomy is regarded as one of the most effective curative treatment of this cancer.[2] Although there have been outstanding advances in the diagnosis, surgical treatment and perioperative treatment of hepatocellular carcinoma in recent years, the recurrence rate remains high, and the long-term recurrence rate is still far from satisfactory.[2] Therefore, it is necessary to conduct further

research on the factors affecting the postoperative prognosis of patients with hepatocellular carcinoma and to identify those at high risk for recurrence and poor survival.

The spleen, the largest lymphoid organ and an important source of antibodies, is closely related to the liver anatomically, histologically and immunologically. Anatomically, the 2 organs are the main components of the portal vein system. Histologically, they possess similar reticuloendothelial structures. Immunologically, they both play important roles in immune homeostasis.[3] Previous studies have shown that splenic volume increased after major hepatectomy.[4–6] Cortez-Retamozo and colleagues[7] found that removal of the spleen, before or after tumour origination, significantly reduced the responses of tumour-associated macrophages and neutrophils, and delayed tumour growth, which confirmed the close connection between the spleen and the hepatic tumour. Splenic volume may affect the prognosis of patients with hepatocellular carcinoma after hepatectomy. To the best of our knowledge, the potential prognostic value of postoperative splenic volume increase (PSVI) has not been evaluated specifically in patients with hepatocellular carcinoma after curative hepatectomy. Therefore, the purpose of this study was to investigate the impact of PSVI on the prognosis of patients with hepatocellular carcinoma after curative hepatectomy.

METHODS

Between January 2007 and May 2013, 1053 adult patients with hepatocellular carcinoma underwent hepatectomy in the Department of Hepatopancreatobiliary Surgery at The First Affiliated Hospital of Fujian Medical University. Hepatocellular carcinoma was diagnosed according to the American Association for the Study of Liver Disease guidelines.[8]

Patients were included in this retrospective study if they 1) had a diagnosis of primary hepatocellular carcinoma at Barcelona Clinic Liver Cancer (BCLC) stage 0, A or B,[9] 2) had undergone curative hepatectomy (R0 resection, with no macroscopic cancerous thrombus in the portal vein, hepatic veins or bile duct) and 3) had appropriate liver functional reserve (Child–Pugh class A or B). Patients were excluded if they 1) had a diagnosis of other malignant diseases, 2) experienced hepatocellular carcinoma recurrence, 3) had hematopathy, connective tissue disease, schistosomiasis or perioperative infection, 4) had a history of malignant disease, chemotherapy or transarterial chemoembolization, 5) had a history of splenectomy or intraoperative splenectomy, 6) died perioperatively, 7) presented with a splenic vascular anomaly, 8) experienced preoperative or intraoperative tumour rupture, 9) presented with preoperative extrahepatic metastasis or 10) were lost to follow-up.

The surgical treatment was chosen by the patient after being informed by the doctor of the risks, benefits, complications and prognoses of the currently available treatments. Patients with elevated hepatitis B virus DNA levels received nucleoside analogue antiviral treatment before and after the operation. Patients underwent anatomic resection unless they were at high risk for postoperative liver failure, in which case nonanatomic resection was performed. The following data were collected before the operation: age, gender, presence of hepatitis B surface antigen (HBsAg), presence of cirrhosis, platelet count, and levels of α-fetoprotein (AFP), total bilirubin, albumin, alanine transaminase and γ-glutamyl transpeptidase. The following data were collected postoperatively: tumour size, presence of microvascular invasion, presence of multiple lesions, tumour differentiation status and BCLC stage. The platelet count 2 months after the operation was also recorded.

Image analysis

Portal venous phase contrast-enhanced computed tomography (CT) scans were used instead of arterial or delayed phase scans because the former produces better images for depicting the outlines of the liver and spleen.[10] Serial transverse enhanced CT scans were obtained at 3.0-mm intervals. Two radiologists blinded to the clinical data independently measured the scans. Each transverse contour of the spleen was traced by hand on the transverse CT scans before and 2 months after the operation (Fig. 1), and the area of the spleen was calculated with the associated software (Picture Archiving and Communications System version 3.6.51, Yilianzhong Corporation). The splenic area in each section was determined by taking the average of the measurements of the 2 radiologists. Each splenic area was then multiplied by the slice thickness to calculate the volume. Finally, total splenic volume was calculated by adding the volume of each slice through the spleen according to a previously described method.[11] We calculated PSVI using

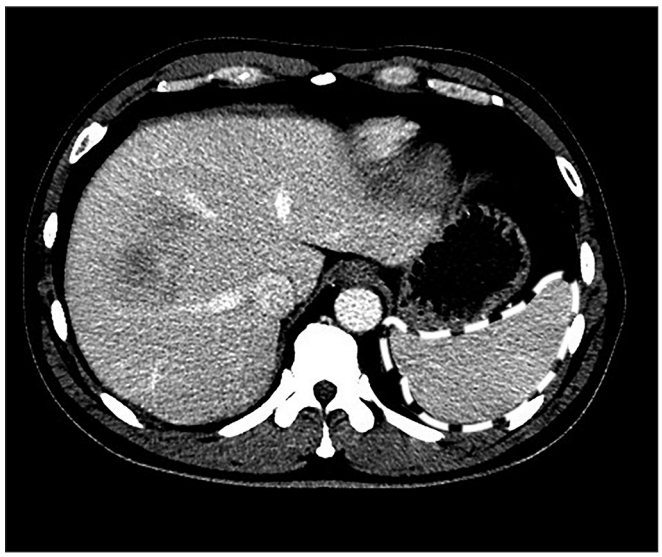

Fig. 1. The transverse contour of the spleen was traced by hand on portal venous phase computed tomography images, and the area of the spleen was then calculated.

the following formula: PSVI = (splenic volume 2 mo after operation – splenic volume before operation)/splenic volume before operation × 100. We defined splenomegaly as splenic volume greater than 300 mL[12] and clinically significant portal hypertension as the presence of esophageal or gastric varices, or thrombocytopenia (platelet count < 100 × 10^9/L) accompanied by splenomegaly.[13]

Follow-up

All patients returned to the hospital 2 months after their operation and underwent re-examination, which included physical examination, routine blood tests, liver function tests, determination of the AFP level, and pulmonary and epigastrium CT. Except for patients with cancer at BCLC stage 0 and those with postoperative hepatic dysfunction, all patients received prophylactic transarterial chemoembolization treatment. After reexamination, all patients underwent routine blood tests, liver function tests, determination of the AFP level and radiological examinations (ultrasonography, CT or magnetic resonance imaging) every 3 months for the next 2 years, after which the frequency of reexamination was changed to every 6 months. Patients positive for hepatitis B virus also received hepatitis B virus DNA tests during their follow-up visits. Bone single photoemission tomography was performed in patients who experienced chronic bone pain. Patients who experienced repeated headaches underwent head CT; if the AFP level rose continuously and the results of head CT were negative, 18F-fludeoxyglucose positron emission tomography/CT was performed. We defined postoperative recurrence or metastasis as 2 typical imaging results, or 1 typical imaging result combined with increased AFP level or a positive result of biopsy/resection pathological examination. Treatments for postoperative recurrence or metastasis included additional surgery, radiofrequency ablation, iodine-125 radioactive seed implantation, transarterial chemoembolization, radiotherapy, sorafenib therapy and supportive care. We defined overall survival as the interval between curative hepatectomy and death or the last follow-up visit. We defined disease-free survival as the interval between curative hepatectomy and the first incidence of detectable recurrence or metastasis. The last follow-up visit was at the end of May 2018.

Statistical analysis

We performed all statistical analyses using SPSS software version 25.0 (IBM Corporation). Continuous variables were expressed as the mean and standard deviation and were compared between groups by means of *t* tests. We compared continuous variables with abnormal distributions and categorical data between groups using the χ^2 test. We used a receiver operating characteristic curve to establish the cut-off value for the prediction of death according to the PSVI. We analyzed disease-free and overall survival rates with the Kaplan–Meier method and analyzed the differences with the log-rank test. Univariate and multivariate analyses were performed with the Cox proportional hazards model. We entered potential risk factors with $p < 0.05$ in the univariate analysis into the Cox model. Two-tailed p values < 0.05 were considered statistically significant.

Ethics approval

This research was approved by the Ethics Committee of The First Affiliated Hospital of Fujian Medical University, and all treatments were performed in accordance with the relevant guidelines and regulations.

RESULTS

A total of 471 patients were included in the study, 411 men (87.3%) and 60 women (12.7%) with a median age of 53 (range 21–84) years. Of the 471, 326 (69.2%) had cirrhosis, 150 (31.8%) had AFP levels greater than 400 ng/mL, 413 (87.7%) were positive for hepatitis B virus, and 179 (38.0%) had microvascular invasion. There were 69 patients (14.6%) with BCLC stage 0 cancer, 165 (35.0%) with BCLC stage A cancer and 237 (50.3%) with BCLC stage B cancer. Nine patients (1.9%) had clinically significant portal hypertension preoperatively, and 29 (6.2%) had clinically significant portal hypertension 2 months after the operation ($p = 0.005$). More patients had thrombocytopenia 2 months after the operation than before the operation (37 [7.8%] v. 108 [22.9%], $p < 0.001$).

The receiver operating characteristic curve for the prediction of death according to the PSVI is shown in Fig. 2.

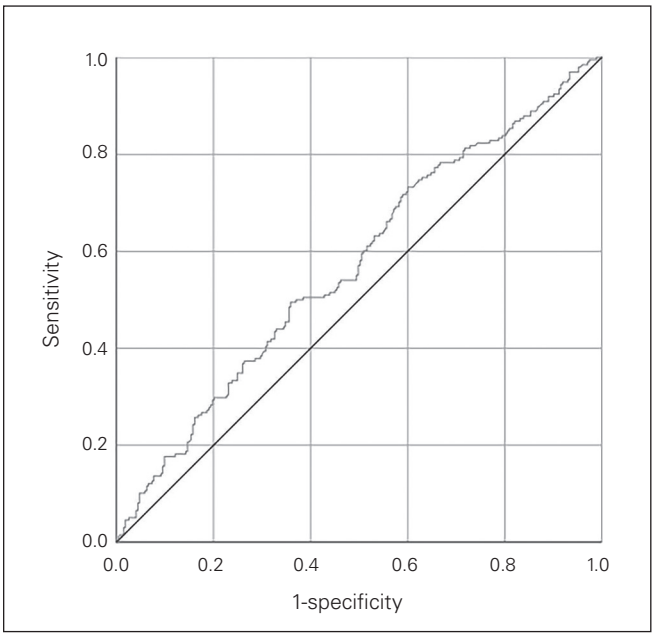

Fig. 2. Receiver operator characteristic curve of postoperative splenic volume increase predicting death, showing the cut-off value of 19.0% (sensitivity = 0.495, specificity = 0.641, $p = 0.008$).

The area under the curve was 0.571, and the p value was 0.008. We categorized the patients into 2 groups based on their PSVI value as follows: group A, PSVI less than 19.0% (n = 275); group B, PSVI 19.0% or greater (n = 196). Except for the presence of cirrhosis, there were no significant differences in the baseline and clinicopathological characteristics between the 2 groups (Table 1).

Impact of postoperative splenic volume increase on disease-free and overall survival

We used univariate Cox proportional hazards modelling to identify the factors associated with disease-free and overall survival (Tables 2 and 3). The 1-, 3- and 5-year disease-free survival rates were 69.5%, 48.0% and 40.3%, respectively, in group A and 58.1%, 36.5% and 29.8%, respectively, in group B (log-rank test, p = 0.01). The corresponding overall survival rates were 98.9%, 74.9% and 63.6%, and 97.4%, 65.3% and 49.8% (log-rank test,

Table 1. Baseline clinicopathological characteristics of groups A and B*

Characteristic	No. (%) of patients† Group A n = 275	Group B n = 196	p value
Age, yr, mean ± SD	52.3 ± 11.6	52.7 ± 11.4	0.7
Male sex	240 (87.3)	171 (87.2)	0.99
Preoperative α-fetoprotein level ≥ 400 ng/mL	86 (31.3)	64 (32.6)	0.8
Hepatitis B surface antigen positive	241 (87.6)	172 (87.8)	0.97
Preoperative platelet count, $\times 10^9$/L, mean ± SD	193.2 ± 83.3	188.2 ± 67.6	0.5
Preoperative total bilirubin level, μmol/L, mean ± SD	15.2 ± 6.7	15.8 ± 6.5	0.3
Preoperative albumin level, g/L, mean ± SD	40.5 ± 3.8	40.8 ± 4.5	0.6
Preoperative alanine transaminase level ≥ 50 U/L	70 (25.4)	53 (27.0)	0.7
Preoperative γ-glutamyl transpeptidase level ≥ 75 U/L	101 (36.7)	59 (30.1)	0.1
Tumour size, cm, mean ± SD	5.9 ± 3.7	6.2 ± 4.0	0.4
Multiple lesions	29 (10.5)	29 (14.8)	0.2
Cirrhosis	213 (77.4)	113 (57.6)	< 0.001
Microvascular invasion	105 (38.2)	74 (37.8)	0.9
Tumour differentiation			0.97
Well	32 (11.6)	24 (12.2)	
Moderate	175 (63.6)	125 (63.8)	
Low	68 (24.7)	47 (24.0)	
BCLC stage			0.1
0	48 (17.4)	21 (10.7)	
A	96 (34.9)	69 (35.2)	
B	131 (47.6)	106 (54.1)	

BCLC = Barcelona Clinic Liver Cancer; SD = standard deviation.
*Group A: postoperative splenic volume increase less than 19.0%; group B: postoperative splenic volume increase 19.0% or greater.
†Except where noted otherwise.

Table 2. Host- and tumour-related prognostic factors associated with disease-free survival on univariate analysis

Factor	No. of patients	Disease-free survival rate, % 1 yr	3 yr	5 yr	p value
Age, yr					0.05
< 50	186	68.3	49.8	41.2	
≥ 50	285	62.5	38.9	32.5	
Preoperative albumin level, g/L					0.02
< 35	37	54.1	23.8	20.8	
≥ 35	434	65.7	45.1	37.2	
Postoperative splenic volume increase, %					0.0
< 19.0	275	69.5	48.0	40.3	
≥ 19.0	196	58.1	36.5	29.8	
Microvascular invasion					< 0.001
Present	179	53.1	32.4	27.4	
Absent	292	71.9	49.5	41.2	
BCLC stage					< 0.001
0	69	84.0	60.4	48.7	
A	165	71.5	48.4	38.6	
B	237	54.0	34.2	30.4	

BCLC = Barcelona Clinic Liver Cancer.

Table 3. Host- and tumour-related prognostic factors associated with overall survival on univariate analysis

Factor	No. of patients	Overall survival rate, % 1 yr	3 yr	5 yr	p value
Age, yr					0.02
< 50	186	98.4	75.3	64.5	
≥ 50	285	98.2	68.0	53.6	
Preoperative albumin level, g/L					0.001
< 35	37	94.6	51.4	35.1	
≥ 35	434	98.6	72.6	59.9	
Postoperative splenic volume increase, %					0.004
< 19.0	275	98.9	74.9	63.6	
≥ 19.0	196	97.4	65.3	49.8	
Cirrhosis					0.03
Present	326	98.2	69.6	54.3	
Absent	145	99.3	74.5	66.1	
Microvascular invasion					< 0.001
Present	179	96.6	54.2	44.1	
Absent	292	99.3	81.2	66.4	
Tumour differentiation					0.006
Well	56	96.4	87.5	75.0	
Moderate	302	99.0	70.5	57.5	
Low	113	96.5	62.8	50.4	
BCLC stage					< 0.001
0	69	98.6	91.3	84.1	
A	165	99.4	75.8	60.6	
B	237	97.0	60.3	48.4	

BCLC = Barcelona Clinic Liver Cancer.

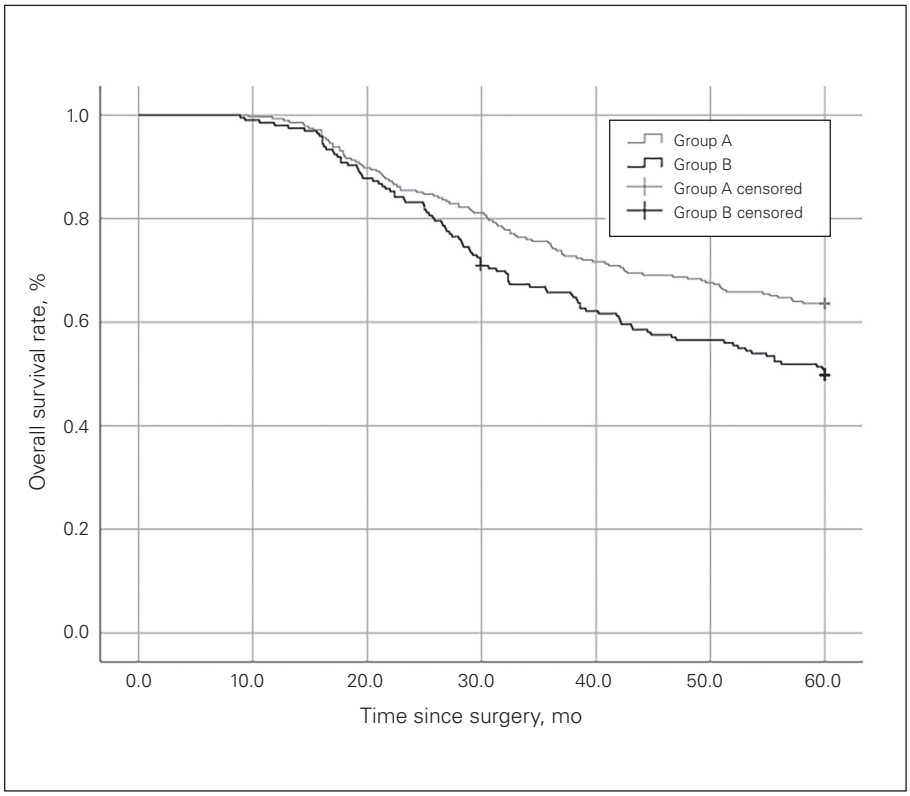

Fig. 3. Overall survival rates of group A (postoperative splenic volume increase < 19.0%) and group B (postoperative splenic volume increase ≥ 19.0%).

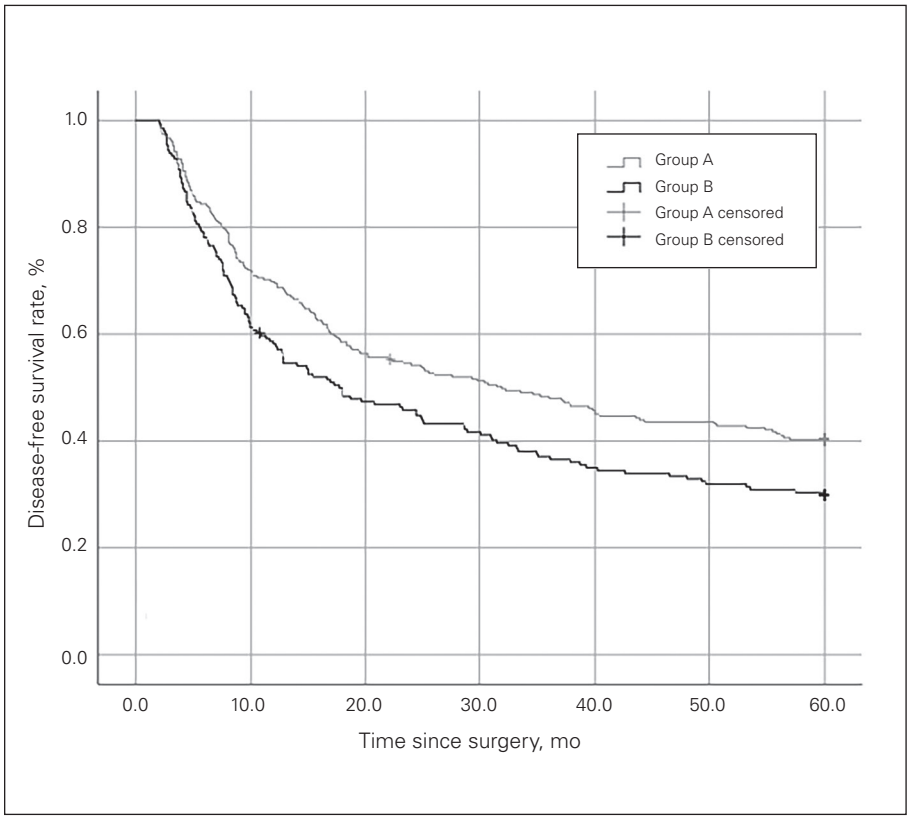

Fig. 4. Disease-free survival rates of group A (postoperative splenic volume increase < 19.0%) and group B (postoperative splenic volume increase ≥ 19.0%).

p = 0.004). The 1-, 3- and 5-year overall survival rates of patients in group A were significantly better than those of patients in group B (p = 0.004) (Fig. 3). The 1-, 3- and 5-year disease-free survival rates of patients in group A were significantly better than those of patients in group B (p = 0.01) (Fig. 4).

Risk factors for prognosis

Univariate analysis showed that age 50 years or more, preoperative albumin level less than 35 g/L, PSVI 19.0% or greater, presence of microvascular invasion and high BCLC stage were all significantly associated with poor disease-free survival (Table 2). No association was found for gender (p = 0.8), preoperative AFP level (p = 0.7), HBsAg positivity (p = 0.6), preoperative platelet count (p = 0.8), platelet count at 2 months (p = 0.1), preoperative total bilirubin level (p = 0.4), preoperative alanine transaminase level (p = 0.9), preoperative γ-glutamyl transpeptidase level (p = 0.6), tumour size (p = 0.6), presence of multiple lesions (p = 0.2), presence of cirrhosis (p = 0.2) or tumour differentiation (p = 0.5). On univariate analysis, age 50 years or more, preoperative albumin level less than 35 g/L, PSVI 19.0% or greater, presence of cirrhosis, presence of microvascular invasion, low level of tumour differentiation and high BCLC stage were all significantly associated with poor overall survival (Table 3). No association was found for gender (p = 0.5), preoperative AFP level (p = 0.2), HBsAg positivity (p = 0.6), preoperative platelet count (p = 0.1), platelet count at 2 months (p = 0.07), preoperative total bilirubin level (p = 0.4), preoperative alanine transaminase level (p = 0.5), preoperative γ-glutamyl transpeptidase level (p = 0.7), tumour size (p = 0.5) or presence of multiple lesions (p = 0.2).

Multivariate analysis identified the following factors as being significantly associated with poor disease-free

survival: PSVI 19.0% or greater (hazard ratio [HR] 1.293, 95% confidence interval [CI] 1.029–1.624), presence of microvascular invasion (HR 1.443, 95% CI 1.139–1.828) and high BCLC stage (HR 1.312, 95% CI 1.106–1.556) (Table 4). The following factors were significantly associated with poor overall survival: preoperative albumin level less than 35.0 g/L (HR 1.839, 95% CI 1.193–2.835), PSVI ≥ 19.0% (HR 1.594, 95% CI 1.197–2.122), presence of cirrhosis (HR 1.660, 95% CI 1.191–2.315), presence of microvascular invasion (HR 1.702, 95% CI 1.279–2.264), low level of tumour differentiation (HR 1.342, 95% CI 1.062–1.697) and high BCLC stage (HR 1.676, 95% CI 1.336–2.102) (Table 5).

Table 4. Independent prognostic factors for disease-free survival on multivariate analysis

Factor	HR (95% CI)
Age	1.218 (0.961–1.544)
Preoperative albumin level	1.392 (0.945–2.049)
Postoperative splenic volume increase	1.293 (1.029–1.624)
Microvascular invasion	1.443 (1.139–1.828)
BCLC stage	1.312 (1.106–1.556)

BCLC = Barcelona Clinic Liver Cancer; CI = confidence interval; HR = hazard ratio.

Table 5. Independent prognostic factors for overall survival on multivariate analysis

Factor	HR (95% CI)
Age	1.307 (0.969–1.762)
Preoperative albumin level	1.839 (1.193–2.835)
Postoperative splenic volume increase	1.594 (1.197–2.122)
Cirrhosis	1.660 (1.191–2.315)
Microvascular invasion	1.702 (1.279–2.264)
Tumour differentiation	1.342 (1.062–1.697)
BCLC stage	1.676 (1.336–2.102)

BCLC = Barcelona Clinic Liver Cancer; CI = confidence interval; HR = hazard ratio.

Discussion

We found that splenic volume had clearly increased in some patients with hepatocellular carcinoma 2 months after curative hepatectomy (Fig. 5) and that PSVI of 19.0% or greater was an independent and significant predictive factor for poor prognosis in patients with hepatocellular carcinoma after curative hepatectomy.

Previous studies showed that postoperative volume of the spleen increased after hepatectomy in living donors[5,6] and patients with cirrhosis.[3] Several potential mechanisms may explain why splenic volume increases postoperatively. In our study and in previous studies,[4–6] it was noted that the spleen enlarges during liver regeneration. Both the liver and the spleen belong to the reticuloendothelial system and may share common regulatory pathways, including regulation by the same cytokines.[14] Some researchers have suggested that hepatectomy stimulates DNA synthetic activity in the spleen, probably through hepatotrophic factors such as hepatocyte growth factor and epidermal growth factor.[15,16]

Long-term splenomegaly may lead to poor prognosis via latent mechanisms. Recent research showed that erythroblast-like cells (Ter-cells) were enriched in the enlarged spleen and facilitated tumour progression and metastasis by secreting neurotrophic factor artemin into the blood.[17] After blockade of Ter-cell–derived artemin, hepatocellular carcinoma growth was inhibited.[17] In addition, splenomegaly is closely related to hypersplenism.[18] The spleen plays an immune regulatory role. There are increased numbers of CD4(+) T cells and cells expressing programmed death ligand 1 and 2 in patients with splenomegaly, which means that they have poor tumour immunity and suggests a potential mechanism by which splenomegaly may cause recurrence of hepatocellular carcinoma.[19,20] In cases of hypersplenism, an increased CD4/

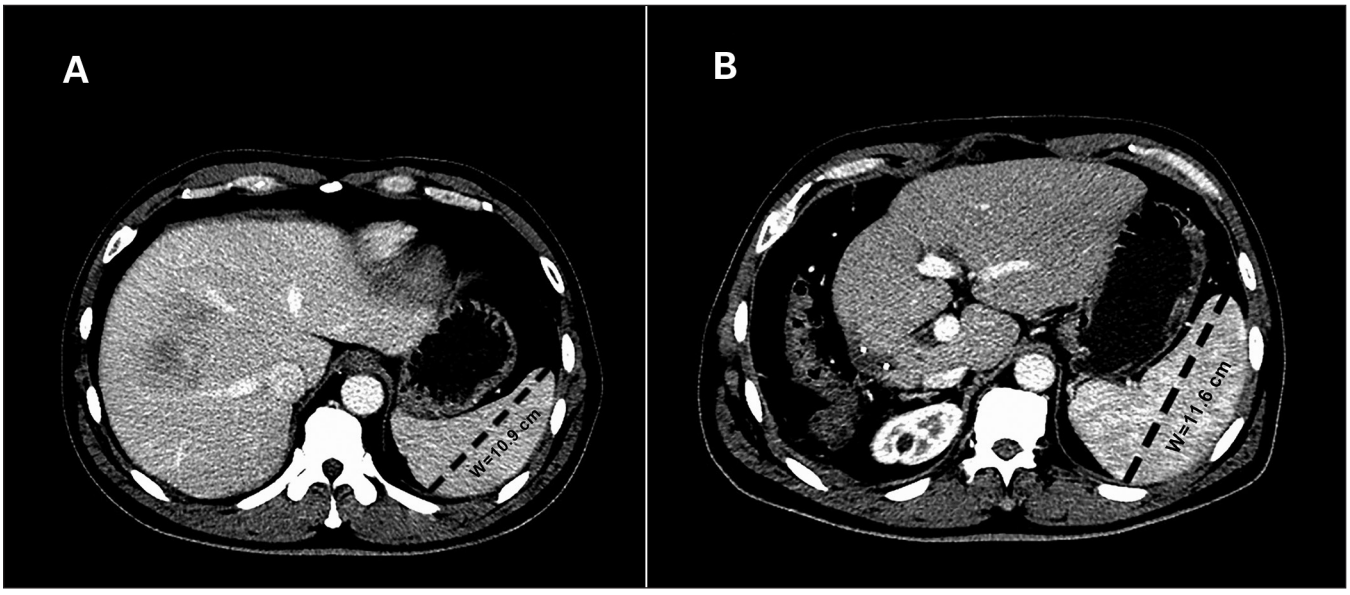

Fig. 5. Maximal width of spleen on portal venous phase computed tomography images before (A) and 2 months after (B) curative hepatectomy. The spleen slowly enlarged during the 2 months after the operation.

CD8 ratio is observed, which may promote hepatocellular carcinoma progression.[21] Furthermore, it has been shown that nuclear factor kappa-light-chain-enhancer of activated B cells p65/cRel signalling is significantly upregulated in hypersplenic macrophages, promoting increased phagocytosis and the secretion of both proinflammatory and profibrogenic factors (e.g., interleukin-1β, interferon-γ, tumour necrosis factor-α and transforming growth factor-β1) in patients with cirrhosis and hypersplenism.[22] Inflammation and hepatic fibrosis are strongly associated with hepatocellular carcinoma.[23,24]

Tumour-associated macrophages and neutrophils, which descend from immature monocytic and granulocytic cells, respectively, can control cancer growth and exist in almost all solid neoplasms. Cortez-Retamozo and colleagues[7] found that removal of the spleen (a reservoir of monocytes) could delay tumour growth. Splenomegaly may lead to increased storage of monocytes, resulting in tumour progression and poor prognosis. Moreover, splenomegaly, which indicates increased storage of blood cells and a higher phagocytic capacity of splenic macrophages, results in lower peripheral blood counts.[25] In the current study, more patients had thrombocytopenia combined with splenomegaly 2 months after surgery than before surgery. Platelet-derived growth factor is stored in platelets. When widespread destruction of platelets occurs during splenomegaly, platelet-derived growth factor is released into the hematologic system and contributes to hepatic carcinogenesis.[26] In previous studies, decreased platelet levels were found to be significantly associated with the risk of hepatocellular carcinoma recurrence.[27,28]

Besides PSVI, a low preoperative albumin level was another risk factor for poor prognosis in our study. This result was consistent with that of Nojiri and colleagues.[29] In vitro results have indicated that albumin itself suppresses the proliferation of hepatocellular carcinoma.[30] It has the ability to stabilize cell growth and DNA replication.[31] Low albumin levels can weaken the immune system and affect long-term disease-free survival and overall survival in patients with cancer.[32] The presence of cirrhosis was also associated with poor overall survival in our study. Most cases of hepatocellular carcinoma develop in the presence of liver cirrhosis. After tumour recurrence, impaired liver function will limit treatment options and cause poor prognosis.[33]

In addition to host-related factors, tumour-related factors are influential in determining the prognosis of patients with hepatocellular carcinoma after curative hepatectomy. Microvascular invasion facilitates the dissemination of hepatocellular carcinoma cells and tends to indicate the presence of intra- and extrahepatic metastasis. The presence of microvascular invasion and low levels of tumour differentiation are markers of aggressive hepatocellular carcinoma. Microvascular invasion, low levels of tumour differentiation and high BCLC stage were related to poor prognosis in our study. These results were identical to those of previous studies.[34–36]

Limitations

This study has limitations. First, it was a retrospective single-centre study. Second, because the platinum drugs used in transarterial chemoembolization may be associated with splenomegaly,[37] we did not continue to measure the volume of the spleen throughout the follow-up period.

Conclusion

We have shown that PSVI correlates with poor prognosis in patients with hepatocellular carcinoma after curative hepatectomy. As a latent marker for predicting postoperative outcomes, PSVI could serve as a simple index for identifying patients with poor prognosis and be incorporated into novel individualized follow-up strategies to improve the outcomes of patients with hepatocellular carcinoma. Further studies are warranted to further elucidate the relation between the change in postoperative splenic volume and the prognosis of patients with hepatocellular carcinoma after surgery.

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Contributors: J. Lin and S.-G. Weng designed the study. J. Lin, M.-H. Chi and X. Zhang acquired and analyzed the data. J. Lin and S.-G. Weng wrote the article, which all authors reviewed and approved for publication.

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