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ORIGINAL RESEARCH

Tumor Compression of the Hepatic or Portal Vein Predicts the Presence of Microvascular Invasion and Satellite Nodules in Hepatocellular Carcinoma: A Retrospective Study

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Purpose: This study aimed to evaluate the association of tumor compression in the hepatic or portal vein with the presence of microvascular invasion (MVI) and satellite nodules in patients with hepatocellular carcinoma (HCC).

Patients and Methods: HCC patients at the Barcelona Clinic Liver Cancer (BCLC) stages 0-A who underwent a radical liver resection in our hospitals from January 2016 to December 2022 were collected. The tumor compression of the portal or hepatic vein in individual patients was analyzed by preoperative imaging and postoperative pathology. Their MVI, satellite nodules, overall survival (OS), and recurrence-free survival (RFS) were analyzed, and the potential risk factors for the MVI and satellite nodules of patients were analyzed by univariable and multivariable logistic analyses.

Results: A total of 390 patients were included with 333 male and 263 patients <60 years old. Of them, 51 (13.1%) HCC patients had tumor venous compression, which was not significantly associated with OS and RFS, but significantly related to higher positive rates of MVI and satellite nodules than those without tumor-venous compression (MVI, 51.0% vs 36.6%, $P = 0.025$; satellite nodules, 19.6% vs 9.1%, $P = 0.023$). Tumor venous compression was an independent risk factor for the development of MVI (OR = 1.902, 95% CI: 1.049–3.447; $P = 0.034$) and satellite nodules (OR = 2.871, 95% CI: 1.277–6.458; $P = 0.011$).

Conclusion: Preoperative tumor venous compression is an independent predictor of MVI and satellite nodules in HCC patients at BCLC stages 0-A and may serve as an imaging biomarker for determining the resection margin and treatment planning.

Keywords: hepatocellular carcinoma, microvascular invasion, perivascular, prognosis, satellite nodules, venous compression

Introduction

Hepatocellular carcinoma (HCC) is a globally prevalent malignancy with high incidence and mortality rates.[1–3] Currently, HCC patients at very early or early stages are treated with radical resection, ablation, or liver transplantation, according to the Barcelona Clinic Liver Cancer (BCLC) staging and treatment strategy.[4,5] Although the patients with HCC at very early or early stages have the highest post-operative 5-year overall survival (OS) rate of 75.2%, nearly half (43.9%) of these patients suffer from recurrence within 5 years post radical resection.[6] Microvascular invasion (MVI) is

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the presence of HCC cells in small blood or lymphatic vessels of the liver.[7] Approximately, MVI can be detected in 15–57% of surgical specimens from HCC patients with liver resection and transplantation,[8] and nearly half (49%) of HCC patients with MVI suffer from HCC recurrence within 6 months post liver resection.[9] Furthermore, satellite nodules are small HCC lesions located in the liver parenchyma, typical surrounding within 2 cm of the primary tumor.[10] Approximately, satellite nodules are detected in 19–41% of surgical specimens from HCC patients with liver tumor resection and transplantation,[11,12] and the presence of satellite nodules is also an important predictor of HCC recurrence after liver tumor resection and liver transplantation.[12,13] Mechanistically, satellite nodules are considered to be derived from MVI.[14] MVI and satellite nodules are difficult to be pre-operatively determined by CT or MRI, and the unresected MVI and satellite nodules in the residual liver will lead to inevitable HCC recurrence of those with liver tumor resection. Therefore, accurate and preoperative evaluation of the presence of MVI and satellite nodules is of great significance for guiding personalized and precise therapies for HCC patients.[15]

Previous studies have explored pre-operatively non-invasive evaluation of MVI and satellite nodules of HCC in the clinic. High levels of serum alpha-fetoprotein (AFP), low levels of serum albumin, liver cirrhosis, high tumor burden score, non-smooth tumor margin, absent radiological capsule on MRI, and intratumoral artery are independent risk factors of MVI development in HCC.[16–18] Multimodal AI models by integrating clinical, imaging, and radiomics features have shown excellent performance in predicting MVI in HCC.[19–23] Our recent studies have also shown that low levels of blood supply in the portal veins are associated with the development of MVI in HCC.[24,25] Furthermore, the prevalence of satellite nodules is significantly associated with the single nodular type of HCC with extranodular growth, the confluent multinodular type of HCC, and the poor differentiated HCC, compared to the early HCC with a vaguely nodular type, the single nodular type of HCC, and the well and moderately differentiated HCC.[11] Moreover, a maximal standardized uptake value (SUVmax) >8.8 of glucose metabolism on 18F-FDG PET/CT is a significantly independent factor for the development of distant satellite nodules >1 cm from the main tumor.[26]

A recent study has elucidated the biomechanical process of MVI of tumors, including tumor vascular compression, intravasation, and thrombus formation.[27] Theoretically, tumor vascular compression is a risk factor of MVI and satellite nodules in HCC. Although tumor venous compression in patients with HCC at very early or early stages is common, yet its association with the development of MVI and satellite nodules in patients with HCC at very early and early stages remains unexplored.

This study retrospectively analyzed the association between preoperative tumor venous compression and postoperative MVI as well as satellite nodules in patients with HCC at very early and early stages. This study aimed at determining whether the presence of tumor vascular compression was a useful preoperative biomarker to predict the development of MVI and satellite nodules in the liver of HCC patients.

Methods

Patients

The study was approved by the Ethics Committee of the Second Affiliated Hospital of Kunming Medical University (approval No. PJ-SCIENCE-2024-4). Informed consent was waived due to its retrospective design. Data in the study were anonymized, and particular attention was paid to protecting patient privacy and ensuring data confidentiality and security. The study complied with the *Declaration of Helsinki* adopted by the World Medical Association.[28–30]

Inclusion criteria were: patients with newly diagnosed HCC at very-early or early stages (BCLC stages 0 or A) underwent radical liver tumor resection at the Second Affiliated Hospital of Kunming Medical University between January 2016 and December 2022; HCC and its R0 margin were confirmed by postoperative pathology; and triphasic liver CT or MRI scans were performed within 2 weeks before liver tumor resection. The exclusive criteria included HCC patients with preoperative transcatheter arterial chemoembolization (TACE), transcatheter arterial embolization (TAE), transcatheter arterial infusion (TAI), hepatic artery infusion chemotherapy (HAIC), or radiotherapy, as well as systemic treatments with targeted therapy or immunotherapy before liver tumor resection; they had concurrent diagnoses of other malignancies; or their clinical or survival data missed.

Grouping

Tumor venous compression is defined as the presence of a tumor contacting with the hepatic or portal vein, compressing the vein to the point of luminal narrowing or even complete occlusion without a visible tumor thrombus within the venous lumen by imaging (Figure 1A). The presence of tumor venous compression in the portal veins or hepatic veins of individual HCC patients was examined using preoperative triphasic liver CT or MRI scans (Figure 1B–E), reviewed by two experienced radiologists, and the absence of tumor thrombus in the portal veins or hepatic veins in individual HCC patients was confirmed by postoperative pathology. The included HCC patients were divided into the tumor venous compression and non-venous compression groups.

Pathological Evaluation of MVI and Satellite Nodules

The pathological examination was conducted by two experienced pathologists. The surgical liver specimens were fixed in 10% formalin, and paraffin-embedded. The liver tissue sections (4 μm) were serially sectioned with an interval of 10 mm and stained with hematoxylin and eosin. The presence of MVI in individual sections was examined and defined as a cluster of cancer cells in the microvascular lumen.[31] The presence of satellite nodules was analyzed and defined as small cancerous foci located in the liver parenchyma within 2 cm from the main tumor, which was separated by non-tumor liver tissues.[32] When it was difficult to distinguish MVI from satellite nodule by pathology, a diagnosis of satellite nodule was made.[14]

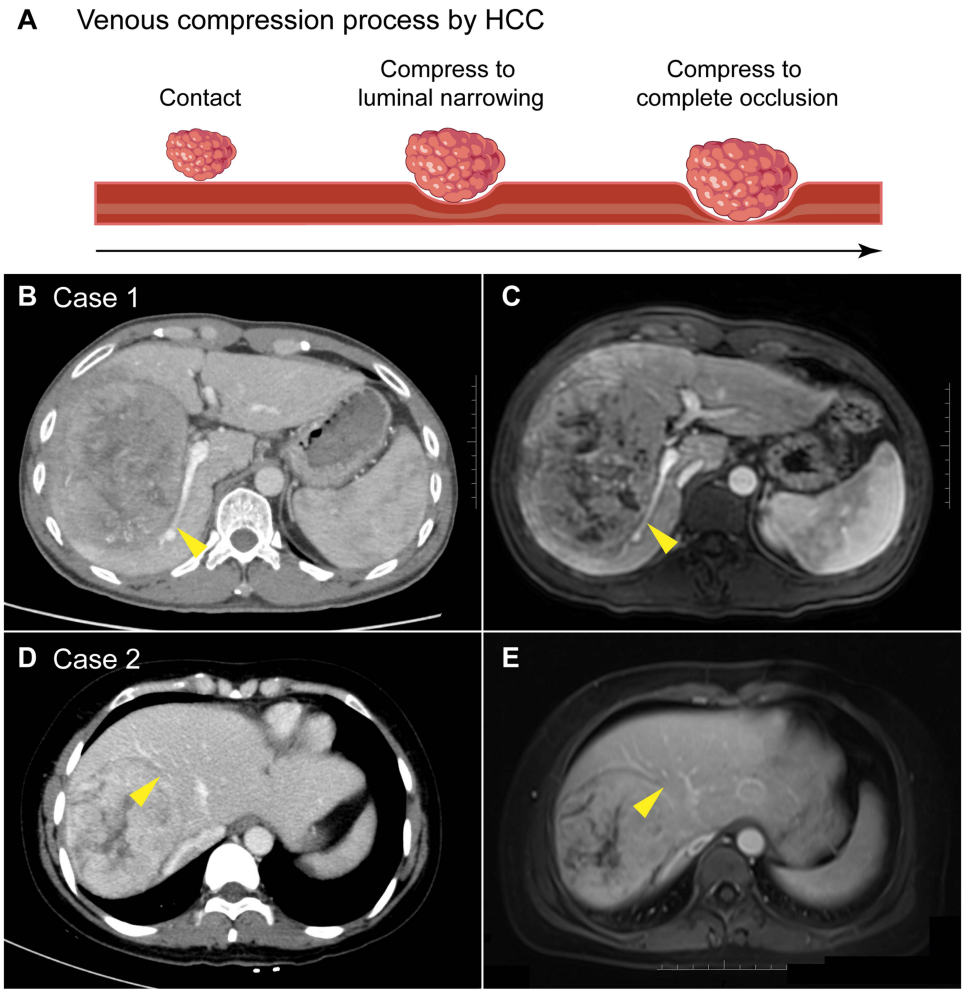

Figure 1 Venous compression of HCC. (**A**) A schematic diagram illustrates the process of venous compression by HCC. (**B** and **C**) A case of HCC with tumor venous compression of the right portal vein branch on CT (**B**) and MRI (**C**). (**D** and **E**) A case of HCC with tumor venous compression of the middle hepatic vein on CT (**D**) and MRI (**E**). Yellow arrowheads indicate the typical sites of tumor venous compression.
Abbreviation: HCC, hepatocellular carcinoma.

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Data Collection

The data at admission were obtained from the medical record system of the Second Affiliated Hospital of Kunming Medical University, and they included age, which was stratified into ≤60 or >60 years old;[33] sex;[34] preoperative laboratory parameters containing hepatitis B or C virus infection,[24] the albumin-bilirubin (ALBI) grade, which is a simpler, more objective, and discriminatory method to assess liver function in HCC patients than Child-Pugh score and stratified into 1, 2, 3 grades,[35] and serum AFP levels, which were stratified into ≤400 ng/mL or >400 ng/mL;[36,37] preoperative imaging parameters including liver cirrhosis, the maximum tumor diameter, and the number of macroscopic tumor nodules.[38,39]

Post-operative data were obtained from all patients when they were subjected to a standard follow-up until December 2024, including every 1–2 months for the first 6 months after discharge, every 3–4 months thereafter until 2 years post-surgery, and every 5–6 months after 2 years.[24,40] During the each follow-up visiting, all patients were subjected to physical examination, liver function tests, tumor marker tests, chest X-ray or CT, and at least one abdominal imaging of liver ultrasound, or triphasic liver CT or MRI. The tumor recurrence was defined as imaging evidence of HCC.[41] HCC patients with recurrence were treated with liver transplantation, repeat liver resection, radio-frequency ablation, TACE, targeted therapy, immunotherapy, or best supportive care as appropriate.[42–45] Recurrence-free survival (RFS) was calculated from the date of hepatectomy to the date of HCC recurrence or death. OS was determined from the date of hepatectomy to the date of death from any cause.

Statistical Analysis

Data were analyzed using SPSS 26.0 (SPSS, Chicago, IL, USA). Continuous variables with normal distribution were expressed as mean ± standard deviation; continuous variables with skewed distribution were expressed as median (interquartile range, IQR); discrete variables were expressed as number and percentage. Inter-group difference was analyzed by Student's t-tests, Mann–Whitney *U*-tests, or χ^2-tests, as appropriate. The difference in survival between two groups was estimated by Kaplan-Meier method and tested by Log-rank test. The potential pre-operative risk factors for MVI and satellite nodules in HCC were analyzed by univariable logistic regression and individual factors with $P < 0.1$ from univariable logistic regression were further analyzed by the multivariable logistic regression using backward Likelihood Ratio (LR) method.[46] A two-tailed *P*-value of <0.05 indicated statistical significance.

Results

Baseline Characteristics

During the studying period, there were 861 HCC patients with liver tumor resection at the Second Affiliated Hospital of Kunming Medical University. Of them, 371 patients were excluded because of HCC at BCLC stages B-C (Figure 2), 39 due to pre-operatively locoregional therapies or systemic therapies, 29 without survival data, 14 with comorbid life-threatening cardiac, cerebral, renal, or other hepatic diseases, 13 with R1/R2 resection, and 5 with other concurrent malignancies. The remaining 390 patients were included into the data analysis.

Analysis of triphasic liver CT or MRI images unveiled that there were 51 (13.1%) HCC patients with the evidence of tumor portal vein or hepatic vein compression (Table 1). Of them, there were 14 (27.4%) patients with the portal vein compression, 21 (41.2%) patients with the hepatic vein compression, and 16 (31.4%) patients with both the portal vein and hepatic vein compression. The remaining 339 (86.9%) patients had neither the portal vein nor the hepatic vein compression in this population. There was no statistically significant difference in their demographic and clinical data between the tumor venous compression and non-venous compression groups (all $P > 0.05$).

Effect of Tumor Venous Compression on OS and RFS

The median follow-up period of those patients was 60.0 months (95% CI, 55.3–64.8 months). During the follow-up period, 156 (40.0%) patients suffered from tumor recurrence and 99 (25.4%) patients died. The median OS and RFS in the study population were >60.0 months and 27.2 months (95% CI, 19.0–35.3 months), respectively. The 1-, 3-, and 5-year OS rates were 95.0%, 82.1%, and 74.9% in the non-venous compression group, and 94.1%, 76.0%, and 71.5% in

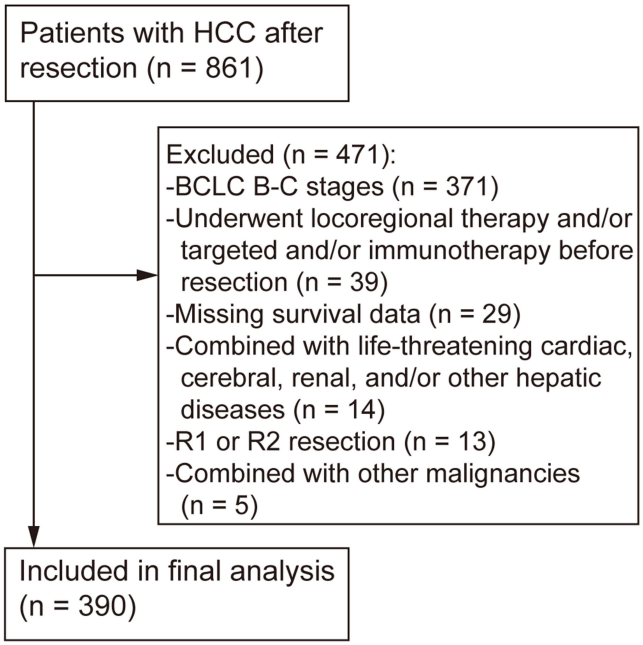

Figure 2 Flowchart of patient selection of the study.

the tumor venous compression group, respectively ($P = 0.514$, Figure 3A). The median OS was >60.0 months in the two groups. The 1-, 3-, and 5-year RFS rates were 72.2%, 46.4%, and 37.0% in the non-venous compression group, and 72.2%, 42.2%, and 42.2% in the tumor venous compression group, respectively ($P = 0.533$, Figure 3B). The median RFS

Table 1 The Demographic and Clinical Characteristics of Patients at Admission

Variables	Total n, (%)	Compression Group (n = 51)	Non-Compression Group (n = 339)	P
Age (year)				0.140
<60	263 (67.4%)	39 (76.5%)	224 (64.3%)	
≥60	127 (32.6%)	12 (23.5%)	115 (35.7%)	
Sex				0.816
Male	333 (85.4%)	43 (84.3%)	290 (85.5%)	
Female	57 (14.6%)	8 (15.7%)	49 (14.5%)	
ALBI grade				0.409
1	244 (62.6%)	29 (56.9%)	215 (63.4%)	
2	123 (31.5%)	20 (39.2%)	103 (30.4%)	
3	23 (5.9%)	2 (3.9%)	21 (6.2%)	
HBV and/or HCV infection	303 (77.7%)	36 (70.6%)	267 (78.8%)	0.191
Cirrhosis				0.075
Yes	250 (64.1%)	27 (52.9%)	223 (65.8%)	
No	140 (35.9%)	24 (47.1%)	116 (34.2%)	
AFP (ng/mL)				0.619
≤400	295 (75.6%)	40 (78.4%)	255 (75.2%)	
>400	95 (24.4%)	11 (21.6%)	84 (24.8%)	
Single nodule	381 (97.7%)	50 (98.0%)	331 (97.6%)	0.860
Maximum tumor diameter (cm)				0.332
<2	18 (4.6%)	1 (2.0%)	17 (5.0%)	
≥2	372 (95.4%)	50 (98.0%)	322 (95.0%)	

Abbreviations: AFP, alpha fetoprotein; ALBI, albumin and total bilirubin; HBV, hepatitis B virus; HCV, hepatitis C virus.

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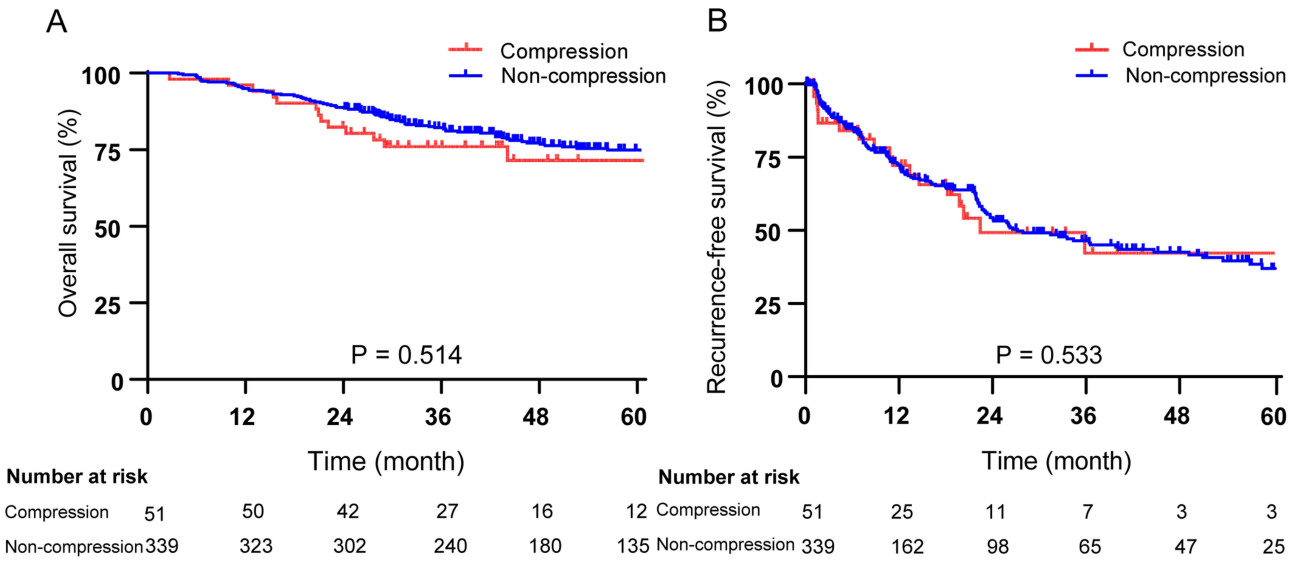

Figure 3 Effect of tumor venous compression on (**A**) overall survival and (**B**) recurrence-free survival of patients with HCC at BCLC stages 0-A after liver tumor resection.
Abbreviations: BCLC, Barcelona Clinic Liver Cancer staging system; HCC, hepatocellular carcinoma.

was 27.2 months (95% CI, 18.6–35.7 months) in the non-venous compression group and 22.4 months (95% CI, 4.1–40.8 months) in the tumor venous compression group. Further stratification analyses indicated that there was no statistically significant difference in OS (P = 0.593) or RFS (P = 0.625) among the groups of non-venous compression, hepatic venous compression alone, portal venous compression alone, and hepatic venous plus portal venous compression (Figure 4). Apparently, the presence of tumor portal vein and/or hepatic vein compression did not significantly affect the OS and RFS of patients with HCC at very early and early stages following liver tumor resection.

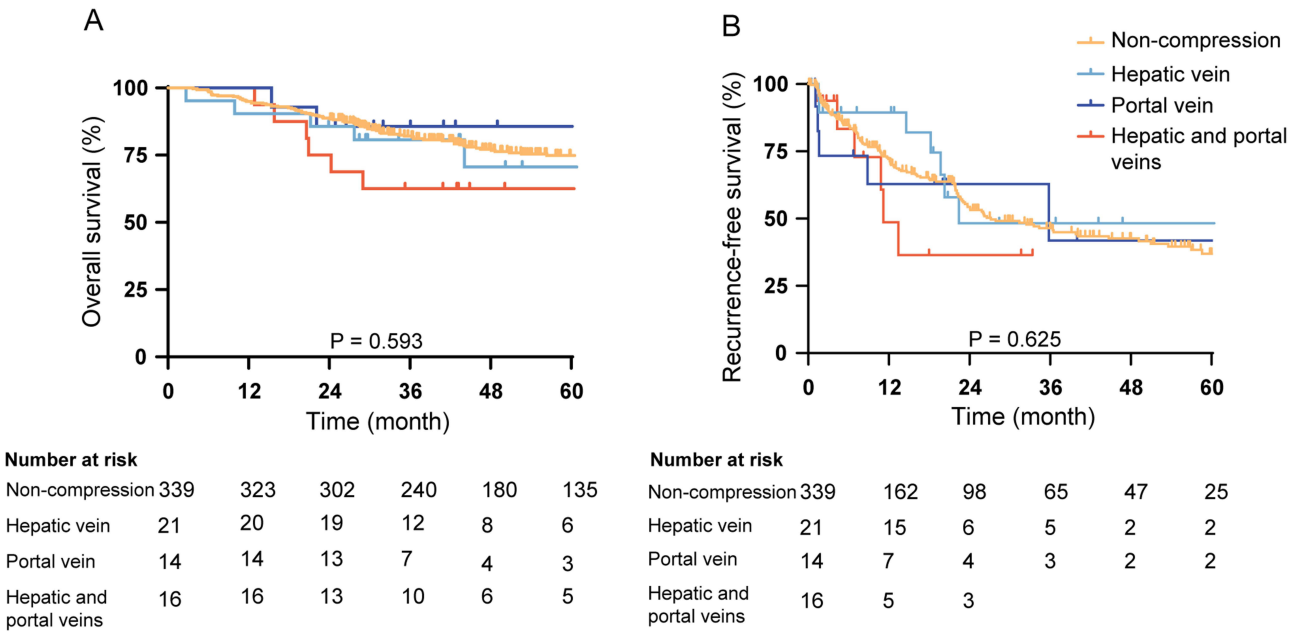

Figure 4 Effect of sub-types of tumor venous compression on (**A**) overall survival and (**B**) recurrence-free survival of patients with HCC at BCLC stages 0-A after liver tumor resection. The sub-types of tumor venous compression included tumor hepatic vein compression alone, portal vein compression alone, and combined hepatic and portal vein compression.
Abbreviations: BCLC, Barcelona Clinic Liver Cancer staging system; HCC, hepatocellular carcinoma.

Association of Tumor Venous Compression with the Development of MVI

MVI is a risk factor of HCC recurrence and metastasis. Analyses of surgical liver sections revealed that there were 150 (38.5%) HCC patients with MVI and the percentage of HCC cases with MVI in the tumor venous compression group (26 cases, 51.0%) was significantly higher than 36.6% (124 cases) in the non-venous compression group ($P = 0.025$, Figure 5A), highlighting that tumor venous compression of the portal veins or hepatic veins was associated significantly with the development of MVI in HCC. The univariable logistic regression analyses of multiple demographic and clinical factors revealed that the presence of tumor venous compression, but not other factors tested, was significantly associated with the development of MVI (OR = 1.951, 95% CI: 1.078–3.528, $P = 0.027$, Table 2). Further multivariable analysis indicated that the presence of tumor venous compression was an independent risk factor of MVI development in HCC (OR = 1.902, 95% CI: 1.049–3.447, $P = 0.034$). Stratification analyses unveiled that the percentage of HCC cases with MVI in the portal vein compression group was significantly higher than those in the non-venous compression group ($P = 0.009$, Figure 5B), implying that the presence of tumor portal vein compression was significantly related to the development of MVI in HCC.

Association of Tumor Venous Compression with the Development of Satellite Nodules

Next, we analyzed the value of tumor venous compression in the predicting satellite nodules in HCC. Pathological examinations indicated satellite nodules in 41 (10.5%) patients, including 10 (19.6%) cases in the tumor venous compression group and 31 (9.1%) cases in the non-venous compression group, implying that the percentage of satellite nodules in HCC with tumor venous compression was significantly higher than that in the non-venous compression group ($P = 0.023$, Figure 6A). The univariable logistic regression analysis of the demographic and clinical factors unveiled that the presence of liver cirrhosis (OR = 2.137, 95% CI: 0.989–4.617, $P = 0.053$), higher serum AFP levels (OR = 1.94, 95% CI: 0.980–3.840, $P = 0.057$), and positive tumor venous compression (OR = 2.423, 95% CI: 1.107–5.306, $P = 0.027$, Table 3) trended to be

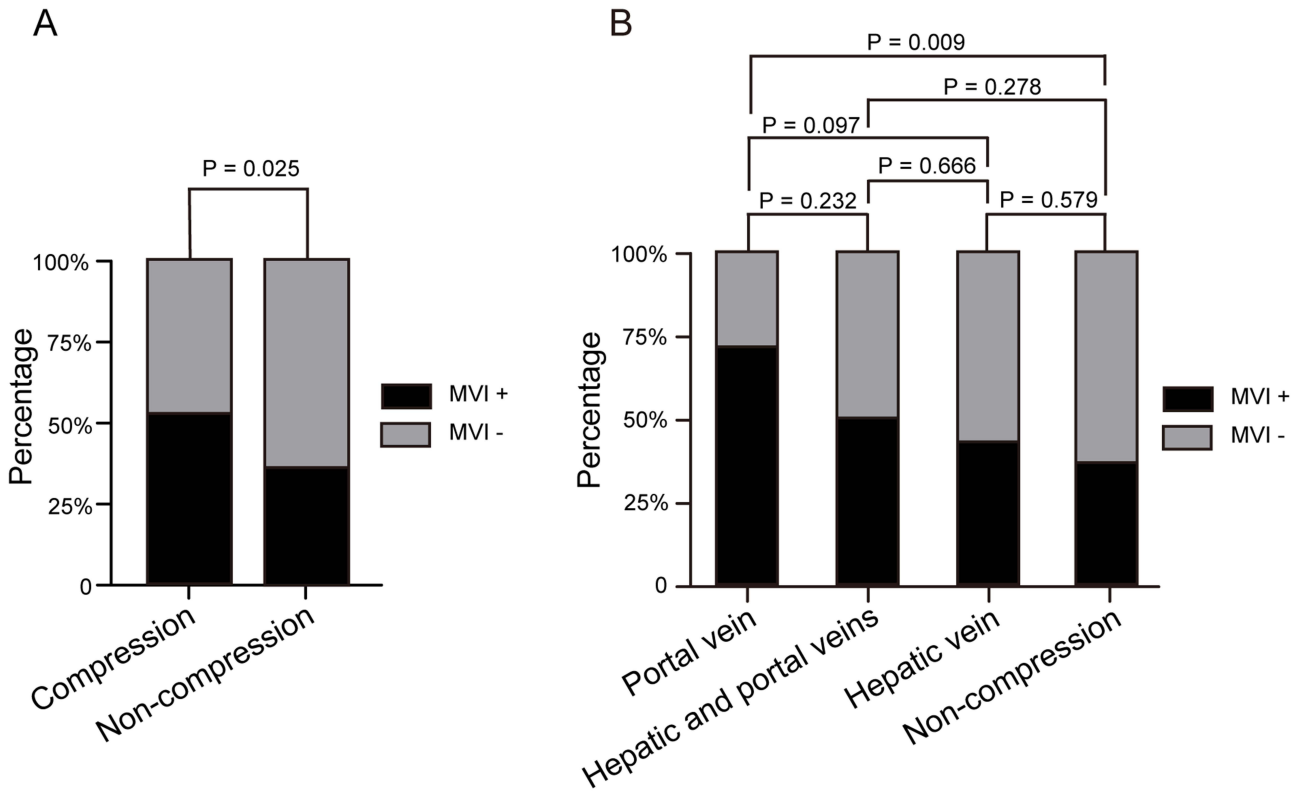

Figure 5 Association of tumor venous compression with microvascular invasion in patients with HCC at BCLC stages 0-A after liver resection. (**A**) Overall analysis. (**B**) Sub-group analysis according to non-tumor compression or tumor compression of the hepatic vein alone, the portal vein alone, and combined the hepatic and portal veins. **Abbreviations**: BCLC, Barcelona Clinic Liver Cancer staging system; HCC, hepatocellular carcinoma; MVI, microvascular invasion.

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Table 2 Univariate and Multivariate Analysis for Microvascular Invasion

Variables	Univariate Analysis			Multivariate Analysis		
	P	OR	95% CI	P	OR	95% CI
Sex (male vs female)	0.138	1.584	0.862–2.911			
Age (≥60 year vs <60 year)	0.584	0.886	0.576–1.365			
Cirrhosis (yes vs no)	0.260	1.28	0.833–1.966			
ALBI (1 vs 2)	0.335	0.802	0.512–1.256			
ALBI (1 vs 3)	0.327	0.63	0.250–1.587			
HBV and/or HCV infection (yes vs no)	0.243	1.348	0.816–2.226			
AFP (>400 ng/m vs ≤400 ng/m)	0.308	1.277	0.798–2.042			
Single nodule (yes vs no)	0.317	2.248	0.461–10.967			
Maximum tumor diameter (≥2 cm vs <2 cm)	0.062	3.304	0.940–11.610	0.074	3.154	0.894–11.121
Compression (yes vs no)	0.027	1.951	1.078–3.528	0.034	1.902	1.049–3.447

Abbreviations: AFP, alpha fetoprotein; ALBI, albumin and total bilirubin; HBV, hepatitis B virus; HCV, hepatitis C virus.

significantly associated with the development of satellite nodules in HCC. Further multivariate analysis indicated that liver cirrhosis (OR = 2.527, 95% CI: 1.144–5.584, $P = 0.022$), higher serum AFP levels (OR = 2.184, 95% CI: 1.084–4.401, $P = 0.029$), and positive tumor venous compression (OR = 2.871, 95% CI: 1.277–6.458, $P = 0.011$) were independent risk factors of the development of satellite nodules in HCC. Stratification analyses revealed that the percentage of satellite nodules in HCC

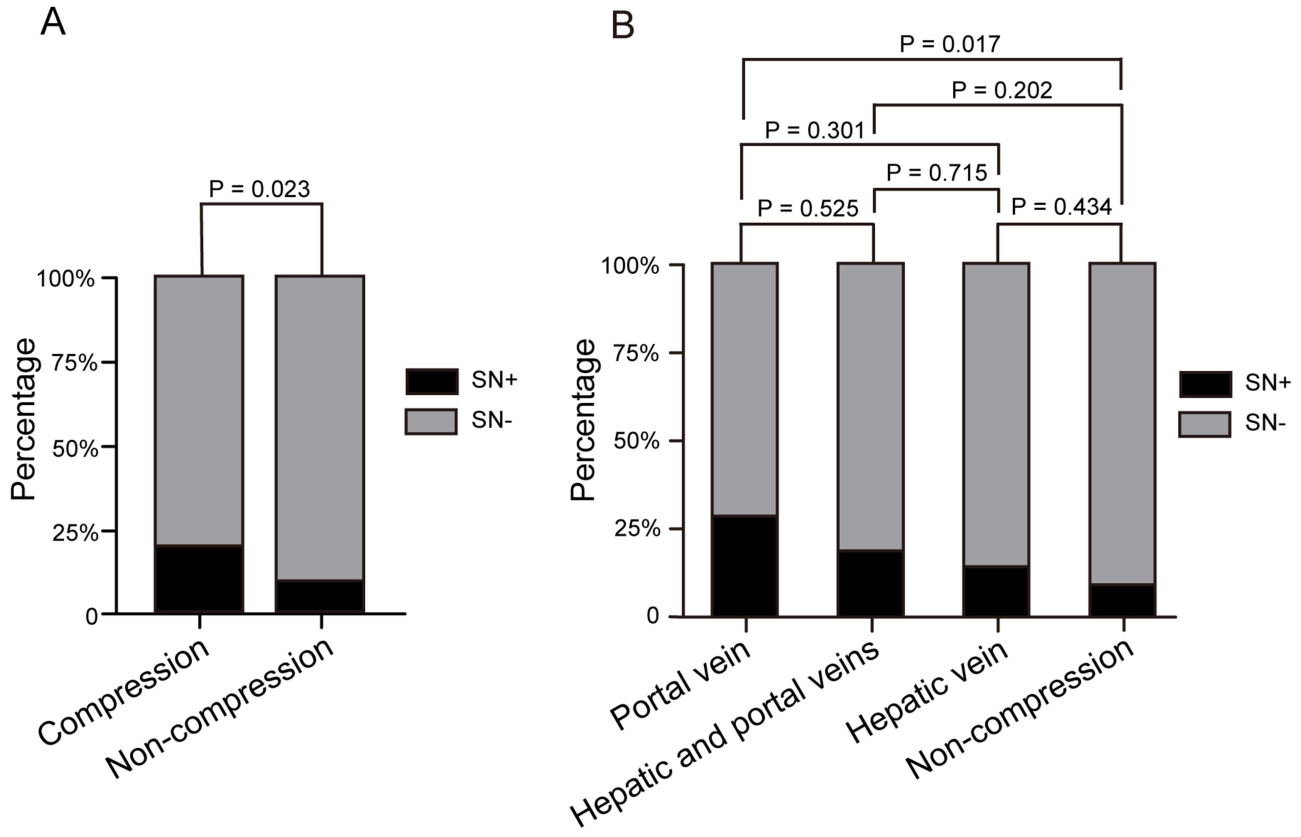

Figure 6 Association of tumor venous compression with satellite nodules in patients with HCC at BCLC stages 0-A after liver resection. (**A**) Overall analysis. (**B**) Sub-group analysis according to non-tumor compression or tumor compression of the hepatic vein alone, the portal vein alone, and combined the hepatic and portal veins.
Abbreviations: BCLC, Barcelona Clinic Liver Cancer staging system; HCC, hepatocellular carcinoma; SN, satellite nodule.

Table 3 Univariate and Multivariate Analysis for Satellite Nodule

Variables	Univariate Analysis			Multivariate Analysis		
	P	OR	95% CI	P	OR	95% CI
Sex (male vs female)	0.643	1.261	0.473–3.361			
Age (≥60 year vs <60 year)	0.723	1.129	0.576–2.214			
Cirrhosis (yes vs no)	0.053	2.137	0.989–4.617	0.022	2.527	1.144–5.584
ALBI (1 vs 2)	0.444	0.742	0.346–1.593			
ALBI (1 vs 3)	0.122	2.329	0.798–6.797			
HBV and/or HCV infection (yes vs no)	0.954	1.023	0.469–2.235			
AFP (>400 ng/m vs ≤400 ng/m)	0.057	1.94	0.980–3.840	0.029	2.184	1.084–4.401
Single nodule (yes vs no)	0.953	0.938	0.114–7.698			
Maximum tumor diameter (≥2 cm vs <2 cm)	0.492	2.048	0.265–15.804			
Compression (yes vs no)	0.027	2.423	1.107–5.306	0.011	2.871	1.277–6.458

Abbreviations: AFP, alpha fetoprotein; ALBI, albumin and total bilirubin; HBV, hepatitis B virus; HCV, hepatitis C virus.

from the tumor portal vein compression group was significantly higher than that in the non-venous compression group (P = 0.017, Figure 6B). Thus, the presence of tumor venous compression, particularly with the tumor portal vein compression, was significantly associated with the development of satellite nodules in HCC. These results are consistent with the hypothesis that "tumor venous compression promotes vascular invasiveness of HCC".

Discussion

MVI and satellite nodules are well-known predictors of tumor recurrence and poor survival in HCC patients.[47–49] However, MVI and satellite nodules are only detected by post-operative microscopy of a surgical liver specimen.[50] Accordingly, there is little chance to take useful and timely action in response to positive MVI and satellite nodules before and during operation.[51–53] Tumor venous compression is an early step of vascular invasion,[27] and it is common to see in the very early and early stages of HCC. Currently, little is known on whether tumor venous compression can act as a predictor for the development of MVI and satellite nodules in HCC.

Our pre-operative study of CT and MRI images found that 13.1% of HCC patients at the very early and early stages had either positive tumor portal vein and/or hepatic vein compression. Interestingly, the percentage of MVI in the tumor venous compression group, particularly in the tumor portal vein compression group was significantly higher than that in the non-venous compression group of HCC patients. Multivariable analysis revealed that tumor venous compression was the only independent risk factor of MVI development in patients with HCC at BCLC stages 0-A. Compared to the traditional predictors, like higher levels of serum AFP, tumor number, and maximum tumor diameter, the pre-operative non-invasive detection of tumor venous compression may be better to predict MVI development for HCC patients at the very early and early stages.[16]

Similarly, the percentage of HCC cases with satellite nodules in the tumor venous compression group, particularly in the tumor portal vein compression group, was significantly higher than that in the non-venous compression group of patients with HCC at very early and early stages. Multi-variable analysis unveiled that tumor venous compression, like liver cirrhosis and higher serum AFP levels, was an independent risk factor of satellite nodule development in patients with HCC at very early and early stages. Consistently, our preliminary studies found that liver cirrhosis was accompanied by lymphangiogenesis,[54] especially by the ones surrounding HCC, which can increase the prevalence of satellite nodules in HCC.[55,56] To the best of our knowledge, our findings provided scientific evidence that the presence of tumor venous compression was associated significantly with the development of MVI and satellite nodules in patients with HCC at very early and early stages. Conceivably, pre-operative measurements of tumor venous compression may be valuable for

predicting the development of MVI and satellite nodules in HCC at early stages, and these results are consistent with the hypothesis that "tumor venous compression promotes vascular invasiveness of HCC".

Why does tumor venous compression promote the development of MVI and satellite nodules in early stages of HCC? First, tumor compression surrounding blood and lymphatic vessels can impair blood flow, oxygen delivery, and therapy efficacy, which enhance tumor invasiveness.[57,58] Second, tumor compression surrounding blood and lymphatic vessels can elevate interstitial fluid pressure in the tumor microenvironment, which results in edema and enables tumor cells and growth factors to invade nearly tissues.[59,60] Third, tumor cells can also respond to mechanical forces through the mechanosensitive pathways, such as the YAP/TAZ, which are activated under a physical stress and promote tumor growth and invasiveness.[59,61,62] Fourth, tumor compression surrounding blood and lymphatic vessels can disrupt their normal architecture and increase vascular permeability, which creates a more favorable environment for tumor cells to spread into surrounding tissues.[27]

Interestingly, tumor venous compression did not significantly influence the survival of patients with HCC at very early or early stages following radical liver tumor resection, though the percentages of HCC patients with MVI and satellite nodules were significantly higher in the tumor venous compression group than in the non-venous compression group. One possible explanation is that HCC patients with tumor venous compression generally received a larger extent of liver tissue resection, which may counteract the higher percentages of HCC patients with MVI and satellite nodules. The results were also supported by the findings that radiofrequency ablation as the first line treatment of small HCC with a maximum diameter of <3 cm achieves similar long-term OS and disease-free survival between patients with perivascular HCC and non-perivascular HCC.[63] However, radiofrequency ablation of patients with periportal HCC causes higher local tumor progression rates and worse OS than those with non-periportal HCC.[64] The different effects of radiofrequency ablation for HCC may be attributed to the different "heat sink effect" in these studies, which takes thermal energy away from the tumor by veins and limits therapeutic outcomes.[65,66] Given that tumor venous compression is common to see in HCC at BCLC stages 0-A and a preliminary step of vascular invasion, the different steps of vascular invasion have different influences on OS of HCC patients. It is critical to re-consider for defining the BCLC stage C by "vascular invasion"[67] because the preliminary step of vascular invasion did not affect the survival of patients with HCC at early stages following liver tumor resection. The China Liver Cancer (CNLC) staging system has utilized "vascular tumor thrombus" instead of "vascular invasion" for defining the similarly advanced BCLC stage C.[68] Obviously, "vascular tumor thrombus" is more precise than "vascular invasion" to describe the disease progression of HCC at BCLC stage C.

Clearly, the findings of this study should be interpreted with caution due to several limitations. First, the single-center design may limit the generalizability of the results, as the sample may not be representative of the broader patient population. Secondly, the relatively small sample size may change the statistical power, increasing the potential Type II errors. Thirdly, the retrospective nature of the study introduces inherent biases in patient selection and data collection, which could affect the reliability and validity of the conclusions. Fourthly, there is a potential bias in the imaging evaluation due to the difference of multiple radiologists. Therefore, further prospective, multi-center studies with a larger sample size are warranted.

Conclusion

Preoperative measurement of tumor venous compression is valuable for predicting the development of MVI and satellite nodules in patients with HCC at BCLC stages 0-A. Tumor venous compression may be a useful imaging biomarker for determining the resection margin and the treatment planning for HCC.

Abbreviations

AFP, Alpha-fetoprotein; ALBI, Albumin and total bilirubin; BCLC, Barcelona Clinic Liver Cancer; CI, confidence interval; CT, Computed Tomography; HAIC, Hepatic Artery Infusion Chemotherapy; HCC, Hepatocellular carcinoma; HBV, hepatitis B virus; HCV, hepatitis C virus; IQR, interquartile range; LR, Likelihood Ratio; MRI, Magnetic Resonance Imaging; MVI, Microvascular invasion; OS, Overall survival; RFS, Recurrence-free survival; SN, satellite nodules; SUVmax, Maximal standardized uptake values; TACE, Transcatheter Arterial Chemoembolization; TAI, Transcatheter Arterial Infusion; TAE, Transcatheter Arterial Embolization; 18F-FDG PET/CT, Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author Yang Ke upon a reasonable request.

Ethics Approval and Informed Consent

This study was approved by the Ethics Committee of the Second Affiliated Hospital of Kunming Medical University (approval No. PJ-SCIENCE-2024-4). Written informed consent was waived by the Ethics Committee due to the retrospective nature of the study. Data in the study were anonymized, and particular attention was paid to protecting patient privacy and ensuring data confidentiality and security. The study complied with World Medical Association *Declaration of Helsinki*.

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Disclosure

All authors declare no competing interests in this work.

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