Original Article

Comparison of the effect on the prognosis of HCC in terms of different surgical approaches for hepatic inflow occlusion

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Background: To investigate the effect of surgical approaches for hepatic inflow occlusion performed during hepatectomy on postoperative tumor-free survival (TFS) in patients treated with R0 resection.

Methods: In total, 343 hepatocellular carcinoma (HCC) patients who underwent hepatectomy (R0) with different surgical approaches for hepatic inflow occlusion were analyzed retrospectively.

Results: In total, 68.80% of the patients underwent hepatic inflow occlusion, including 46.65% with a routine Pringle maneuver and 22.16% with selective hemi-hepatic vascular exclusion (SHVE), during surgery. The TFS did not significantly differ among the Pringle group, the SHVE group and the no hepatic inflow occlusion group. After further stratifying the patients according to the Barcelona clinic liver cancer (BCLC) staging system, the patients with BCLC stage A disease in the SHVE group and no hepatic inflow occlusion group displayed better TFS than those in the Pringle maneuver group (P=0.04; P=0.002), but the patients with BCLC stage B–C disease did not show significant differences among the groups. Furthermore, all 214 patients with BCLC stage A disease were classified into two subgroups according to the microvascular invasion (MVI) status. Interestingly, among the patients with MVI, those in the SHVE group and no hepatic inflow occlusion group had significantly longer TFS than those in the Pringle group (P=0.025; P=0.006); however, the patients without MVI did not show differences among the groups. Additionally, the multivariate analysis revealed that a tumor size ≥5 cm, an absent capsule, a low Edmondson grade, MVI positivity and performance of the Pringle maneuver were independent risk factors of the prognosis in patients with BCLC stage A disease.

Conclusions: Hepatic inflow occlusion and the surgical approach used to address this issue may have an impact on HCC prognosis in patients with BCLC stage A disease, especially among those with MVI positivity. No hepatic inflow occlusion or an SHVE approach rather than the Pringle maneuver should be considered first during hepatectomy for patients with BCLC stage A disease.

Keywords: Hepatocellular carcinoma (HCC); hepatectomy; Barcelona clinic liver cancer (BCLC); microvascular invasion (MVI); hepatic inflow occlusion

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Introduction

Seriously threatening human public health, the incidence of hepatocellular carcinoma (HCC) has increased worldwide (1). Hepatectomy is regarded as the first-line curative treatment for HCC and has improved postoperative survival outcomes (2,3). However, the rates of postoperative recurrence and

metastasis continue to be high (4,5). Appropriate approaches for treating hepatic inflow occlusion have generally been thought to be important and necessary to guarantee a smooth surgery (6).

Two methods, i.e., the Pringle maneuver and selective hemi-hepatic vascular exclusion (SHVE), have become routine during surgery for HCC. These techniques effectively reduce intraoperative blood loss. The Pringle maneuver prevents bleeding from the liver by clamping the hepatoduodenal ligament and has been used for more than 100 years (7). However, the Pringle maneuver is controversial because of the potential for severe ischemia-reperfusion (IR) injury, which usually causes reversible or irreversible liver and multiple organ dysfunction and other complications (8,9). By occluding the bleeding inflow from the hemi-hepatic tissue in which the tumor is situated, SHVE is useful, but IR injury is also unavoidable (10,11). To decrease blood loss and accelerate the postoperative recovery of patients, surgical approaches for hepatic inflow occlusion have been proposed but remain controversial, especially regarding the effects of these approaches on the prognosis of HCC patients (12-16). Therefore, further exploration of these surgical approaches is necessary and imperative.

Previous studies have reported that hepatic inflow occlusion influences postoperative liver function, but the effects of hepatic inflow occlusion on tumor-free survival (TFS) remain unclear. The Barcelona clinic liver cancer (BCLC) staging system is commonly used to direct treatment at different stages of disease (17). Hence, we explored the effects of hepatic blood flow occlusion on the prognosis of HCC patients undergoing surgery. We performed a retrospective study to investigate whether hepatic inflow occlusion could affect the TFS of HCC patients according to the BCLC stage.

Methods

Patients

In total, 343 patients undergoing R0 resection between March 2013 and June 2018 at our hospital were enrolled, and the follow-up deadline was October 1, 2018. The inclusion criteria were as follows: (I) R0 resection indicated that the macroscopic tumor was completely removed, the resection margin was negative, and no detectable intrahepatic and extrahepatic metastasis lesions remained; (II) the disease stages were distinguished according to the BCLC staging system; (III) a definitive pathological diagnosis of HCC was made based on the World Health Organization (WHO) criteria; (IV) no other treatment was performed before surgery; (V) the patient's liver function was not beyond the Child-Pugh stage A, and the performance status test (PST) score was less than 1; (VI) the tumor differentiation grade was identified according to the Edmondson-Steiner criteria (18); (VII) finally, the criteria for microvascular invasion (MVI) were that the tumor thrombus was whole or partly covered by the endothelium and visible only under microscopy. The endothelium-covered tumor thrombi had to be located inside the tumor or close to the tumor edge and extend into the portal vein or hepatic vein branches to be considered MVI (19).

Surgical approaches

Hepatectomy (R0) and hepatic inflow occlusion were performed by surgeons with considerable clinical experience. The surgeons occluded the blood flow by blocking the portal blood flow (Pringle maneuver). A flexible tourniquet was used to clamp the whole hepatoduodenal ligament. A relaxed interval of 5 minutes was alternated with intermittent vascular interruption, which lasted less than 25 minutes each time. The right or left Glisson's pedicle was blocked for SHVE.

Follow-up

Postoperative follow-up was performed every 1–2 months during the first year and every 3 months thereafter. The serum alpha-fetoprotein (AFP) levels were measured regularly, and imaging examinations, including ultrasonography and computed tomography (CT)/magnetic resonance imaging (MRI), were performed regularly. Recurrence was defined as meeting one of the following criteria: (I) AFP levels significantly increased along with one typical imaging finding, (II) two types of imaging showing a lesion simultaneously, or (III) lesion biopsy implemented due to a new episode of recurrence. The final time to recurrence (either intrahepatic or extrahepatic) was estimated by clinical doctors. The final follow-up data included in this study were collected in June 2018.

Statistical analysis

All statistical analyses were performed with IBM SPSS Statistics 23. TFS curves were constructed using the

Table 1 Clinical characteristic of all patients

Variables	Value
Age (years), mean ± SD [range]	47.830±0.587 [24–80]
Sex, n (%)	
Male	298 (86.88)
Female	45 (13.12)
HBsAg, n (%)	
Positive	295 (86.00)
Negative	48 (14.00)
HBV DNA, n (%)	
≥500 copies/mL	226 (65.89)
<500 copies/mL	117 (34.11)
AFP, n (%)	
≥400 ng/mL	181 (52.77)
<400 ng/mL	162 (47.23)
Tumor size, n (%)	
≥5 cm	270 (78.70)
<5 cm	73 (21.30)
Edmondson grade, n (%)	
Low	122 (35.57)
High	221 (64.43)
Capsule, n (%)	
Complete	229 (66.76)
Absent	114 (33.24)
Cirrhosis degree, n (%)	
Low	221 (64.43)
High	122 (35.57)
MVI, n (%)	
Positive	211 (61.52)
Negative	132 (38.48)
PVTT, n (%)	
Positive	54 (15.74)
Negative	289 (84.26)
Surgical approaches, n (%)	
No occlusion	107 (31.20)
SHVE	76 (22.16)
Pringle maneuver	160 (46.64)
Tumor number, n (%)	
Number >1	105 (30.61)
Number ≤1	238 (69.39)

SD, standard deviation; HBsAg, serum hepatitis B surface antigen; HBV, hepatitis B virus; AFP, alpha-fetoprotein; MVI, microvascular invasion; PVTT, portal vein tumor thrombus; SHVE, selective hemi-hepatic vascular exclusion.

Kaplan-Meier method and compared with a log-rank test. A Cox proportional hazard model was established to evaluate the independent risk factors for postoperative recurrence. A two-tailed P value <0.05 was considered significant.

Results

Patient characteristics

The characteristics of the 343 patients are described in *Table 1*. The tumor size in 52.77% of the patients was greater than or equal to 5 cm, and 78.70% of the patients had serum AFP levels greater than 400 ng/mL. The positivity rates for hepatitis B surface antigen (HBsAg) and hepatitis B virus (HBV) DNA were 86.00% and 65.89%, respectively. In total, 122 (35.57%) patients and 221 (64.43%) patients had low Edmonson grades and cirrhosis stages, respectively. The capsule was absent in 114 (33.24%) patients. The tumor number in 30.61% of the patients was greater than one. In total, 211 (61.52%) patients and 54 (15.74%) patients had MVI and a portal vein tumor thrombus (PVTT), respectively. In total, 214 patients and 129 patients had BCLC stage A disease and BCLC stage B–C disease, respectively. The median age of all patients was 47.830±0.587 [24–80] years. The 1-, 2-, and 3-year TFS rates were 54.7%, 39.9%, and 30.6% (median TFS: 14 months), respectively.

Surgical approaches had no impact on the prognosis of all patients

SHVE and the Pringle maneuver were performed in 76 patients and 160 patients, respectively. Additionally, 107 patients underwent surgery without hepatic inflow occlusion. The 1-, 2-, and 3-year TFS rates in all patients without occlusion were 58.7%, 44.9%, and 35.7% (median

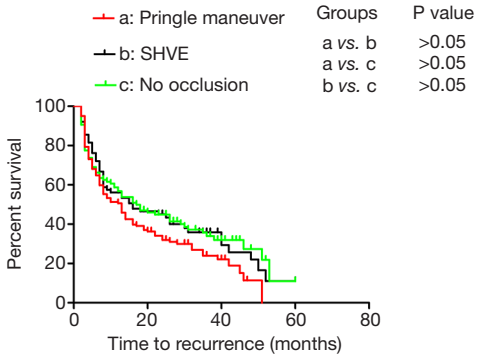

Figure 1 No difference was shown in TFS among patients who underwent the three different surgical approaches for all patients. TFS, tumor-free survival.

Table 2 Clinical characteristic of patients in BCLC stage A

Variables	Value
Age (years), mean ± SD [range]	49.270±0.770 [24–80]
Sex, n (%)	
Male	178 (83.18)
Female	36 (16.82)
HBsAg, n (%)	
Positive	178 (83.18)
Negative	36 (16.82)
HBV DNA, n (%)	
≥500 copies/mL	135 (63.08)
<500 copies/mL	79 (36.92)
AFP, n (%)	
≥400 ng/mL	101 (47.20)
<400 ng/mL	113 (52.80)
Tumor size, n (%)	
≥5 cm	153 (71.50)
<5 cm	61 (28.50)
Edmondson grade, n (%)	
Low	60 (28.04)
High	154 (61.96)
Capsule, n (%)	
Complete	169 (78.97)
Absent	45 (21.03)
Cirrhosis degree, n (%)	
Low	137 (64.02)
High	77 (35.98)
MVI, n (%)	
Positive	111 (51.87)
Negative	103 (48.13)
Surgical approaches, n (%)	
No occlusion	58 (27.10)
SHVE,	59 (27.57)
Pringle maneuver	97 (45.33)
Tumor number, n (%)	
Number >1	7 (3.30)
Number ≤1	207 (96.70)

Table 2 *(continued)*

BCLC, Barcelona clinic liver cancer; SD, standard deviation; HBsAg, serum hepatitis B surface antigen; HBV, hepatitis B virus; AFP, alpha-fetoprotein; MVI, microvascular invasion; PVTT, portal vein tumor thrombus; SHVE, selective hemi-hepatic vascular exclusion.

TFS: 17 months), respectively, and those in the patients who underwent surgery with SHVE were 56.1%, 45.0%, and 35.9% (median TFS: 16 months), respectively. In addition, the 1-, 2-, and 3-year TFS rates in all patients who underwent surgery with the Pringle maneuver were 51.3%, 34.1%, and 24.0% (median TFS: 13 months), respectively. There was no difference in TFS among the patients who underwent the three different surgical approaches (*Figure 1*).

Characteristics of the patients with BCLC stage A disease

The characteristics of the patients with BCLC stage A disease are described in *Table 2*. The median patient age was 49.270±0.770 [24–80] years. Approximately 47.20% and 71.50% of the patients had AFP levels ≥400 ng/mL and a tumor size ≥5 cm, respectively. The positivity rates for HBsAg and HBV DNA were 83.18% and 63.08%, respectively. There were 60 (28.04%) and 137 (64.02%) patients with low Edmonson grade and cirrhosis stage, respectively. The capsule was absent in 45 (21.03%) patients, and MVI was detected in 111 (51.87%) patients.

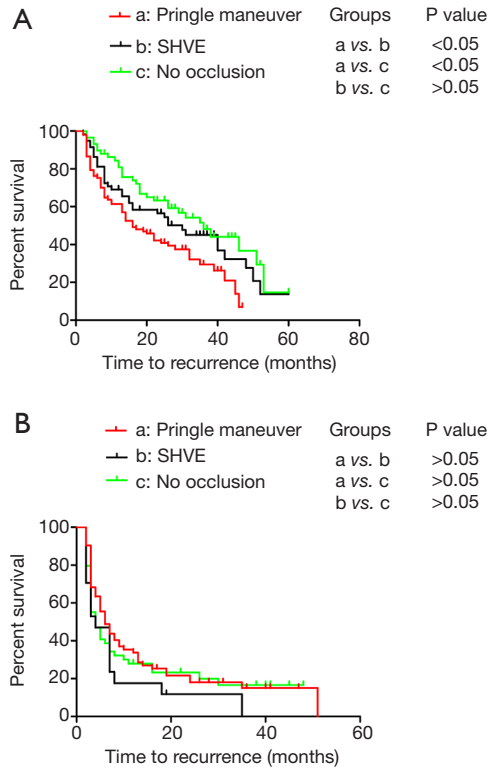

Figure 2 Analysis of patients in BCLC stage B–C. (A) For patients in BCLC stage A, patients treated with Pringle maneuver had the worst TFS compared with those treated with SHVE and those treated without hepatic inflow occlusion; (B) no difference in TFS was observed among patients treated without hepatic inflow occlusion, those treated with the Pringle maneuver and those treated with SHVE. BCLC, Barcelona clinic liver cancer; SHVE, selective hemi-hepatic vascular exclusion; TFS, tumor-free survival.

The tumor number in 3.3% of the patients was greater than one. Additionally, SHVE was performed in 59 (27.57%) patients, 97 (45.33%) patients underwent the Pringle maneuver, and 58 (27.10%) patients underwent surgery without hepatic inflow occlusion.

Performance of the Pringle maneuver had a negative impact on TFS in patients with BCLC stage A disease

By the end of follow-up, 131 of the 214 patients (61.21%) developed recurrence. Among all patients, the median TFS was 26 months, and the 1-, 2-, and 3-year TFS rates were 69.8%, 51.9%, and 40.4%, respectively. Among the patients with no inflow occlusion, the 1-, 2-, and 3-year TFS were 84.4%, 63.3%, and 51.5%, respectively, and those among the patients who underwent surgery with SHVE were 69.0%, 56.5%, and 45.1%, respectively. Among the patients treated with the Pringle maneuver, the 1-, 2-, and 3-year TFS rates were 61.5%, 42.2%, and 29.4%, respectively. The Kaplan-Meier analysis revealed that the patients treated with the Pringle maneuver had the worst TFS compared with those treated with SHVE and those treated without hepatic inflow occlusion (median: 16 *vs.* 30 months and 16 *vs.* 36 months; P<0.05) (*Figure 2A*). There was no difference in TFS between the patients treated with SHVE and those treated without inflow occlusion (median: 30 *vs.* 36 months; P>0.05) (*Figure 2A*). Additionally, as described in *Table 3*, the multivariate analysis revealed that a tumor size ≥5 cm, an absent capsule, a low Edmondson grade, MVI positivity and the Pringle maneuver were independent risk factors of

Table 3 Factors associated with TFS in BCLC stage A patients

Variables	Kaplan-Meier analysis	Multivariate Cox analysis	
	Log rank (mantel-Cox)	HR (95% CI)	P value
Age (years)	0.243		
≥50			
<50			
Sex	0.318		
Male			
Female			
HBsAg	0.020		
Positive			
Negative			

Table 3 *(continued)*

Table 3 *(continued)*

Variables	Kaplan-Meier analysis	Multivariate Cox analysis	
	Log rank (mantel-Cox)	HR (95% CI)	P value
HBV DNA	0.050		
≥500 copies/mL			
<500 copies/mL			
AFP	0.009		
≥400 ng/ml			
<400 ng/mL			
Tumor size	0.004	1.857 (1.168–2.979)	0.009
≥5 cm			
<5 cm			
Edmondson grade	0.007	1.610 (1.081–2.400)	0.019
Low			
High			
Capsule	0.000	2.401 (1.549–3.723)	0.000
Complete			
Absent			
Margin	0.285	0.668 (0.449–0.996)	0.048
Positive			
Negative			
Cirrhosis degree	0.560		
Low			
High			
MVI	0.001	1.661 (1.137–2.425)	0.009
Positive			
Negative			
Hepatic blood flow occlusion	0.005	1.277 (1.005–1.622)	0.046
No occlusion			
SHVE			
Pringle maneuver			
Tumor number	0.640		
Number >1			
Number ≤1			

TFS, tumor-free survival; BCLC, Barcelona clinic liver cancer; HR, hazard ratio; CI, confidence interval; HBsAg, serum hepatitis B surface antigen; HBV, hepatitis B virus; AFP, alpha-fetoprotein; MVI, microvascular invasion; SHVE, selective hemi-hepatic vascular exclusion.

Table 4 Clinical characteristic of patients in BCLC B–C

Variables	Value
Age (years), mean ± SD [range]	45.440±0.870 [20–69]
Sex, n (%)	
Male	120 (93.02)
Female	9 (6.98)
HBsAg, n (%)	
Positive	117 (90.70)
Negative	12 (9.30)
HBV DNA, n (%)	
≥500 copies/mL	91 (70.54)
<500 copies/mL	38 (29.46)
AFP, n (%)	
≥400 ng/mL	80 (62.02)
<400 ng/mL	49 (37.98)
Tumor size, n (%)	
≥5 cm	117 (90.70)
<5 cm	12 (9.30)
Edmondson grade, n (%)	
Low	67 (51.94)
High	62 (48.06)
Capsule, n (%)	
Complete	60 (46.51)
Absent	69 (54.00)
Cirrhosis degree, n (%)	
Low	84 (65.12)
High	45 (34.88)
MVI, n (%)	
Positive	100 (51.90)
Negative	29 (48.10)
PVTT, n (%)	
Positive	54 (41.86)
Negative	75 (58.14)
Hepatic blood flow occlusion, n (%)	
No occlusion	49 (37.98)
SHVE	17 (13.18)
Pringle maneuver	63 (48.84)
Tumor number, n (%)	
Number >1	98 (75.97)
Number ≤1	31 (24.03)

BCLC, Barcelona clinic liver cancer; SD, standard deviation; HBsAg, serum hepatitis B surface antigen; HBV, hepatitis B virus; AFP, alpha-fetoprotein; MVI, microvascular invasion; PVTT, portal vein tumor thrombus; SHVE, selective hemi-hepatic vascular exclusion.

the prognosis in the patients with BCLC stage A disease.

Characteristics of the patients with BCLC stage B–C disease

The characteristics of the patients with BCLC stage B–C disease are described in *Table 4*. The median patient age was 45.440±0.870 [20–69] years. Approximately 62.02% and 37.98% of the patients had AFP levels ≥400 ng/mL and a tumor size ≥5 cm, respectively. The positivity rates for HBsAg and HBV DNA were 90.70% and 70.54%, respectively. There were 67 (51.94%) and 84 (65.12%) patients with low Edmonson grades and cirrhosis stages, respectively. The capsule was absent in 69 (54.00%) patients, MVI was detected in 100 (51.90%) patients, and PVTT was detected in 54 (41.86%) patients. The tumor number in 75.97% of the patients was greater than one. Additionally, SHVE was performed in 17 (13.18%) patients, 63 (48.84%) patients underwent the Pringle maneuver, and 49 (37.98%) patients underwent surgery without hepatic inflow occlusion.

Effect of hepatic inflow occlusion on TFS in the patients with BCLC stage B–C disease

By the end of follow-up, 107 of the 129 patients (82.95%) developed recurrence. The median TFS rate was 5 months, and the 1-, 2-, and 3-year TFS rates were 30.1%, 20.8%, and 13.7%, respectively. Among the patients without inflow occlusion, the 1-, 2-, and 3-year TFS rates were 27.9%, 23.3%, and 16.6%, respectively, and those among the patients who underwent surgery with SHVE were 17.6%, 11.8%, 0%, respectively. Among the patients treated with the Pringle maneuver, the 1-, 2-, and 3-year TFS rates were 35.4%, 21.6%, and 15.0%, respectively. As displayed, the Kaplan-Meier analysis revealed that there was no significant

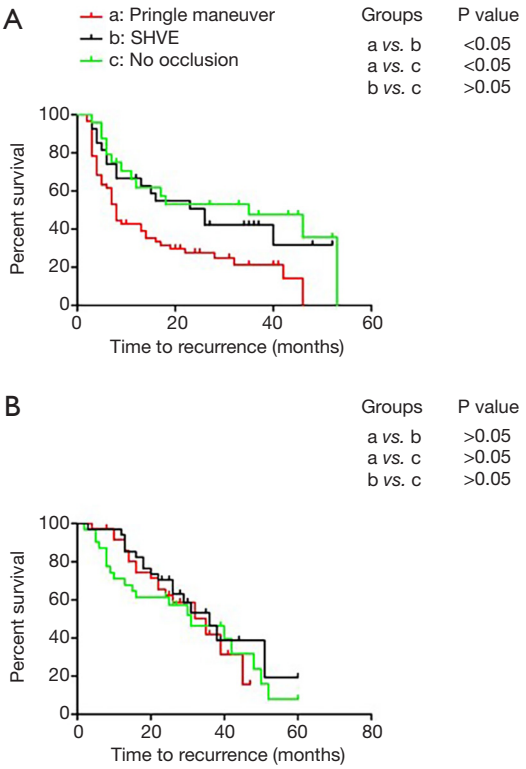

Figure 3 Analysis of patients in BCLC stage A. (A) In the MVI-positive subgroup, patients treated with Pringle maneuver had the worst TFS compared to those treated with SHVE and those treated without blood flow occlusion. No difference was observed in TFS between patients treated with hemi-hepatic vascular occlusion and patients treated without inflow occlusion; (B) there was no significant difference in TFS among patients treated with different approaches for hepatic inflow occlusion in the MVI-negative subgroup. BCLC, Barcelona clinic liver cancer; MVI, microvascular invasion; SHVE, selective hemi-hepatic vascular exclusion; TFS, tumor-free survival.

difference in TFS among the patients with BCLC stage B–C disease treated with the different approaches for hepatic inflow occlusion (*Figure 2B*).

Performance of the Pringle maneuver had a negative impact on the TFS of patients with MVI with BCLC stage A disease

In this analysis, the 214 patients were subdivided into an MVI-positive subgroup (n=111) and an MVI-negative subgroup (n=103). The Kaplan-Meier method was used to analyze the relationship between the different surgical approaches for hepatic inflow occlusion and the prognosis of the HCC patients with MVI. In the MVI-positive group, the 1-, 2-, and 3-year TFS rates were 53.7%, 38.9%, and 32.6%, respectively (median TFS: 13 months). In the MVI-negative group, the 1-, 2-, and 3-year TFS rates were 87.2%, 65.9%, and 47.8%, respectively (median TFS: 32 months). In the MVI-positive group, SHVE was performed in 27 (24.32%) patients, 60 (54.05%) patients underwent the Pringle maneuver, and 24 (21.63%) patients underwent surgery without hepatic inflow occlusion. In the MVI-negative group, SHVE was performed in 32 (31.07%) patients, 37 (35.92%) patients underwent the Pringle maneuver, and 34 (33.01%) patients underwent surgery without hepatic inflow occlusion. As described, in the MVI-positive subgroup, the patients treated with Pringle maneuver had the worst TFS compared to those treated with SHVE and those treated without blood flow occlusion (median: 8 *vs.* 26 months/8 *vs.* 35 months) (*Figure 3A*). No difference was observed in TFS between the patients treated with SHVE and the patients treated without inflow occlusion (P>0.05). However, there was no significant difference in TFS among the patients treated with different approaches for hepatic inflow occlusion in the MVI-negative subgroup (P>0.05) (*Figure 3B*).

Discussion

It has been one hundred years since the Pringle maneuver was developed, and this technique still has both pros and cons. With the introduction of precision therapy, SHVE has also been frequently used during hepatectomy, and sometimes, performing surgery without hepatic vascular occlusion is feasible (10). However, the effect of the surgical approach on the prognosis of HCC patients has been continuously disputed.

In contrast to a previous study, this study separated patients into three groups, including a Pringle maneuver group, hemi-hepatic vascular occlusion group and no hepatic vascular occlusion group (20). Special analyses of patients with early stage disease and those with intermediate/advanced disease were performed. The present study demonstrated that there was no significant difference in the recurrence rate or TFS among the three groups. These results are consistent with the outcomes reported in a previous study (20). We also found that the patients treated with the Pringle maneuver had the worst median TFS among the three groups, although no significant association was found between the surgical

approach and prognosis. Hence, further analysis involving patients with different BCLC stages was performed. In the present study, there was no significant difference in TFS among the BCLC B–C stage patients treated with different approaches for hepatic inflow occlusion. This result indicated that surgical approaches for hepatic inflow occlusion have no influence on the prognosis of HCC patients with intermediate/advanced disease. High intracorporal tumor dissemination and PVTT are commonly found in patients with BCLC B–C stage disease, and both are indicative of more serious disease before surgery, which may offset the effect of the operative method. Therefore, it seems reasonable that there was no significant difference in TFS among the three groups of patients with advanced stage disease (BCLC stage B–C).

However, among the patients with BCLC A stage disease, a significant difference in prognosis was observed between the patients treated with the Pringle maneuver and those treated with SHVE or without hepatic inflow occlusion. However, there was no significant difference in TFS between the patients treated with SHVE and those treated without hepatic inflow occlusion. These outcomes indicate that the surgical approach possibly had an impact on the survival of HCC patients with early-stage disease. The presence of MVI ranges from 15% to 57% in HCC patients after liver resection or liver transplantation and significantly shorten prognostic survival for HCC patients even in early stage (21,22). In the present study, the early-stage HCC patients were stratified according to the MVI status, and a subgroup analysis was performed. We found that compared with SHVE or without hepatic inflow occlusion, the Pringle maneuver in liver resection significantly decreased the TFS in patients with MVI. However, in the case of patients without MVI in our study, the surgical approaches for hepatic inflow occlusion did not significantly affect TFS. Among the patients with BCLC stage A disease, the Pringle maneuver had an impact on the prognosis of the patients with MVI but not on those without MVI. Currently, there is no clear reason to explain the phenomenon. MVI may promote metastasis by acting as a "seed" that gives rise to micro-metastases in the liver parenchyma (23). Changes in the hepatic microenvironment caused by IR promote "seeding" and the development of metastases. Furthermore, the proinflammatory response induced by IR may play an important role in the formation and growth of metastases at both local and remote sites through changes in the hepatic microenvironment (24,25). In addition, The level of reactive oxygen species (ROS) was upregulated by hypoxia caused by the Pringle maneuver, spurring the development of remaining tumor lesions and promoting HCC recurrence after hepatectomy (26). Therefore, we inferred that IR injury and hypoxia caused by the Pringle maneuver harmed liver function and had an adverse impact on the postoperative prognosis of the HCC patients in the early stage (8,27). Because MVI was undetectable preoperatively, given our findings, no hepatic inflow occlusion or the SHVE approach rather than the Pringle maneuver should be considered first during hepatectomy for all patients with BCLC stage A disease.

The limitations of our study should be discussed. First, our study claimed that hepatic inflow occlusion and the surgical approach may have an impact on HCC prognosis in patients with BCLC stage A disease, especially those with MVI positivity. However, our sample size is not large enough, our conclusion may lack persuasive power in a way. In the future, we will continue to expand the sample size and use propensity score to avoid bias. Second, among the patients with BCLC stage B–C disease, those treated with SHVE had shorter median TFS than those treated with the Pringle maneuver; however, no statistically significant difference was observed between the groups. We believe that a limited number of cases of patients with BCLC stage B–C disease were selected. However, the Pringle maneuver contributed to a poor prognosis in the HCC patients with BCLC stage A disease, especially those with MVI, as demonstrated in our study.

Conclusions

Hepatic inflow occlusion and the surgical approach may have an impact on HCC prognosis in patients with BCLC stage A disease, especially those with MVI positivity. No hepatic inflow occlusion or SHVE rather than the Pringle maneuver should be considered first during hepatectomy for patients with BCLC stage A disease.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tcr.2019.07.44). The authors have no conflicts of interest to declare.

Ethics Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. In accordance with the Declaration of Helsinki (as revised in 2013), this study was approved by the Institutional Review Board of the Affiliated Tumor Hospital of Guangxi Medical University (No. LW2019019). Informed consent was obtained from all voluntary participants for their clinical cases to be used in the present study.

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