Int Surg 2016;**101**:437–442
DOI: 10.9738/INTSURG-D-15-00248.1

Portal Vein Pressure Change Predicts Posthepatectomy Liver Failure Following Right Lobectomy

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The aim of this study was to evaluate the usefulness of intraoperative portal venous pressure (PVP) as a predictor of posthepatectomy liver failure (PHLF). Hepatic functional reserve is typically evaluated by using parameters such as albumin level, platelet count, prothrombin activity level, or indocyanine green retention rate at 15 minutes. Low hepatic functional reserve can enhance the risk of PHLF. We retrospectively analyzed the outcomes of 35 patients who underwent right lobectomy and intraoperative PVP measurements between April 2004 and August 2012. According to preoperative prediction scores, all patients were within a safe limit for right lobectomy. The patients were grouped into uncomplicated (n = 22) and PHLF (n = 13) groups by postoperative course. PHLF was defined as grade B or C according to International Study Group of Liver Surgery criteria. Patient background, intraoperative bleeding, operative time, and PVP elevation after hepatectomy (ΔPVP) grade were compared between the groups. No cases of in-hospital death occurred. Univariate analysis revealed significant differences in preoperative white blood counts, intraoperative bleeding, and ΔPVP between the groups ($P < 0.05$). The ΔPVP was an independent risk factor on multivariate analysis. A ΔPVP >3 cmH_2O was associated with PHLF at 69.2% sensitivity and 90.9% specificity. Following right lobectomy, a ΔPVP >3 cmH_2O indicates a risk of PHLF and warrants careful postoperative management.

Key words: Portal vein pressure – Posthepatectomy liver failure – Hepatectomy

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Following hepatic resection, it is typically necessary to spare >30% of the future liver remnant (FLR) volume for patients with a normal liver compared with >50% of FLR volume for patients with a cirrhotic liver.[1] Several parameters are currently used to assess the hepatic function reserve, including albumin level, platelet count, prothrombin activity level, hyaluronic acid, indocyanine green retention rate at 15 minutes (ICGR 15), and Child-Pugh score. In our institution, we typically calculate the required hepatic resection amount by using Yamanaka's prognosis score, a numeric formula based on resection rate, patient age, and ICGR 15.[2] However, the presence of an anteroposterior shunt or constitutional excretory defect can affect the ICGR 15 value.

Interestingly, several reports have described a correlation between portal vein pressure (PVP) and hepatic function reserve, hyaluronic acid, liver activity at 15 minutes (LHL 15), technetium-99m galactosyl human serum albumin scintigraphy, ICGR 15, and liver stiffness.[3–7] Therefore, we chose to examine intraoperative PVP as an additional tool for evaluating hepatic function reserve and predicting posthepatectomy liver failure (PHLF) following right lobectomy.

Methods

We retrospectively examined the records of 35 patients whose PVP was monitored before and after right lobectomies conducted between April 2004 and August 2012. At our institution, right lobectomy is indicated using a scoring formula established by Yamanaka *et al*[2] ($Y = -84.6 + 0.933 \times$ resection rate [%] $+ 1.11 \times$ ICGR [%] $+ 0.999 \times$ patient age). Using this formula, patients with a value of $Y < 45$ points are deemed safely resectable; $Y < 55$ points, borderline resectable; and $Y \geq 55$ points, unresectable. This study included patients who underwent right lobectomy with a Y value indicative of borderline resectability. As part of this study, we assessed patient age, preoperative laboratory data, presence or absence of diabetes, intraoperative bleeding, operative time, PVP prior to resection, and grade of PVP elevation after hepatectomy (ΔPVP). All patients provided written informed consent before treatment, and the study was approved by the institutional review board of our hospital.

Measuring PVP

The PVP was assessed according to the water-gauge pressure (cmH_2O) obtained by using a round ligament from the patient's liver that was cut and reopened following laparotomy. We inserted a 6-Fr silicon tube into the cut end of the round ligament; after reverse blood flow was confirmed, we filled the tube with saline and measured the height of the column of water at the portal vein (Fig. 1).

PHLF Criteria

PHLF was defined and graded by using International Study Group of Liver Surgery (ISGLS) criteria.[8] In short, PHLF was characterized by an increased prothrombin-international normalized ratio and concomitant hyperbilirubinemia on or after postoperative day 5. PHLF severity was graded based on its impact on clinical management, with grade A PHLF resulting in no change in clinical management. Grade B PHLF results in deviation from the regular course of management and requires non-invasive therapy (*e.g.*, administration of diuretics or fresh-frozen plasma). Grade C PHLF requires invasive treatment such as tracheal intubation or dialysis.

In the present study, the uncomplicated group included 22 patients with absent or grade A PHLF, while the PHLF group included 13 patients with grade B or C PHLF.

Statistical Analysis

In the univariate analyses, the data were analyzed by using the Mann-Whitney *U*-test and the χ^2 test. Multivariate logistic regression was used for the multivariate analysis, and factors with a value of $P < 0.05$ on univariate analysis were entered into the multivariate model. Receiver operator characteristic (ROC) curve analysis was used to determine optimal cutoff values. The level of significance for all tests was set at $P < 0.05$. All analyses were performed using statistical software (JMP version 9.0.2, SAS Institute, Tokyo, Japan).

Results

The results of our univariate analysis are listed in Table 1. The mean patient age was 64.1 ± 8.1 years and 60.1 ± 12.7 years for the uncomplicated and PHLF groups, respectively, a difference that was not statistically significant. There were also no significant intergroup differences regarding preoperative albumin level, total bilirubin level, aspartate aminotransferase (AST), alanine aminotransferase (ALT), platelet count, prothrombin activity, or ICGR

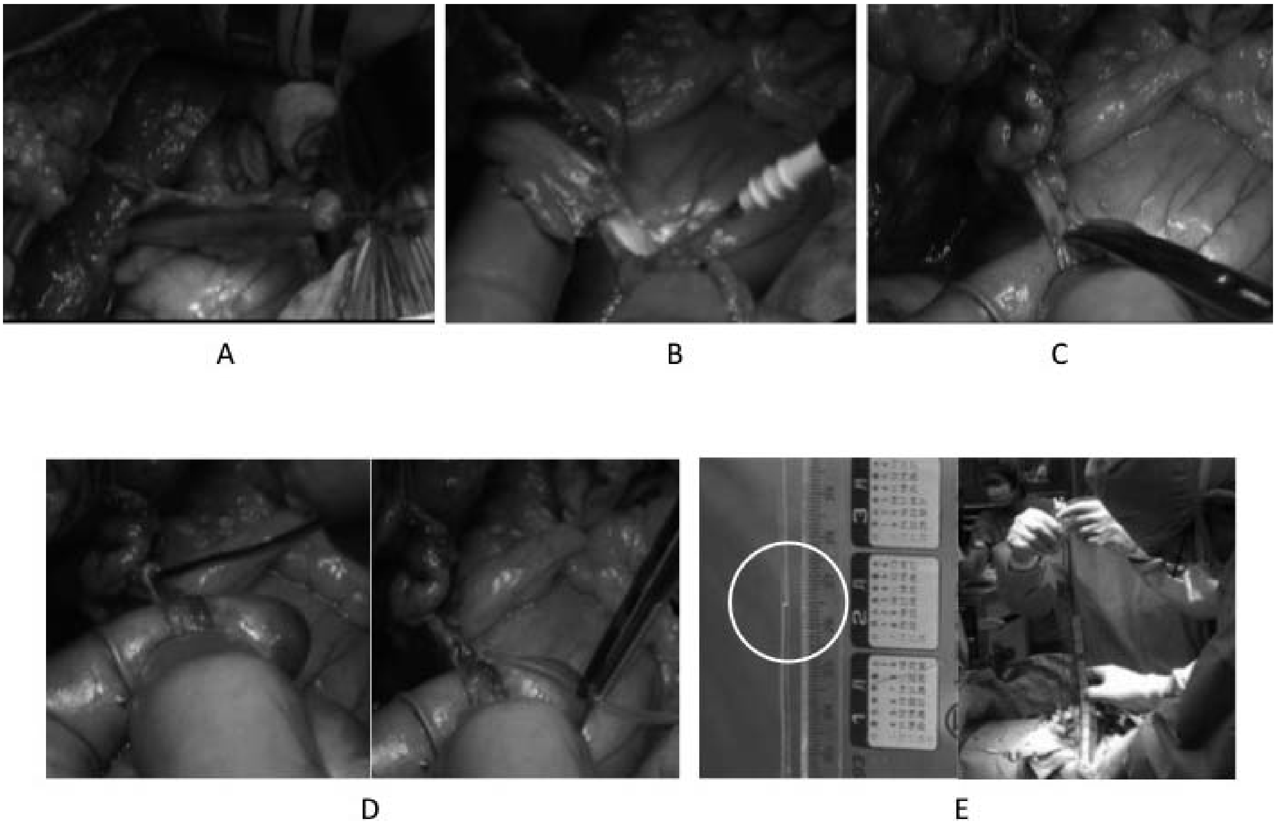

Fig. 1 Evaluating PVP. (A) Round ligament. (B) Skeletonization of the round ligament. (C) Excision of the round ligament. (D) Reopening of the round ligament and insertion of the silicon tube into the portal vein. (E) Measurement of PVP.

15. Diabetes was present in 18% (4/22) of patients in the uncomplicated group and 31% (4/13) of patients in the PHLF group. No significant difference in operative time was observed between the uncomplicated and PHLF groups (306 ± 83 and 351 ± 100 minutes, respectively). The preoperative white blood cell count for the uncomplicated group was 5672 ± 2095/μL compared with 8550 ± 4432/μL for the PHLF group ($P = 0.04$). Mean intraoperative blood loss was 1155 ± 688 mL and 2216 ± 1728 mL for the uncomplicated and PHLF groups, respectively ($P = 0.04$). The PVP prior to resection was similar in the uncomplicated and PHLF groups, although ΔPVP following resection was higher in

Table 1 Univariate analysis between uncomplicated group and PHLF group

	Uncomplicated group (n = 22)	PHLF group (n = 13)	*P* value
Age, y	64.1 ± 8.1	60.1 ± 12.7	0.51
Albumin, g/dL	3.9 ± 0.4	3.6 ± 0.4	0.14
Total bilirubin, mg/dL	0.6 ± 0.2	0.8 ± 0.4	0.20
AST, IU/L	58 ± 67	40 ± 21	0.91
ALT, IU/L	51 ± 62	36 ± 18	0.59
White blood count, per μL	5672 ± 2095	8550 ± 4432	0.04
Platelet count, $\times 10^4/\mu L$	22.1 ± 10.6	22.5 ± 13.7	0.88
Prothrombin activity, %	88.8 ± 9.9	85.4 ± 12.0	0.60
ICGR 15, %	9.2 ± 4.3	13.2 ± 9.4	0.47
Diabetes, +/−	4/18	4/9	0.39
Intraoperative bleeding, mL	1155 ± 688	2216 ± 1728	0.04
Operative time, min	306 ± 83	351 ± 100	0.17
PVP prior to resection, cm	15.2 ± 2.3	16.1 ± 4.6	0.74
ΔPVP, cm	0.88 ± 0.97	2.92 ± 1.55	0.0004

Table 2 Multivariate analysis of predicting PHLF

	Odds ratio	95% confidence interval	*P* value
White blood count, per µL	1.00	0.999–1.000	0.26
Intraoperative bleeding, mL	1.00	0.999–1.000	0.35
ΔPVP, cm	3.11	1.536–8.183	0.006

the PHLF group (0.88 ± 0.97 and 2.92 ± 1.55 cmH_2O, respectively; $P = 0.0004$).

The results of our multivariate analysis of the risk factors for PHLF are shown in Table 2. White blood cell count, intraoperative bleeding, and PVP elevation were included in this analysis, as they were identified as significant ($P < 0.05$) on the univariate analysis. However, only ΔPVP was identified as an independent risk factor for PHLF ($P = 0.031$). The optimal cutoff value was evaluated using ROC curve analysis, and a cutoff of 3 cmH_2O of ΔPVP provided a sensitivity of 69.2% and specificity of 90.9% (Fig. 2).

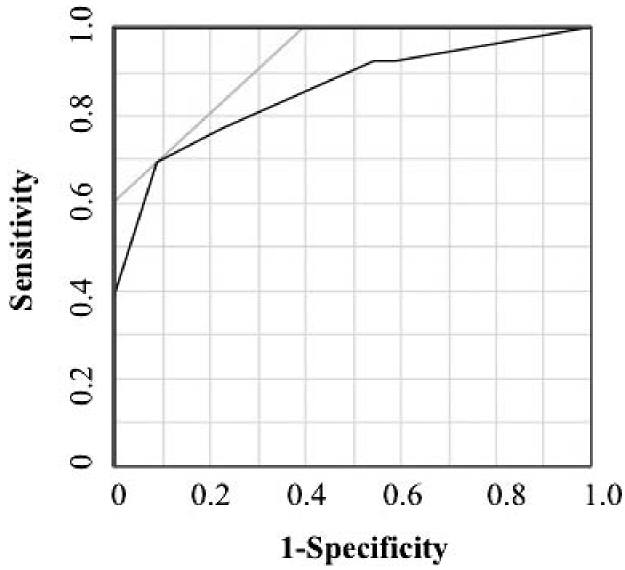

Fig. 2 ROC for elevated PVP. An elevation of 3 cmH_2O provided a sensitivity of 69.2% and a specificity of 90.9%.

Discussion

Several studies have reported a correlation between PVP and hepatic functional reserve,[1,3–7] which we have also studied using 221 patients treated at our institution between April 2004 and August 2012. The results of that study indicated that PVP was correlated with ICGR 15 ($r = 0.44$, $P < 0.0001$); AST level ($r = 0.46$, $P < 0.0001$); and pathologic fibrosis grade ($r = 0.52$, $P < 0.0001$).

The postoperative ΔPVP is interesting. Some studies have reported that the PVP typically becomes elevated immediately after hepatic resection but quickly returns to baseline.[9–11] Additionally, some reports have suggested that a moderate PVP elevation is necessary to regenerate liver tissue,[11,12] although abnormally elevated PVP and decreased portal blood flow can result if a large portion of the liver is resected.[13–15]

On the other hand, other studies have reported that elevated PVP is a risk factor for PHLF[16–18] and that the long-term prognosis is poor for patients with an elevated postoperative PVP.[19] In addition, one study reported that a postoperative PVP >20 cmH_2O is a risk factor for PHLF[20]; thus, some researchers have attempted the use of simultaneous splenectomy to decrease postoperative PVP, which resulted in fewer complications and improved hepatic functional reserve.[21,22] Furthermore, ligation of the splenic artery reportedly leads to decreased postoperative PVP,[23] and a portosystemic shunt may also decrease postoperative PVP, thereby preventing early PHLF.[24,25]

Our result suggested that an elevated posthepatectomy PVP indicates a risk of PHLF. The average postoperative day 5 total bilirubin level was 3.7 ± 1.3 mg/dL, while prothrombin activity level was 59.8% ± 10.7% in the PHLF group. On the other hand, total bilirubin level was 1.64 ± 0.56 mg/dL and prothrombin activity level was 80.6% ± 8.8% in the uncomplicated group.

The PHLF group included 8 grade B patients and 5 grade C patients. All PHLF patients had severe ascites that required drainage and the administration of diuretics. Additionally, all patients needed an intravenous drip infusion of albumin and fresh-frozen plasma. Four grade C patients needed an abdominal puncture for severe ascites. One grade C patient needed a plasma exchange. Fortunately, no patients in the PHLF group died during the study. However, the average postoperative hospital stay was 41.9 ± 21.9 days in the PHLF group versus 15.8 ± 3.4 days in the uncomplicated group ($P > 0.0001$).

The posthepatectomy mortality rate has recently decreases to as low as 0.8% to 2.6% in Japan because of improvements in liver resection and preoperative indications for hepatectomy.[26,27] Some preoperative indicators of hepatectomy have been identified in Japan. Among these, Makuuchi's criteria using the presence or absence of ascites, total bilirubin level, and ICGR 15,[27] as well as Yamanaka's criteria 2 are the most popular. Using these criteria, postoperative mortality has been successfully avoided. In the present study, all patients were discharged from hospital upon recovery.

However, among this cohort, the PHLF group patients needed severe postoperative management and an extended hospital stay, which resulted in high medical bills. Therefore, we should aim to identify methods to avoid PHLF.

We are currently attempting to prospectively evaluate the use of PVP by clamping the right portal vein and evaluating PVP prior to initiating hepatic resection. To date, only 6 such cases have been evaluated. Two patients developed PHLF following right lobectomy, and both had a 2 cmH_2O elevation in PVP after clamping of the right portal vein. The remaining 4 patients had a normal postoperative course; among them, 3 had a 0 to 1 cmH_2O elevation in PVP after clamping of the right portal vein. Although we cannot currently provide a suitable conclusion regarding these data, clamping of the right portal vein and evaluating PVP prior to hepatic resection might enable the prediction of PHLF.

The limitations of the present study are its small size, retrospective nature, and single-center design. Therefore, we cannot confirm causality. We hope to investigate this phenomenon in a larger and prospective multicenter study.

In conclusion, a PVP elevation >3 cmH_2O following right lobectomy is a risk factor for PHLF. Thus, if a PVP elevation >3 cmH_2O is observed, careful postoperative management is advised.

Acknowledgments

Drs. Hiroya Iida, Tsukasa Aihara, Shinichi Ikuta, and Naoki Yamanaka declare no conflicts of interest. The authors declared that there was no support in the forms of grants, equipment, and drugs.

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