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Original Article

The impact of portal vein resection on outcome of hilar cholangiocarcinoma

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Backgrounds/Aims: Portal vein resection (PVR) with major hepatic resection can increase the rate of curative resection for hilar cholangiocarcinoma (HC). However, the oncologic role and safety of PVR is still debatable. This study aims to analyze PVR in terms of safety and therapeutic effectiveness. **Methods:** We retrospectively analyzed 235 patients who had undergone major hepatic resection for HC with curative intent, including patients with PVR (PVR, *n*=35) consisting of PV invasion (PVR-A, *n*=9), No PV invasion (PVR-B, *n*=26); and patients without PVR (No PVR, *n*=200). **Results:** There was no significant difference in the 30-day mortality or postoperative morbidity between PVR and No PVR (2.9% vs. 1.0%; *p*=0.394 and 34.3% vs. 35.0%; *p*=0.875). The rate of advanced HC (T3: 40% vs. 12%; $p<0.001$ and nodal metastasis: 60% vs. 28%; $p<0.001$) was higher in PVR compared to No PVR. There was no significant difference in the 5-year overall survival rates and disease-free survival between PVR-A vs. PVR-B vs. No PVR. In multivariate analysis, estimated blood loss >600 ml (*p*=0.010), T3 diseases (*p*=0.001), nodal metastasis (*p*=0.001) and poor differentiation (*p*=0.002) were identified as independent risk factors for survival. **Conclusions:** PVR does not increase postoperative mortality or morbidity. It showed a similar oncologic outcome, despite a more advanced disease state in patients with HC. Given these findings, PVR should be actively performed if necessary, after careful patient selection. **(Ann Hepatobiliary Pancreat Surg 2021;25:221-229)**

Key Words: Hilar cholanagiocarcinoma; Portal vein resection; Mortality; Morbidity; Oncologic outcome

INTRODUCTION

Hilar cholangiocarcinoma (HC) is known to account for 60% of all biliary tract malignancy.[1] Adjuvant treatment for HC does not appear to have any practical treatment effect,[2] and curative surgical resection is accepted as the best option for treatment. Despite the high morbidity rate after liver resection,[3,4] the extent of resection for HC has been extended from resection of the bile duct with affected liver parenchyma to the radical resection accompanying major hepatectomy. Over the past decades, several tertiary institutions have demonstrated that hepatectomy combined with bile duct resection can lead to improved oncologic outcomes.[5-8]

Recently, attempts have been made to extended surgery with portal vein resection (PVR) to overcome the high recurrence rate[2] and to obtain a clear resection margin. The tumor growth of HC acts as an obstacle to achieving a clear margin because of anatomical features of the hilar portion adjacent to the vascular structure, such as the hepatic artery or the portal vein. Theoretically, HC's tumor progression is likely to anatomically invade vascular structures such as the portal vein. A multicenter study reported that approximately 32% of patients with PVR had a pathological tumor invasion in the portal vein.[9] Although some institutions have proposed PVR as a standard treatment for HC under the concept of no-touch resection, it is still debatable whether PVR has a superior oncologic effect. Numerous studies to date have shown conflicting results for perioperative risk, mortality, and the oncologic

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role brought about by PVR.[10-15]

In this regard, the purpose of this study is to verify the therapeutic role of PVR for HC. To this end, we compared perioperative morbidity, mortality rate, and long-term survival outcomes between patients who received PVR and those who did not. In addition, we analyzed the risk factors affecting the prognosis of HC after surgery.

MATERIALS AND METHODS

Patients selection

We retrospectively analyzed 418 patients who had undergone surgery for HC during January 2005 through December 2016 at a single center. Of these patients, we excluded 176 patients with Bismuth type Ⅰ and Ⅱ and included 242 patients with Bismuth type Ⅲa, Ⅲb and Ⅳ. Of these 242 patients, we excluded 7 patients (4 with palliative surgery, 2 with biopsy only, and 1 with R2 resection). We enrolled the remaining 235 patients for analysis in this study. Among the finally enrolled 235 patients, 35 received PVR and 200 did not receive PVR. Of the 35 PVR patients, 9 (25.7%) were found to have portal vein invasion on the final pathological examination (PVR-A), and 26 (74.3%) were found to have no portal vein invasion (PVR-B) (Fig. 1). This study was approved by Institutional Review Board of Samsung Medical Center, Seoul, Republic of Korea (approval number: 2020-05-167).

Preoperative management

If preoperative hyperbilirubinemia (total bilirubin level above 3.0 gm/dl) was present before surgery, we performed preoperative bile drainage (PBD). The procedures we performed were percutaneous transhepatic biliary drainage, endoscopic retrograde biliary drainage, and endoscopic nasobiliary drainage. For hypertrophy of the future remnant liver after liver resection, preoperative portal vein embolization (PVE) was performed in patients with a future remnant volume of less than 20% as measured in CT liver volumetry. We evaluated the volumetry again 2 to 3 weeks following PVE, and we undertook surgical treatment when the future remnant liver volume was 20% or more of the total liver volume.

Surgical management

We established our strategy for liver resection and PVR after considering the Bismuth type and the vascular tumor

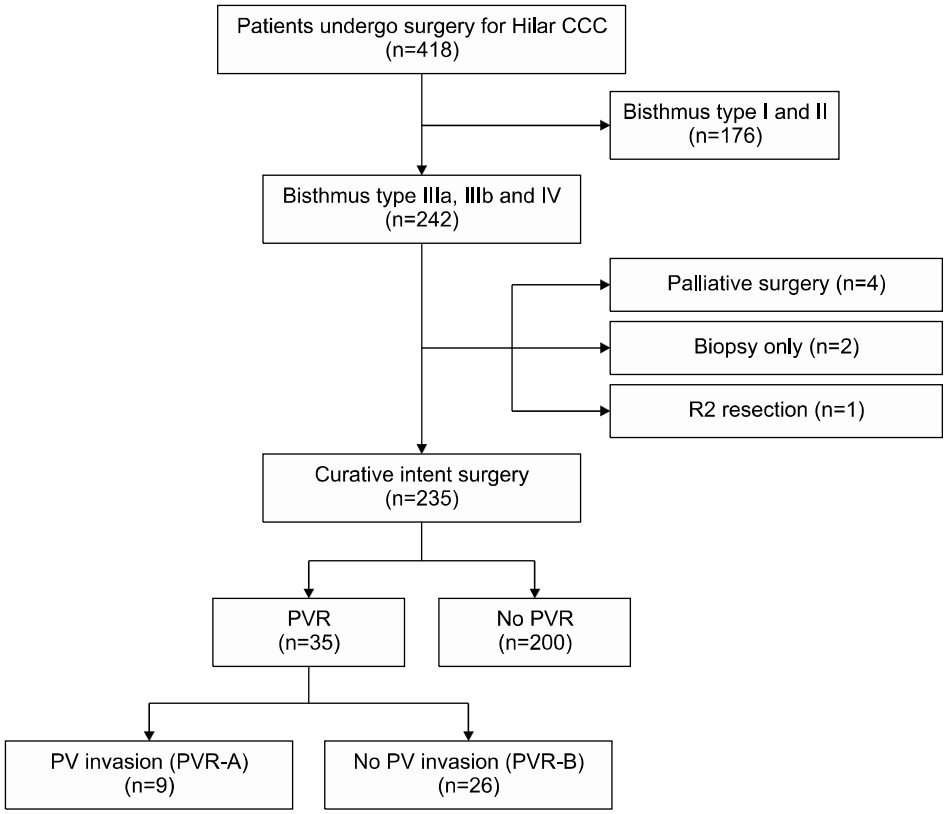

Fig. 1. Patients selection.

invasion as identified in the preoperative imaging. We made our final decision based on intraoperative findings. We resected the proximal bile duct along with the liver parenchyma as an en-bloc specimen. We executed PVR by using methods such as wedge resection with patch graft (1 patient) or segmental resection and end-to-end anastomosis (34 patients). We also performed hepatic artery resection and anastomosis in 5 patients. To confirm that the patency of the portal vein flow to the remnant liver, we took an intraoperative Doppler sonogram before the end of surgery. We performed transection of the liver parenchyma according to the method we had described in our previous study.[16] We executed a Roux-en-Y bilioenteric anastomosis to maintain bile flow from the remnant liver to the alimentary tract. We routinely performed lymph node dissection to achieve radical surgery. The extent of the Lymph node dissection was as follows; lymph nodes around the celiac trunk, the common hepatic artery, peripancreatic area and hepatoduodenal ligament.

Pathologic examination and adjuvant treatment

After histological examination, we performed tumor TNM staging, using the AJCC, 7th edition.[17] We microscopically determined the margin status of the ductal margin and the radial margin. The ductal margin was evaluated by the cut margins of the distal bile duct and the proximal bile duct. We defined R0 as being pathologically tumor-free at the margins mentioned above. We defined R1 as having the presence of invasive carcinoma. This institution considers carcinoma in situ at the margin to be R0. We did not provide adjuvant treatment to all cohorts. But, after considering TNM staging, margin status, and patient performance in multidisciplinary approach, we provided adjuvant treatment to 65 (27.7%) patients.

Investigated variables and definition

The analyzed variables were age, sex, body mass index (BMI), ASA class, follow-up duration, comorbidity, PBD, PVE, preoperative laboratory tests, adjuvant treatment, operating time, estimated blood loss (EBL), type of liver resection, positive resection margin, T stage by AJCC 7th edition, tumor size, node metastasis, differentiation type, perineural invasion, lymphovascular invasion, 30-day mortality, and postoperative complications. We divided postoperative complications into general complications and procedure-related complications. We described the former according to the Clavien-Dindo classification.[18] The latter consisted of portal vein thrombosis, liver failure, bile leak, bleeding, intraabdominal fluid collection, intraabdominal abscess and wound problems. Liver failure defined as the development of severe acute liver damage accompanied by hepatic encephalopathy and synthetic dysfunction (INR of ≥ 1.5) in patients without cirrhosis or liver disease and its cutoff is an illness duration of < 26 weeks. And preoperative bilirubin was defined as the last bilirubin level before operation.

Statistical analysis

We performed statistical analyses by using the PASW Statistics version 23.0 (SPSS, IBM Corp., Armonk, NY, USA). We used the Kaplan-Meier method to calculate the overall survival rate (OSR) and median survival times. We performed the log rank test to compare survival curves. We included all recurrences and tumor-related deaths in the disease-free survival rates (DFS) analysis. We also performed univariate and multivariate Cox regression analysis to identify prognostic factors for OSR and DFS. In univariable analysis, we considered $p < 0.1$ to be significant. We included parameters with $p < 0.1$ in a multivariable Cox proportional hazards regression analysis to identify the risk factors for prognosis. Statistical significance was indicated at $p < 0.05$ in multivariate analysis.

RESULTS

Demographics and perioperative details

Table 1 summarizes the demographics and perioperative details of the PVR group (n=35) and the No PVR group (n=200). The proportion of preoperative biliary drainage was significantly higher in PVR than in No PVR (85.7% vs. 61.5%; p=0.006). There was no significant difference in the proportion of preoperative PVE between the two groups (22.8% vs. 18.5%; p=0.642). The median value of the estimated blood loss of the PVR group was significantly greater than that of No PVR group (1143.2± 1034.51 vs. 688.0±442.3 ml; $p < 0.001$). Right hepatectomy was performed more frequently in the PVR than in the No PVR group (94.3% vs. 72%; p=0.001). In detail, right trisectionectomy (45.7% vs. 19%), extended right hemihepatectomy (22.9% vs. 28%), right hemihepatectomy (20%

Table 1. Demographics and perioperative details

	PVR (*n*=35)	No PVR (*n*=200)	*p* value
Age (years, mean±SD)	63.9±9.2	64.3±8.4	0.823
Sex (male/female (N, %))	20 (57.1)/15 (42.9)	132 (66)/68 (34)	0.341
BMI (kg/m^2, mean±SD)	23.8±5.4	24.1±5.3	0.403
ASA class 1/2/3 (%)	8/22/3	40/152/8	0.733
Follow up duration (months, mean±SD)	34.4±31.6	40.1±33.4	0.355
Comorbidity (N, %)			
Cardiovascular disease	14 (40.0)	92 (46.0)	0.514
Diabetes mellitus	6 (17.1)	50 (25.0)	0.308
Tuberculosis	2 (5.7)	10 (5.0)	0.632
Chronic liver disease	1 (2.8)	6 (3.0)	0.768
Previous abdominal surgery	3 (8.6)	33 (16.5)	0.179
PBD (N, %)	30 (85.7)	123 (61.5)	0.006
Preoperative PVE (N, %)	8 (22.8)	37 (18.5)	0.642
Preoperative laboratory test (mean±SD)			
Hb (g/dl, mean±SD)	12.2±1.4	12.4±1.6	0.568
Albumin (g/dl, mean±SD)	3.8±0.3	3.7±0.4	0.470
T.Bil (mg/ml)	2.6±2.4	2.3±3.2	0.625
CEA (ng/ml)	3.3±2.3	2.5±2.2	0.358
CA 19-9 (U/ml)	946.9±1969.9	392.1±1489.3	0.066
Adjuvant treatment (N, %)	10 (28.6)	55 (27.5)	0.460
Operating time (min±SD)	432.0±79.1	404.1±89.2	0.150
EBL (ml, mean±SD)	1143.2±1034.5	688.0±442.3	<0.001
Right/Left hepatectomy (N, %)	33 (94.3)/2 (5.7)	144 (72)/56 (28)	0.001
Caudate lobectomy (N, %)	34 (97.1)	189 (94.5)	0.700
Positive resection margin (N, %)[a]	2 (5.7)	23 (11.5)	0.386
T stage 1/2/3 (N, %)[b]	1 (2.8)/20 (57.2)/14 (40)	25 (12.5)/151 (75.5)/24 (12)	<0.001
Tumor size (cm, mean±SD)	3.3±1.4	3.1±1.7	0.586
Node metastasis (N, %)	21 (60.0)	56 (28.0)	<0.001
Differentiation (N, %)			0.498
Well	8 (22.8)	28 (14)	
Moderate	16 (45.7)	110 (55.0)	
Poor	10 (28.6)	53 (26.5)	
Perineural invasion (N, %)	13 (37.1)	62 (31.0)	0.225
Lymphovascular invasion (N, %)	32 (91.4)	142 (71.0)	0.065
30-day mortality (N, %)	1 (2.9)	2 (1.0)	0.394
Moderate to severe complication (≥C-D grade 3) (N, %)	12 (34.3)	68 (35.0)	0.875
General complication (N, %)			
Cardiovascular	0 (0)	2 (1.0)	0.933
Pulmonary	4 (11.4)	17 (8.5)	0.810
Cerebrovascular	0 (0)	2 (1.0)	0.933
Renal failure	2 (5.7)	8 (4.0)	0.842
Procedure related complication (N, %)			
Portal vein thrombosis	1 (2.8)	3 (1.5)	0.910
Postoperative liver failure	2 (5.7)	3 (1.5)	0.284
Bile leak	1 (2.8)	5 (2.5)	0.765
Bleeding	1 (2.8)	2 (1.0)	0.392
Intra-abdominal fluid collection	8 (22.9)	45 (22.5)	0.872
Intra-abdominal abscess	1 (2.8)	9 (4.5)	0.336
Wound problem	10 (28.6)	52 (26.0)	0.510

[a]Resection margin positive means invasive carcinoma at margin
[b]According to AJCC 7th edition
BMI, body mass index; PBD, preoperative bile drainage; PVE, portal vein embolization; T. bili, total bilirubin; CEA, carcinoembryonic antigen; CA19-9, cancer antigen 19-9; EBL, estimated blood loss; C-D grade, Clavien-Dindo classification

vs. 25.5%), left trisectionectomy (2.9% vs. 3.5%), extended left hemihepatectomy (8.6% vs. 16%) and left hemihepatectomy (0% vs. 8%) were performed. T3 stage and node metastases were observed more frequently in the PVR than in the No PVR group (40% vs. 12%; $p<0.001$ and 60% vs. 28%; $p<0.001$). There was no significant difference in proportion of positive resection margins between the two groups (5.7% vs. 11.5%; p=0.386).

The 30-day mortality developed in one (2.9%) case in PVR group and two (1.0%) cases in No PVR group (p=0.394). There was no significant difference in proportion between the two groups having portal vein thrombus (2.8% vs. 1.5%; p=0.910), liver failure (5.7% vs. 1.5%; p=0.284), bile leakage (2.8% vs. 2.5%; p=0.765), bleeding (2.8% vs. 1.0%; p=0.392) and intraabdominal fluid collection (22.9% vs. 22.5%; p=0.872).

Survival analysis

There was no significant difference in the 5-year OSR between the PVR and No PVR groups (37.7% vs. 42.6%; p=0.2300) (Fig. 2A). The 5-year DFS of the PVR and No PVR groups was 29.6% and 27.7% (p=0.379) (Fig. 2B). Fig. 2C, D shows a 5-year OSR and DFS for PVR-A, PVR-B and No PVR groups. There was no significant difference in the 5-year OSR and DFS between the three groups. The 5-year OSR for PVR-A, PVR-B and No PVR groups were 33.3%, 40.4% and 42.6%, respectively (p=0.479). The 5-year DFS of the three groups was 44.4%, 22.9% and 27.7%, respectively (p=0.576).

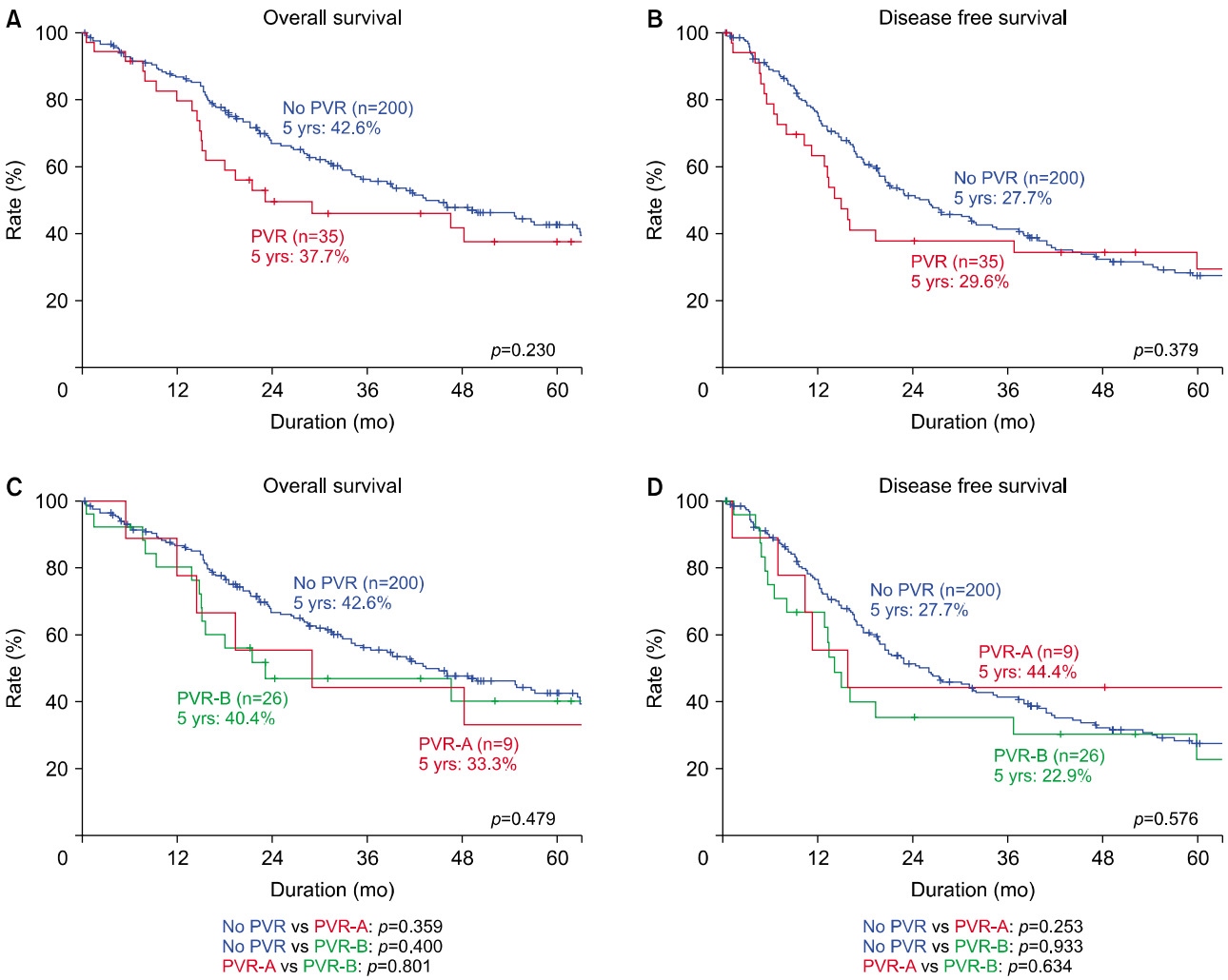

Fig. 2. Kaplan-Meier survival analysis (A) 5-year overall survival rate (OSR) of PVR and No PVR (B) 5-year disease-free survival rates (DFS) of PVR and No PVR (C) 5-year OSR for PVR-A, PVR-B and No PVR (D) 5-year DFS for PVR-A, PVR-B and No PVR.

Risk factor for overall survival rate (OSR)

Table 2 summarizes the risk factor for overall survival rate (OSR). In univariate analysis, preoperative bilirubin ≥3 mg/dl, preoperative CA 19-9 ≥40, tumor size ≥3 cm, operation time >390 min, EBL ≥600 ml, T3 versus T2/T1, node metastasis and poor differentiation significantly affected, OSR (hazard ratio [HR]=1.607, 95% confidence interval [CI] 0.923-2.797; *p*=0.097, HR=1.603, 95% CI 0.973-2.732; *p*=0.068, HR=1.607, 95% CI 0.959-2.695; *p*=0.089, HR=1.655, 95% CI 0.987-2.777; *p*=0.067, HR=2.024, 95% CI 1.202-3.407; *p*=0.009, HR=2.887, 95% CI 1.331-6.261; *p*=0.007, HR=2.422, 95% CI 1.369-4.284; *p*=0.002 and HR=2.666, 95% CI 1.329−4.974; *p*=0.002).

EBL >600 ml (HR=1.688, 95% CI 1.133-2.514; *p*=0.010), T3 versus T2/T1 (HR=2.403, 95% CI 1.540-3.747; *p*=0.001), node metastasis (HR=2.941, 95% CI 1.964-4.386; *p*=0.001), and poor differentiation (HR=1.890, 95% CI 1.260-2.836; *p*=0.002) were identified as independent risk factors in multivariate analysis. PVR and portal vein true invasion were not independent risk factors for OSR.

Risk factor for disease free survival (DFS)

Table 3 summarizes the risk factor for disease free survival (DFS). In univariate analysis, preoperative CA 19-9 ≥40, perineural invasion, positive resection margin, T3 versus T2/T1, node metastasis and poor differentiation significantly affect DFS (HR=1.717, 95% CI 1.002-2.943; *p*=0.048, HR=1.961, 95% CI 1.081-3.557; *p*=0.030, HR=2.123, 95% CI 0.919-4.878; *p*=0.081, HR=1.981, 95% CI 0.889-4.414; *p*=0.099, HR=1.769, 95% CI 0.976-3.203; *p*=0.061, and HR=2.165, 95% CI 1.133-4.136; *p*=0.021).

Perineural invasion (HR=1.684, 95% CI 1.120-2.530; *p*=0.012), positive resection margin (HR=1.874, 95% CI 1.010-3.447; *p*=0.043), node metastasis (HR=2.169, 95% CI 1.540-3.058; *p*=0.001), and poor differentiation (HR=2.096, 95% CI 1.439-3.054; *p*=0.001), were identified as independent risk factors in multivariate analysis. PVR and portal vein true invasion were not independent risk factor for DFS.

Table 2. Univariate and multivariate analysis of risk factor for overall survival rate (OSR)

Characteristics	Univariate			Multivariate		
	HR	95% CI	*p* value	HR	95% CI	*p* value
Age ≥65	1.556	0.927-2.610	0.115			
Male sex	0.918	0.537-1.568	0.785			
BMI ≥25	1.355	0.752-2.441	0.370			
High ASA class (3)	0.667	0.230-1.936	0.596			
Left hepatectomy	1.660	0.903-3.048	0.126			
No Caudate lobectomy	1.811	0.530-3.172	0.387			
Pre-op biliary drainage	1.526	0.890-2.617	0.133			
Pre-op Portal vein embolization	0.881	0.460-1.690	0741			
Pre-op T.bil ≥3	1.607	0.923-2.797	0.097	1.194	0.660-2.162	0.558
Pre-op alb <3.5	0.776	0.464-1.298	0.361			
Pre-op CA 19-9≥40	1.630	0.973-2.732	0.068	1.317	0.762-2.276	0.324
Tumor size ≥3 cm	1.607	0.959-2.695	0.089	1.275	0.738-2.203	0.384
Operation time >390 min	1.655	0.987-2.777	0.067	0.871	0.587-1.292	0.492
EBL ≥600 ml	2.024	1.202-3.407	0.009	1.688	1.133-2.514	0.010
Lymphovascular invasion	2.588	0.893-7.499	0.124			
Perineural invasion	3.359	0.862-13.091	0.115			
Portal vein resection	1.385	0.667-2.876	0.464			
Portal vein true invasion	3.203	0.651-15.756	0.179			
Positive resection margin	0.792	0.345-1.818	0.673			
T3 versus T2/T1	2.887	1.331-6.261	0.007	2.403	1.540-3.747	0.001
Node metastasis	2.422	1.369-4.284	0.002	2.941	1.964-4.386	0.001
Poorly differentiation	2.666	1.329-4.974	0.002	1.890	1.260-2.836	0.002
No Adjuvant treatment	1.230	0.692-2.187	0.558			

HR, hazard ratio; CI, confidence interval; BMI, body mass index; T. Bili, total bilirubin; CA19-9, cancer antigen 19-9; EBL, estimated blood loss

Table 3. Univariate and multivariate analysis of risk factor for disease free survival (DFS)

Characteristics	Univariate			Multivariate		
	HR	95% CI	*p* value	HR	95% CI	*p* value
Age ≥65	0.936	0.547-1.600	0.891			
Male sex	1.481	0.843-2.601	0.205			
BMI ≥25	1.535	0.831-2.838	0.223			
High ASA class (3)	0.583	0.204-1.666	0.416			
Left hepatectomy	1.812	0.954-3.442	0.086			
No Caudate lobectomy	1.424	0.552-3.676	0.297			
Pre-op biliary drainage	1.380	0.824-2.311	0.240			
Pre-op Portal vein embolization	0.690	0.355-1.340	0.299			
Pre-op T.bil ≥3	1.444	0.857-2.436	0.186			
Pre-op alb <3.5	0.924	0.548-1.557	0.791			
Pre-op CA 19-9≥40	1.717	1.002-2.943	0.048	0.616	0.347-1.094	0.098
Tumor size ≥3 cm	1.260	0.738-2.151	0.417			
Operation time >390 min	1.143	0.678-1.925	0.690			
EBL ≥600 ml	1.380	0.817-2.332	0.235			
Lymphovascular invasion	1.206	0.682-2.135	0.566			
Perineural invasion	1.961	1.081-3.557	0.030	1.684	1.120-2.530	0.012
Portal vein resection	1.078	0.507-2.295	0.852			
Portal vein true invasion	1.117	0.272-4.587	1.000			
Positive resection margin	2.123	0.919-4.878	0.081	1.874	1.010-3.447	0.043
T3 versus T2/T1	1.981	0.889-4.414	0.099	1.300	0.853-1.981	0.222
Node metastasis	1.769	0.976-3.203	0.061	2.169	1.540-3.058	0.001
Poorly differentiation	2.165	1.133-4.136	0.021	2.096	1.439-3.054	0.001
No Adjuvant treatment	1.108	0.616-1.992	0.767			

HR, hazard ratio; CI, confidence interval; BMI, body mass index; T. Bili, total bilirubin; CA19-9, cancer antigen 19-9; EBL, estimated blood loss

DISCUSSION

Several previous studies have reported that the proportion of Bismuth type III and IV in HC are at least 31%.[9,19] Extended hepatectomy should be performed for curative resection of this type of advanced HC. The problem is that such aggressive surgical excision increases morbidity and mortality after surgery. Furthermore, frequent tumor invasion into the portal vein because of the anatomical characteristics of HC has been recognized as an important factor limiting R0 resection. Nevertheless, various efforts have been made to achieve R0 resection through extended resection with PVR in several large centers. Two recent meta-analyses on the suitability of PVR have been conducted in terms of oncologic and surgical outcomes. Among these, one meta-analysis that W. Chen et al.[20] conducted included 13 studies (9 Asian groups, 2 USA groups, and 2 European groups). The results of this analysis showed that the PVR groups had a worse OSR than did the No PVR groups (HR=1.90, 95% CI 1.59-2.28; $p<0.00001$). This can be explained by the result of the PVR group having more LN metastases (HR=1.50, 95% CI 1.06-2.13; $p=0.02$) and a higher proportion of perineural invasion (HR=2.95, 95% CI 1.80-4.84; $p<0.0001$) than did the No PVR group. The fact that the curative resection was done in a smaller proportion in the PVR group (HR=0.65, 95% CI 0.46-0.91; $p=0.0$) also seems to have brought about the worse survival outcomes. However, there was no significant difference between the two groups in postoperative mortality and morbidity. Another meta-analysis reported by Bai et al.[21] was based on 21 retrospective studies and 2403 patients. This study showed a similar trend compared to the analysis of Chen et al.[20] The lymphatic invasion (HR=1.14, 95% CI 1.02-1.28; $p=0.02$) and perineural invasion (HR=1.31, 95% CI 1.05-1.64; $p=0.01$) were more frequently observed in the PVR group. The rate of curative resection was lower in the PVR group than in No PVR group (HR=0.89, 95% CI 0.75-0.99; $p=0.03$). Patients undergoing PVR experienced a higher postoperative mortality and a worse OSR (HR=

1.52, 95% CI 1.06-2.18; p=0.02 and HR=0.67, 95% CI 0.49-0.91; $p<0.001$). Postoperative morbidity was not significantly different between the two groups (HR=1.06, 95% CI 0.94-1.02; p=0.35). However, one cannot make these results into a simple generalization that the surgical oncologic outcome of the PVR group is worse than that of the No PVR group. This is because the tendency to have more advanced disease in the patient group undergoing PVR likely caused these results. We urgently need a prospective randomized control study because the above-mentioned meta-analysis used prior retrospective studies. On the other hand, the findings that there were no differences in morbidity in both the PVR and the No PVR groups in two meta-analyses shows us that PVR is acceptable in terms of safety.

In the current study, advanced T stage and LN metastases were observed more frequently in the PVR group than in the No PVR group (40% vs. T3: 12%; $p<0.001$ and 60% vs. 28%; $p<0.001$), which is in the same context as the previous reports. Nonetheless, there was no significant difference in OSR, DFS, 30-day mortality or postoperative morbidity in either group. Of note is that unlike the previous meta-analyses, the prognosis of patients undergoing PVR is not inferior to that of the No PVR group. Considering that the achievement of R0 resection is an important factor for a good prognosis of HC,[22] a surgical strategy that increases the possibility of a negative margin rate through PVR needs to be considered for the long-term survival of the selective cases of HC. Although PVR was not an independent risk factor for OSR and DFS in this study, the findings that R1 status is an independent risk factor for DFS also supports this view.

Among the patients in this study who underwent PVR, the rate of microscopic portal vein invasion was 25.1%. There were no significant differences in OSR and DFS between patients with or without microscopic portal vein invasion. A meta-analysis performed by Abbas et al.[23] reported that true microscopic portal vein invasion did not significantly affect survival using the previous seven retrospective studies (HR=1.59, 95% CI 0.75-3.35; p=0.22).[10-12,15,24-26] The percentage of patients having pathologically confirmed disease with microscopic portal vein invasion in these seven studies ranged from 22% to 88%. Microscopic vascular invasion was not found to have a significant effect on survival in a multicenter study of 305 cases consisting of cohorts in four USA and three European institutions. Our study also revealed that microscopic portal vein invasion is not a risk factor for OSR or DFS.

This study has some limitations. First, the absence of a protocol for adjuvant treatment is likely to have acted as a bias in the analysis of DFS. Although we determined the type of adjuvant treatment considering TNM staging and various oncologic factors, oncologist and radiologist's preferences may have been involved. Second, the number of PVR patients, which is relatively small compared to the No PVR patients, may have made a solid statistical analysis difficult. Finally, as a selection bias, patients in the PVR group were selected for patients with operability, so it is considered that there is a limit to comparison with the non-PVR group. However, this study has implications for comparable survival to No PVR patients when PVR was performed in operable patients with only PV invasion. In the future, large-scale prospective randomized controlled trials will minimize bias in studies that may occur in the patient selection process and will be necessary to validate the outcome of the PVR.

PVR does not increase postoperative mortality or morbidity. Although the PVR group has a more advanced disease state than the No PVR group, the PVR showed similar oncological results compared to the No PVR. Given these findings, PVR should be actively performed if necessary, after careful patient selection.

CONFLICT OF INTEREST

Ki Beom Kim, Dong Wook Choi, Jin Seok Heo, In Woong Han, Sang Hyun Shin, Yunghun You and Dae Joon Park have none to declare.

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Conceptualization: DWC, KBK, JSH, IWH, SHS, YY, DJP. Data curation: KBK, YY, DJP. Methodology: DWC, KBK, JSH, IWH, SHS, YY, DJP. Project administration: DWC, JSH, IWH, SHS. Visualization: KBK. Writing - original draft: KBK. Writing - review & editing: DWC, KBK, JSH, IWH, SHS, YY, DJP.

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