Original Article

Clinical significance of surgical resection for hepatocellular carcinoma with portal vein invasion: a nationwide cohort study

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Background: Hepatocellular carcinoma (HCC) with portal vein invasion (PVI) is considered an advanced stage with a poor prognosis. Although current guidelines recommend systemic treatment for HCC with PVI, surgical resection could produce acceptable outcomes in selected patients. This study aimed to identify the clinical significance of surgical resection for HCC with PVI patients using a large-scale nationwide registry.

Methods: This retrospective, multicenter, observational cohort analyzed data from the Korean Primary Liver Cancer Registry. A total of 16,781 patients who were newly diagnosed with HCC between 2008 and 2018 were enrolled in this study. Patients with worse Child-Turcotte-Pugh scores (≥7) or performance status (≥2) were excluded. Among them, 998 patients who received treatment for HCC with PVI were included in the analysis and were divided into two groups: resection group of 151 (15.1%) and palliative group of 847 (84.9%) who received transarterial and systemic therapy according to the treatment intent. After matching the number and size of the tumors and model for end-stage liver disease (MELD) score between the groups, the final study cohort for analysis comprised 151 (26.6%) patients in the resection group and 417 (73.4%) in the palliative group. The primary endpoints were overall survival (OS) and cancer-specific survival (CSS).

Results: The number and maximum size of HCC did not differ between the resection and palliative groups after matching [1 (range, 1–5) *vs.* 1 (range, 1–6), P=0.11 and 5.5 (range, 1.2–20.6) *vs.* 6.0 (range, 1.0–20.5) cm, P=0.24, respectively]. Tumor markers, including alpha-fetoprotein (AFP) and protein induced by vitamin K absence or antagonist-II (PIVKA-II), also did not differ between the groups (P=0.29 and P=0.36, respectively). The 5-year OS and CSS rates of the resection and palliative groups were 44.8% and 17.4% (P<0.001) and 47.7% and 18.6% (P<0.001), respectively. Multivariate analysis showed that palliative treatment intent was the most significant risk factor for OS and CSS [odds ratio (OR) =2.24; 95% confidence interval (CI): 1.66–3.02; P<0.001 and OR =2.29; 95% CI: 1.68–3.12; P<0.001, respectively].

Conclusions: Surgical resection could significantly improve OS and CSS in selected HCC with PVI patients who have preserved liver function and performance status.

Keywords: Hepatocellular carcinoma (HCC); portal vein invasion (PVI); overall survival (OS); cancer-specific survival (CSS); surgical resection

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Introduction

Hepatocellular carcinoma (HCC) accounts for most primary liver cancers and is one of the leading causes of cancer-related deaths globally (1). Along with the development of screening programs for high-risk patients and advances in imaging studies, early-stage HCC has been increasingly detected and successfully treated over time (2). Because HCC is often asymptomatic, 23–54% of patients are diagnosed at an advanced stage (2,3). Portal vein invasion (PVI), a common form of macrovascular invasion in patients with HCC, is a decisive negative prognostic factor and is associated with higher intrahepatic recurrence and reduced median survival owing to the increased risk of dissemination of tumor cells into the bloodstream and distant metastasis (4,5).

The recently updated Barcelona Clinic Liver Cancer (BCLC) and American Association for the Study of Liver Diseases (AASLD) guidelines also classified HCC with PVI as an advanced stage and suggested systemic treatments as the first line of treatment (6,7). Although the atezolizumab and bevacizumab regimen is regarded as a game changer, it mainly includes unresectable patients, necessitating further investigation (8). The median survival time of patients with advanced HCC who were treated with sorafenib was relatively short at 10.7 months (9). Therefore, assuming that curative treatment can play a potential role in patients with PVI, increasing numbers of studies have reported favorable outcomes of surgical resection for selected patients with PVI (10,11). Because studies directly comparing surgical resection and palliative treatment are limited and the characteristics of patients included in each study are different, identifying the role of surgical resection in patients with PVI remains challenging. Therefore, this study aimed to evaluate the survival benefit of surgical resection for HCC with PVI patients with Child-Pugh class A liver function and preserved performance status using a large-scale nationwide cohort registry. We present this article in accordance with the STROBE reporting checklist (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-23-578/rc).

Highlight box

Key findings

- Surgical resection could significantly improve long-term outcomes in selected hepatocellular carcinoma (HCC) with portal vein invasion (PVI) patients.

What is known and what is new?

- Current guidelines recommend only systemic treatment for HCC with PVI patients.
- Multivariate analysis showed that surgical resection was the most significant prognostic factor for overall and cancer-specific survival in HCC with PVI patients.

What is the implication, and what should change now?

- Surgical resection could be worth considering to achieve favorable long-term outcomes in patients with HCC with PVI who have preserved liver function and performance status.

Methods

Data

The Korean Central Cancer Registry (KCCR) was developed and maintained by the Korean Ministry of Health and Welfare in 1980. All newly diagnosed cancer patients have been registered in the KCCR database. The Korean Primary Liver Cancer Registry (KPLCR) maintained by the Korean Liver Cancer Association randomly extracted and registered HCC cohort data of approximately 15% of patients from the KCCR database using code C22.0 of the International Classification of Disease since 2008. This study was approved by the ethics review board of Korea University Anam Hospital (No. 2023AN0006) and was conducted in accordance with the tenets of the Declaration of Helsinki (as revised in 2013) and Declaration of Istanbul. Informed consent has not been achieved due to the retrospective character and anonymous data collection.

Study population and matching

A total of 16,781 patients registered in KPLCR from 54 hospitals between 2008 and 2018 were enrolled in this study (*Figure 1*). Patients who met the following criteria were excluded: (I) presence of extrahepatic metastasis, (II) those who underwent liver transplantation or radiotherapy only or local ablation therapy for HCC with PVI, (III) those with a Child-Turcotte-Pugh score ≥7, (IV) Eastern Cooperative Oncology Group (ECOG) performance status ≥2, and (V) those with incomplete medical records. Of the remaining 10,083 patients, 1,226 (12.2%) patients with PVI were then included in the study. Furthermore, 228 patients who had received no treatment for HCC with PVI were excluded. Consequently, the final analysis included 998 patients who were divided into two groups: a resection group (n=151, 15.1%) comprising patients who were treated with PVI who had undergone surgical resection, and a palliative group

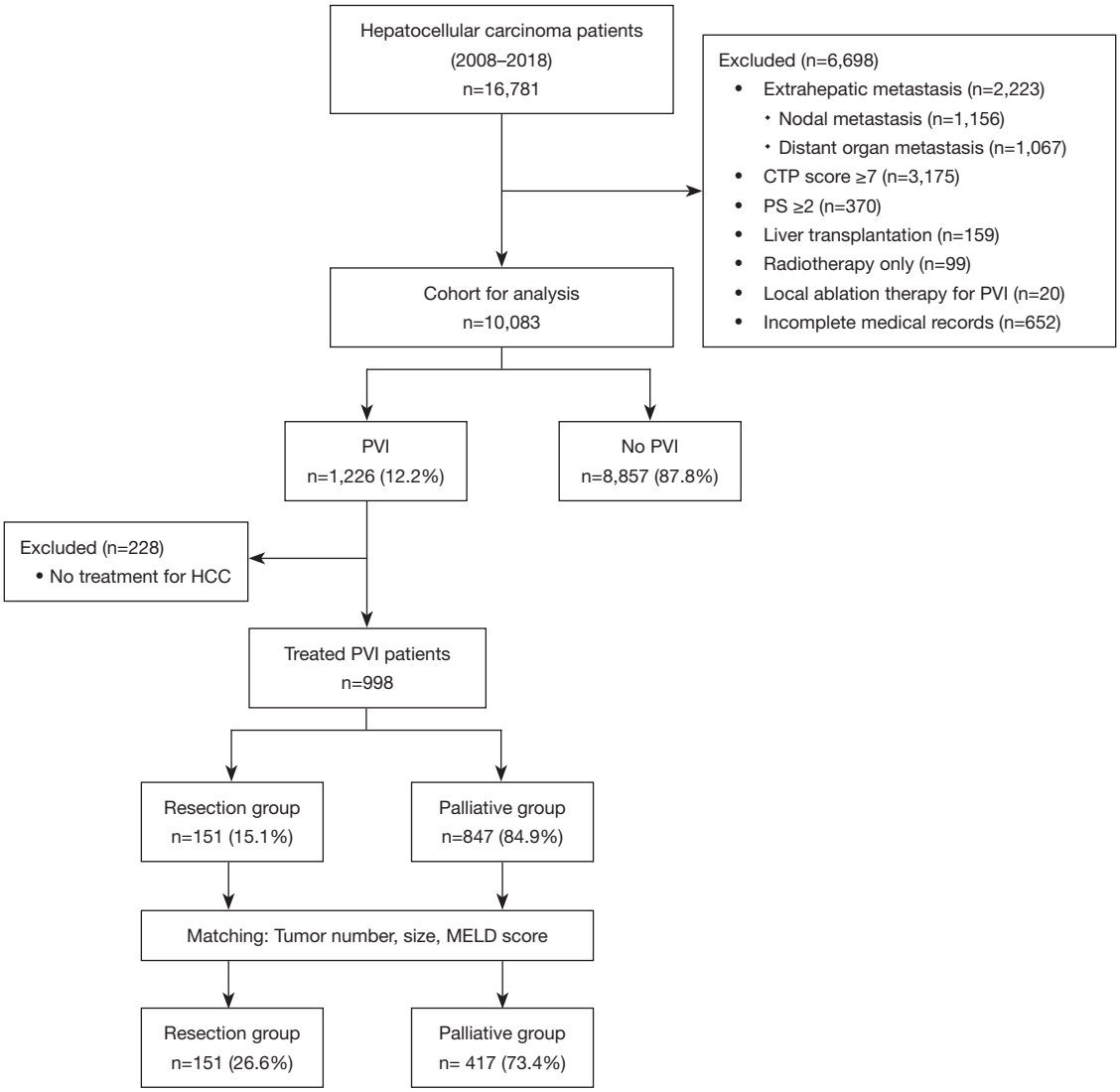

Figure 1 Study population. CTP, Child-Turcotte-Pugh; PS, performance status; PVI, portal vein invasion; HCC, hepatocellular carcinoma; MELD, model for end-stage liver disease.

(n=847, 84.9%) who had received transarterial and systemic therapy according to treatment intent.

However, patients in the palliative group were highly likely to have advanced HCC and poor liver function, making them not feasible to undergo surgical resection. Therefore, we matched the number and maximum size of the tumor and model for end-stage liver disease (MELD) score at the time of diagnosis between the two groups. Finally, the study cohort for analysis comprised 151 (26.6%) patients in the resection group and 417 (73.4%) in the palliative group (*Figure 1*).

Diagnosis and definition

The final analysis included patients who were first diagnosed with HCC and treated for the first time. HCC was diagnosed if the histological and immunological findings after biopsy were positive or if the image findings were consistent with HCC, measuring ≥1 cm in size, hyperenhancement in the arterial phase, and washout at the portal venous or delayed phase on multi-phase computed tomography (CT) and magnetic resonance imaging (MRI) using specific contrast in high-risk patients (12). In patients

who had undergone surgical resection, PVI was confirmed by histological findings, whereas in others, PVI was identified on CT or MRI when HCC invaded the portal vein branch above the segmental branch. However, the database did not include the grade of PVI.

Overall survival (OS) was defined as the time of diagnosis until death or last follow-up, while cancer-specific survival (CSS) was defined as the time of diagnosis until death caused specifically by HCC, using the Korean Standard Classification of Diseases version 7 system, or last follow-up.

Statistical analysis

Continuous variables are presented as medians and ranges and were compared between groups using Student's *t* and Mann-Whitney *U* tests. Categorical variables are presented as numbers with percentages and were compared using the χ^2 or Fisher's exact tests, as appropriate. The OS and CSS were calculated using the Kaplan-Meier analysis and compared using log-rank tests. The number and maximum size of the tumors and MELD score at the time of diagnosis were adjusted using propensity scores. After propensity matching, a standard mean difference suggested an appropriate balance of preoperative variables between the two groups (Figure S1, Table S1). Cox proportional hazards regression analysis was used to assess the prognostic significance of variables for survival. Multivariate analysis was performed on factors with P values ≤0.1 obtained using univariate analysis. P values <0.05 indicated statistical significance. All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

Results

Descriptive analysis and pre-matched cohort

The treatment types of the 998 patients before matching were as follows: surgical resection 151 (15.1%), transarterial treatment 641 (64.2%), and systemic treatment 206 (20.6%). The median follow-up duration was 31 months. In this pre-matched cohort, the tumor number was significantly lower and the maximum size was also smaller in the resection group than in the palliative group [1 (range, 1–5) *vs.* 2 (range, 1–10), P<0.001 and 5.5 (range, 1.2–20.6) *vs.* 8.8 (range, 0.8–22.6) cm, P<0.001, respectively]. The MELD score was lower in the resection group than in the palliative group [7 (range, 6–21) *vs.* 9 (range, 6–22), P<0.001]. Therefore, we matched those three variables between the two groups because significantly different tumor burdens and underlying liver function can critically affect long-term outcomes.

Baseline characteristics of matched cohort

Table 1 shows the baseline characteristics of the resection and palliative groups. Among 417 patients in the palliative group, 351 (84.2%) had undergone transarterial treatment and 66 (15.8%) had received systemic treatment. The combined radiotherapy was rarely performed in the resection group compared to the palliative group [1 (0.7%) *vs.* 81 (19.4%), P<0.001]. The median age was slightly lower in the resection group than in the palliative group [56 (range, 30–80) *vs.* 58 (range, 26–93) years, P=0.001]. Patients with performance status grade 1 were fewer in the resection group than in the palliative group [16 (14.5%) *vs.* 74 (22.2%), P=0.08]. All other patients had a performance status grade of 0. The CTP grade of all patients in both groups was grade A, and no patients had moderate to severe ascites or hepatic encephalopathy. However, the albumin level and platelet counts were slightly higher in the resection group than in the palliative group [4.2 (range, 3.2–5.1) *vs.* 4.0 (range, 2.8–5.1) g/dL, P<0.001 and 180×10^3 (range, 43×10^3–483×10^3) *vs.* 145×10^3 (range, 37×10^3–661×10^3), P<0.001, respectively].

In terms of HCC characteristics, the number and maximum size of tumors were not different between the resection and palliative groups after matching [1 (range, 1–5) *vs.* 1 (range, 1–6), P=0.11 and 5.5 (range, 1.2–20.6) *vs.* 6.0 (range, 1.0–20.5) cm, P=0.24, respectively] (*Table 2*). Moreover, no significant differences in tumor markers, including alpha-fetoprotein (AFP) and protein induced by vitamin K absence or antagonist-II (PIVKA-II) were observed between the groups (P=0.29 and P=0.36, respectively).

OS and CSS and risk factors

The 1-, 3-, and 5-year OS rates of the resection and palliative groups were 79.3% and 59.6%, 55.0% and 28.0%, and 44.8% and 17.4%, respectively (P<0.001) (*Figure 2A*). The 1-, 3-, and 5-year CSS rates of the resection and palliative groups were 79.3% and 59.8%, 57.2% and 28.6%, and 47.7% and 18.6%, respectively (P<0.001) (*Figure 2B*).

Multivariate analysis showed that palliative treatment was the most significant risk factor for OS and CSS [odds ratio (OR) =2.24; 95% confidence interval (CI): 1.66–3.02;

Table 1 Baseline characteristics of resection and palliative groups

Variables	Resection group (n=151)	Palliative group (n=417)	Total (n=568)	P value
Age	56 (30–80)	58 (26–93)	57 (26–93)	0.001
Female	29 (19.2)	73 (17.5)	102 (18.0)	0.64
BMI (kg/m^2)	23.2 (14.9–33.9)	23.5 (15.4–35.3)	23.4 (14.9–35.3)	0.67
Smoking	68 (45.3)	226 (54.2)	294 (51.9)	0.09
PST (grade 1)	16 (14.5)	74 (22.2)	90 (20.3)	0.08
Hypertension	45 (30.0)	138 (33.1)	183 (32.3)	0.48
Diabetes mellitus	31 (20.5)	95 (22.8)	126 (22.2)	0.56
Underlying liver disease (multiple)				
HBV	112 (74.2)	277 (69.6)	389 (70.9)	0.29
HCV	9 (6.4)	40 (10.5)	49 (9.4)	0.15
Alcoholic liver disease	41 (27.9)	141 (34.6)	182 (32.8)	0.14
Ascites				0.70
Mild	15 (9.9)	46 (11.0)	61 (10.7)	
Moderate to severe	0 (0.0)	0 (0.0)	0 (0.0)	
Hepatic encephalopathy	0 (0.0)	0 (0.0)	0 (0.0)	–
CTP grade (A)	151 (100.0)	417 (100.0)	568 (100.0)	–
MELD score	7 (6–21)	8 (6–18)	8 (6–21)	0.22
Laboratory findings				
Total bilirubin (mg/dL)	0.74 (0.14–1.90)	0.80 (0.20–2.60)	0.80 (0.14–2.60)	0.13
PT-INR	1.04 (0.88–1.40)	1.08 (0.85–1.61)	1.07 (0.85–1.61)	0.10
Albumin (g/dL)	4.2 (3.2–5.1)	4.0 (2.8–5.1)	4.0 (2.8–5.1)	<0.001
Platelet (×10^3)	180 (43–483)	145 (37–661)	158 (37–661)	<0.001
Cr (mg/dL)†	0.86 (0.50–4.11)	0.85 (0.27–3.21)	0.85 (0.27–4.11)	0.34

Values are presented as median (range) or n (%). †, Mann-Whitney. BMI, body mass index; PST, performance status test; HBV, hepatitis B virus; HCV, hepatitis C virus; CTP, Child-Turcotte-Pugh; MELD, model for end-stage liver disease; PT-INR, prothrombin time-international normalized ratio; Cr, creatinine.

Table 2 Characteristics of HCC between resection and palliative groups

Variables	Resection group (n=151)	Palliative group (n=417)	Total (n=568)	P value
Tumor number†	1 (1–5)	1 (1–6)	1 (1–6)	0.11
Tumor size (cm)	5.5 (1.2–20.6)	6.0 (1.0–20.5)	6.0 (1.0–20.6)	0.24
Hepatic vein invasion	11 (7.3)	46 (11.0)	57 (10.0)	0.18
Hepatic artery invasion‡	4 (2.6)	1 (0.2)	5 (0.9)	0.01
Bile duct invasion	6 (4.0)	17 (4.1)	23 (4.0)	0.95
AFP (ng/mL)†	156.5 (1.6–101,482.3)	388.9 (1.4–565,662.7)	268.5 (1.4–565,662.7)	0.29
PIVKA-II (mAU/mL)	400.0 (11.0–75,000.0)	1,200.0 (6.0–100,000.0)	930.0 (6.0–100,000.0)	0.36

Values are presented as median (range) or n (%).†, Mann-Whitney; ‡, Fisher's exact. HCC, hepatocellular carcinoma; AFP, alpha-fetoprotein; PIVKA-II, protein induced by vitamin K absence or antagonist-II.

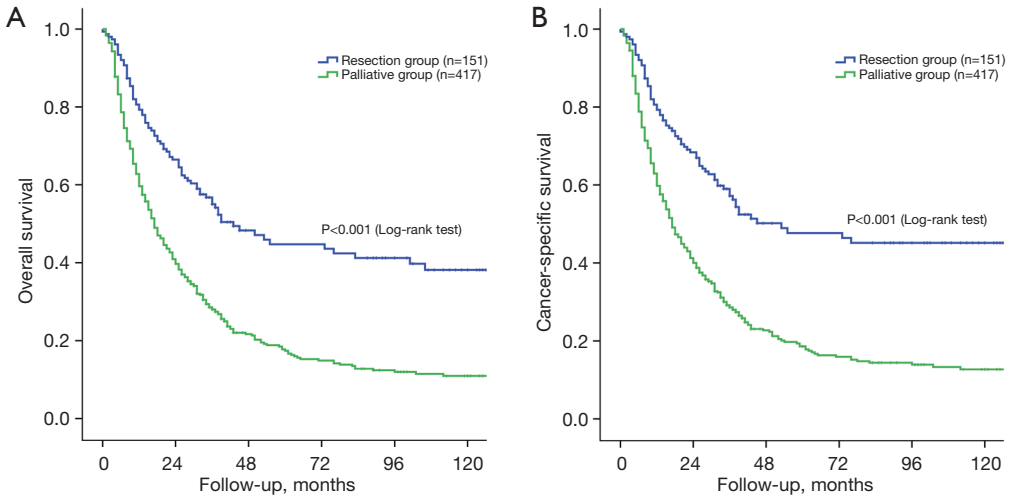

Figure 2 Long-term outcomes of matched PVI patients. (A) Overall survival between the resection and palliative groups (P<0.001). (B) Cancer-specific survival between the resection and palliative groups (P<0.001).

P<0.001 and OR =2.29; 95% CI: 1.68–3.12; P<0.001, respectively] (*Table 3*). Contrarily, maximum tumor size (≥5 cm, OR =1.41; 95% CI: 1.08–1.84; P=0.01) and AFP (≥400 ng/mL, OR =1.34; 95% CI: 1.04–1.72; P=0.02) were independent risk factors for OS. Similarly, maximum tumor size (≥5 cm, OR =1.37; 95% CI: 1.03–1.81; P=0.03) and AFP (≥400 ng/mL, OR =1.33; 95% CI: 1.03–1.71; P=0.02) were also independent risk factors for CSS.

Long-term outcome in a total cohort

In addition, although the degree of tumor burden and underlying liver function could differ among patients who received each treatment, we also analyzed the long-term outcome in a cohort of 10,083 patients to identify the overall trend of the long-term outcomes of patients with PVI. The baseline characteristics are shown in Table S2. Patients with PVI had larger tumor sizes, frequent vascular invasion and bile duct invasion, and significantly higher tumor markers than those without PVI (all P<0.001) (Table S3). The median survival time of the resection, transarterial, systemic treatments, no treatment for PVI, and no PVI groups were 33 (range, 0–161) months, 13 (range, 0–164) months, 6 (range, 0–145) months, 3 (range, 0–123) months, and 39 (range, 0–167) months, respectively. The 5-year OS of the resection, transarterial, systemic treatments, no treatment for PVI, and no PVI groups were 44.8%, 14.4%, 6.5%, 1.7%, and 56.0%, respectively (P<0.001) (*Figure 3A*). The 5-year CSS of the resection, transarterial, systemic treatments, no treatment, and no PVI groups were 47.7%, 15.3%, 7.5%, 2.8%, and 61.4%, respectively (P<0.001) (*Figure 3B*).

Discussion

Among several factors used to define advanced HCC, macrovascular invasion, in particular PVI, is the most important negative risk factor resulting in a poor prognosis. The median survival of patients with untreated portal vein tumor thrombus is 2.4–4.0 months (13). Consistent with previous findings, the median survival time of untreated patients for PVI in this study was 3 months. Considering that portal vein tumor thrombus was found in 44% of patients who died from HCC (14), PVI is an obvious indicator of advanced HCC. PVI adversely affects patients with HCC in two aspects. First, it promotes the spread of HCC through the bloodstream, resulting in aggressive behavior that causes recurrence or distant metastasis (15). In addition, portal vein tumor thrombus, an advanced form of PVI, could induce considerable portal hypertension by obstructing portal blood flow. Furthermore, it worsens liver function, leading to ascites, hepatic encephalopathy, and esophageal varix, thereby reducing treatment compliance and ultimately resulting in a poor prognosis (16).

The BCLC and AASLD, the most widely used consensus guidelines, classify HCC with PVI as an advanced stage with low curability and recommend only systemic treatment (6,7). However, this study revealed that the resection group

Table 3 Univariate and multivariate analysis for overall and cancer-specific survival in matched cohort

Variables	Overall survival				Cancer-specific survival			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Treatment intent (palliative)	2.20 (1.72–2.80)	<0.001	2.24 (1.66–3.02)	<0.001	2.33 (1.81–3.00)	<0.001	2.29 (1.68–3.12)	<0.001
Age (≥65 years)	1.16 (0.94–1.42)	0.15	–	–	1.06 (0.86–1.31)	0.56	–	–
Sex (male)	1.24 (0.96–1.60)	0.09	–	–	1.22 (0.94–1.58)	0.13	–	–
BMI (<18.5 kg/m^2)	1.15 (0.70–1.90)	0.58	–	–	1.11 (0.67–1.87)	0.68	–	–
Smoking	1.14 (0.95–1.38)	0.16	–	–	1.13 (0.93–1.37)	0.23	–	–
PST (≥1)	1.22 (0.94–1.58)	0.14	–	–	1.21 (0.93–1.58)	0.16	–	–
HBV	0.90 (0.73–1.11)	0.34	–	–	0.98 (0.79–1.21)	0.82	–	–
HCV	1.06 (0.76–1.48)	0.72	–	–	1.04 (0.74–1.46)	0.82	–	–
Alcoholic liver disease	1.24 (1.01–1.52)	0.03	–	–	1.23 (1.00–1.52)	0.048	–	–
Ascites (positive)	1.44 (1.08–1.94)	0.01	–	–	1.46 (1.08–1.97)	0.01	–	–
MELD score (≥10)	1.12 (0.86–1.46)	0.40	–	–	1.03 (0.77–1.36)	0.85	–	–
Tumor number (multiple)	1.13 (0.91–1.40)	0.12	–	–	1.12 (0.89–1.40)	0.32	–	–
Tumor size (≥5 cm)	1.59 (1.30–1.95)	<0.001	1.41 (1.08–1.84)	0.01	1.64 (1.33–2.01)	<0.001	1.37 (1.03–1.81)	0.03
Hepatic vein invasion	1.27 (0.93–1.72)	0.12	–	–	1.33 (0.98–1.81)	0.07	–	–
Hepatic artery invasion	5.33 (0.75–37.91)	0.09	–	–	5.10 (0.72–36.33)	0.10	–	–
Bile duct invasion	1.76 (1.03–3.00)	0.03	–	–	1.67 (0.98–2.84)	0.06	–	–
AFP (≥400 ng/mL)	1.62 (1.33–1.97)	<0.001	1.34 (1.04–1.72)	0.02	1.64 (1.34–2.00)	<0.001	1.33 (1.03–1.71)	0.02
PIVKA (≥500 mAU/mL)	1.51 (1.19–1.92)	0.001	–	–	1.57 (1.23–2.01)	<0.001	–	–

OR, odds ratio; CI, confidence interval; BMI, body mass index; PST, performance status test; HBV, hepatitis B virus; HCV, hepatitis C virus; MELD, model for end-stage liver disease; AFP, alpha-fetoprotein; PIVKA, protein induced by vitamin K.

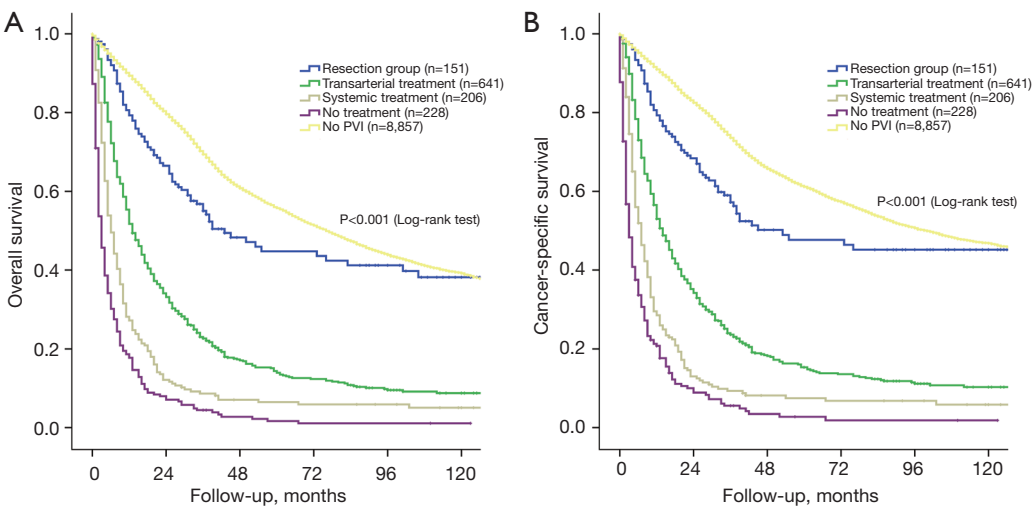

Figure 3 Long-term outcomes of the total cohort after the exclusion. (A) Overall survival of the resection, transarterial, systemic treatments, no treatment for PVI, and no PVI groups (P<0.001). (B) Cancer-specific survival of the resection, transarterial, systemic treatments, no treatment for PVI, and no PVI groups (P<0.001). PVI, portal vein invasion.

showed significantly better OS and CSS rates than those of the palliative group. Patients with more advanced HCC, including PVI, and poor liver function would have tended to choose palliative treatment, which could seriously impact the outcome. Therefore, we tried to correct the differences in underlying liver function and tumor burden between the two groups by matching the tumor number, size, and MELD score. Furthermore, we excluded patients with a higher CTP grade (≥ B) and impaired performance status (≥2) to include only patients potentially eligible for surgical resection. All subgroups in patients with PVI had advanced HCC characteristics (tumor size, other types of vascular invasion, and tumor markers) than those without PVI (Table S3). In long-term survival, the resection group of p atients with PVI showed significantly worse OS and CSS rates than those of the no-PVI group; however, the difference was not great. Considering that PVI is a definite negative prognostic factor for HCC, surgical resection could be worth considering to achieve favorable long-term outcomes.

The recent comprehensive review effectively summarizes the different classifications of portal vein tumor thrombus and the role of surgical resection based on its grade (17). They emphasize the importance of precisely categorizing patients with PVI based on Japanese Vp and Chinese Cheng's classifications to identify those who could benefit from surgical resection (18,19). Although HCC with PVI has been regarded as a contraindication to surgical resection in current guidelines, many surgeons prefer to choose surgical resection as the initial treatment for HCC with Vp1 and Vp2 in real-world practice, especially in Asian countries. Surgical resection could improve the median survival time for PVI confined to the first-order branch with preserved liver function (10,20-22). A previous study with a large sample size reported a median OS of 34.4 months after surgical resection for HCC with PVI (10). Although surgical resection increased the OS time compared to other treatment modalities, its benefit decreased as the extent of PVI became more extensive. For Vp3 and Vp4 patients, the worse median survival in the surgical resection group could be attributed to the aggressive tumor behavior and higher macroscopic margin positive rate of approximately 50%. Therefore, since PVI could lead to different prognoses following surgical resection depending on grade, it is imperative to conduct a thorough evaluation of the extent of PVI and thrombus before treatment.

In addition, the surgical strategy based on the extent of PVI is also crucial for curative surgical resection. We should consider the Vp grade and whether the portal vein tumor thrombus is within or beyond the resection plane. For cases classified Vp1–2, segmental hepatectomy could be feasible for curative resection, but for Vp3 and above, extensive hepatectomy with or without portal vein thrombectomy is necessary (17,23,24). While current classifications do not incorporate liver function, a small remnant liver after an extensive hepatectomy has the potential to affect underlying liver function and is especially fatal in cases of intrahepatic recurrence because treatment options are very limited. Therefore, patient selection for surgical resection and intraoperative strategy should be based on accurate evaluation of Vp grade, underlying liver function, the extent of resection, and the possibility of obtaining a negative margin (17).

Transarterial treatment has also not been recommended for HCC with PVI. Although it varies depending on the degree of portal vein tumor thrombus, damage to the hepatic artery caused by the transarterial treatment could cause irreversible liver ischemia (25). However, several studies showed that transarterial treatment could safely be applied to selected patients with preserved liver function and collateral circulation (26). Although different studies evaluating the effects of transarterial treatment for PVI showed conflicting results, a recent study showed a median OS time of 8.5 months (27). In contrast, acceptable outcomes following transarterial treatment combined with sorafenib for PVI have been reported (28,29). They inferred the mechanism of local tumor control that transarterial treatment could induce extensive intrahepatic tumor necrosis, whereas sorafenib targets the portal vein tumor thrombus and inhibits revascularization. However, although various treatment modalities for HCC are being tried alone or in combination, the treatment outcomes are relatively worse than surgical resection, as shown in this study.

Our study had several limitations. First, despite involving a large number of patients from a national database, more detailed clinical data were limited. If detailed information about the extent of PVI, including portal vein tumor thrombus, had been available, a more comprehensive analysis would have been possible. Additionally, PVI was diagnosed through histologic examination after surgical resection in the resection group, while imaging studies in the palliative group. Although different diagnostic methods for PVI could serve as a bias, we tried to evaluate the prognostic impact of surgical resection in the treatment of HCC with PVI through the most accurate diagnosis possible in both groups. Second, there could be a selection

bias for each treatment modality. In other words, patients in the palliative group may not have been able to consider surgical resection due to liver dysfunction and aggressive tumor characteristics. Although we tried to minimize those selection biases, we could not suggest a clear indication for surgical resection for patients with PVI. Nevertheless, this study could be a cornerstone for more active consideration of the potential role of surgical resection, which is a contraindication in the current guidelines. Despite these limitations, the major strength of our study was the inclusion of large sample size with long-term follow-up and highly reliable clinical information from a multicenter and nationwide cohort, which minimized selection bias. We hope that a prospective multi-center comparative study, including more detailed PVI grades, will be conducted to strengthen the conclusions of the present study.

Conclusions

In conclusion, the surgical resection showed significantly better OS and CSS than the palliative treatment in HCC with PVI patients with preserved liver function and performance status. Although the resection group had higher tumor burdens than the patients without PVI, the long-term survival of both groups did not show as much difference as expected. Therefore, surgical resection, if applied to meticulously selected PVI patients, could produce favorable long-term outcomes.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-23-578/coif). The authors have no conflicts of interest to declare.

Ethical 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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and Declaration of Istanbul. The study was approved by the ethics review board of Korea University Anam Hospital (No. 2023AN0006). Informed consent has not been achieved due to the retrospective character and anonymous data collection.

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