

Original Research

A predictive formula for portal venous pressure prior to liver resection using directly measured values

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Abstract

Purpose: Despite refinements in surgical techniques for liver resection, evaluation of hepatic reserve disparity remains one of the most common problems in liver surgery, especially for hepatic malignancies such as hepatocellular carcinoma (HCC). Portal venous pressure (PVP) is regarded one of the important factors in selecting treatment strategy, although its measurement can be invasive and complex.

Methods: To establish a formula for calculating PVP preoperatively, intraoperative directly measured PVP was used in 177 patients with preoperative factors and liver function tests such as age, sex, virus status, platelet count, prothrombin time, albumin, total bilirubin, alanine aminotransferase (ALT), Child–Pugh grade, liver damage defined by the Liver Cancer Study Group of Japan, indocyanine green retention rate at 15 min (ICG-R15), and the aspartate transaminase (AST)-platelet ratio index (APRI).

Results: After multiple regression analysis, the formula $PVP \text{ (cmH}_2\text{O)} = \text{EXP}[2.606 + 0.01 \times (\text{ICG-R15}) + 0.015 \times \text{APRI}]$ was established from the measured data ($r = .495$ ($p < 0.01$)).

Conclusion: Considering its simplicity of use, we have adopted the formula for predicting PVP in determining treatment strategy for HCC and other hepatic malignancies.

Keywords: portal venous pressure, formula, hepatocellular carcinoma, resection,

prediction

Introduction

Outcomes of liver resection for hepatocellular carcinoma (HCC) have improved due to better surgical techniques and patient selection [1]. We previously reported that intraoperative portal venous pressure (PVP) was a good indicator of postoperative complications after hepatectomy and that measurement of portal venous pressure is useful in selecting the optimal type of resection in cirrhotic patients with HCC [2]. In addition, the value of intraoperative PVP was validated even on recurrence of HCC [3]. In the BCLC (Barcelona Clinic Liver Cancer) criteria established in 2001, Bruix included PVP in selecting a treatment for HCC [4], especially in European facilities. However, in the BCLC criteria, hepatic venous pressure gradient (HVPG) was used as the indicator of PVP [5, 6], but this measurement is not always applicable to all patients because it needs a skillful radiologist and a facility for performing an angiogram [7]. In addition, HVPG is a rather invasive technique which is not standardized outside of Europe, e.g. Asian countries, such as Japan [8].

Recently, various scores have been advocated for assessing basic liver function or hepatic functional reserves over the Child-Pugh score, such as Albumin-Bilirubin (ALBI) Grade and Albumin-Indocyanine Green Evaluation (ALICE) grade [9-

11]. They have been reported to be good indicators in selecting therapeutic modalities or predicting survival upon treatment for HCC. However, if PVP could be estimated to evaluate the timing of treatment of portal hypertension and selecting therapeutic modality for HCC in a cirrhotic liver, it would be of great value, especially when the BCLC criteria are used.

During our previous study, we had collected PVP data along with background factors of patients [3]. In the present study, in an effort to establish a formula to calculate PVP preoperatively, directly measured PVP was used, particularly in patients with liver diseases.

Patients and methods

To establish a formula for calculating PVP, previously collected data for PVP were used in 177 patients who underwent hepatectomy between 2000 and 2009.

Direct portal venous pressure measurement

In the 177 subjects, immediately after celiotomy for liver resection, PVP was measured directly [3]. Briefly, a catheter was inserted into a jejunal mesenteric vein

around 100–120 cm from the Treitz ligament before liver mobilization and resection.

For HCC surgery, we do not dissect the hepatoduodenal ligament, since LN dissection is not needed. Therefore, we did not puncture the portal vein itself directly. PVP was then measured using a water pressure gauge with saline (Fig. 1). The zero points were set at the level of the anterior axillary line. Patients with a history of upper abdominal surgery and mesenteric membrane adhesions were excluded, because intubation could not be done easily after laparotomy.

Preoperative data

Patient data collected before surgery included age, sex, virus status, platelet count, prothrombin time, albumin, total bilirubin, alanine aminotransferase (ALT), Child–Pugh grade, liver damage defined by the Liver Cancer Study Group of Japan (LCSGJ), and indocyanine green retention rate at 15 minutes (ICG-R15) (12). The degree of liver damage, a procedure that was advocated by the LCSGJ as an alternative to the Child–Pugh score, was defined by preoperative measurements of ascites, serum bilirubin level, serum albumin level, indocyanine green retention rate at 15 minutes (ICG R15), and prothrombin activity [13].

Serological presence of hepatitis B antigens was considered evidence for

hepatitis B infection. Serologic presence of hepatitis C antibody was considered an indicator of hepatitis C infection. Serum levels of alpha-fetoprotein (AFP) and des-gamma-carboxy prothrombin (DCP) were measured as tumor markers. Ishak's hepatitis activity score (HAI score: Grading and Staging) were histologically determined. (14)

Hepatic resections were classified according to the terminology of the Liver Cancer Study Group of Japan (12).

The aspartate transaminase (AST)-platelet ratio index (APRI), which is a well-established marker for liver fibrosis, was used as indicators for monitoring esophageal varices [15].

Informed consent was obtained [3], and the study protocol has been approved by the institutional committee on human research.

Statistical analysis

All values are expressed as median and range. Correlation between PVP and clinical factors were calculated using Spearman rank-order correlation. Multiple regression analysis was performed to establish a formula to calculate PVP preoperatively.

Results

The characteristics of the 177 patients with HCC are summarized in Table 1. Almost 90% of the patients were in Child-Pugh classification A because they were fair candidates for hepatic resection, while the grade of liver damage was worse than Child-Pugh classification, probably because of high ICG-R15. Major hepatectomy greater than hemihepatectomy was performed in 30% of the patients. Median APRI (AST/Platelet) was 0.76 (0.08 - 8.01), while median ICG-R15 was 13.0 % (1-40).

In the 177 subjects, immediately after celiotomy for liver resection, PVP was measured directly. Although 90% of the patients were classified as Child-Pugh A, median direct PVP was 16.5cm H₂O (5.5-37.0) and the percentage of PVP greater than 20cm H₂O was 27.1%, reflecting portal hypertension due to liver damage

Four independent factors, that is, platelet counts, serum levels of albumin, ICG-R15, and APRI, were extracted and showed a certain extent of correlation with PVP (Fig. 2). Other factors were not correlated with directly measured PVP. From the measured data, applying multiple regression analysis, PVP (cmH₂O) = EXP[2.606 + 0.01×(ICG-R15)+0.015×APRI] was established (r = .495, p<0.01)) as a predictive formula.

Discussion

As a result, we can advocate the formula of PVP = EXP[2.606 + 0.01×(ICG-

R15)+0.015×APRI]. Considering its simplicity of use, we adopted the formula for predicting PVP in determining treatment strategy for HCC and other hepatic malignancies.

Portal venous pressure has been found to reflect the degree to which the liver parenchyma is damaged [16]. Measuring PVP is useful in determining the final indications for surgery also in cirrhotic patients with HCC [2, 12-15]. In a meta-analysis, morbidity and mortality after hepatectomy were 6.1%, 2.8%, and 41.7%, 34.7%, respectively [17]. In addition, Berigotti et al reported that the rate of liver failure after hepatectomy was much higher in patients with portal hypertension (PHT) than in those without PHT [18]. In those studies, some defined PHT as platelet count less than 100×10^3 and diameter of the spleen greater than 12cm, while some used HVPG [19, 20]. They even reported that long-term recurrence-free survival after hepatectomy was correlated with PVP. Therefore, it is important to know the PVP based on preoperatively measured values with ease [21]. We could make resection smaller if estimated PVP is high, or we would be convinced to perform a larger resections if PVP is within normal range. For those reasons, we established this formula for predicting PVP preoperatively.

The equation for PVP that we calculated contains ICG retention rate at 15 minutes and APRI. ICG-R15 has not been considered to reflect PVP directly as we

reported previously but rather a comprehensive reflection of liver fibrosis and collateral formation in the body [2]. In addition, ICG-R15 has been used as one element of the Japanese assessment of liver function instead of the Child-Pugh classification and has been called a more objective evaluation of the degree of liver damage [22]. On the other hand, APRI consists of AST level and the number of platelets, which has been regarded as one of the most important reflections of PHT as the result of hypersplenism. Therefore, our equation could be a reasonable one calculated from direct measurement of PVP. In the clinical setting, degree of portal hypertension and liver functions such as synthetic function and conjugation are somewhat different and dissociated (23-26). That is why our formula could be of use clinically.

There are some limitations in this study. First, although we reported the relationship between direct PVP and postoperative complications, the patients in this study were a completely different cohort from the previous study [2]. Therefore, we should have performed the same analysis with the current cohort. Second, validation of similarity between the estimated PVP and the directly measured PVP should be done in a prospective manner. Third, the number of calculate PVP was only 177, which ideally should have been bigger to obtain a more reliable formula. Finally, relevant factors such as spleen size etc. should be investigated in future research.

Conclusions

Considering its simplicity of use, we adopted this formula for predicting PVP in determining treatment strategy for HCC or other hepatic malignancies. The formula needs further validation using data from patients of all ethnicities.

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Figure legend

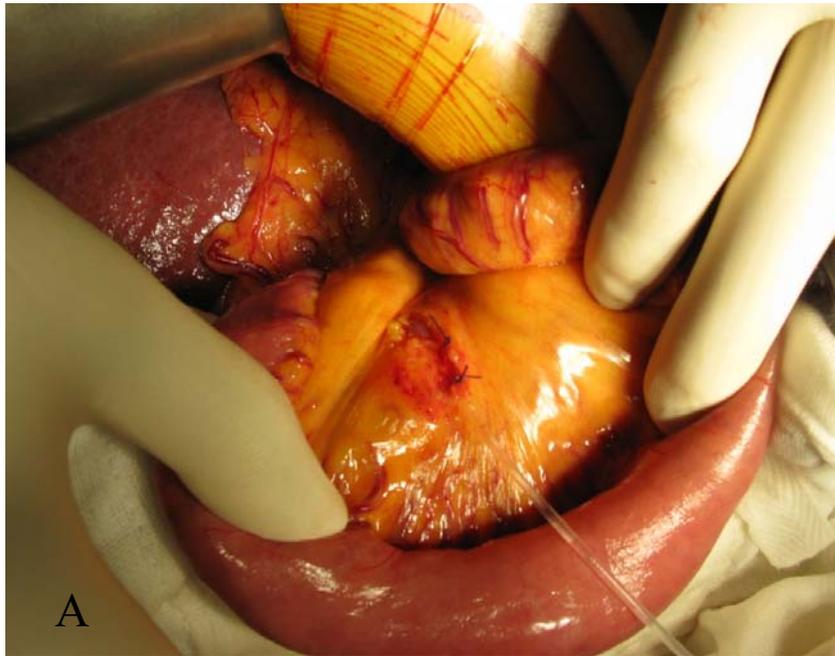
Fig. 1. Direct measurement of portal venous pressure in patients undergoing hepatectomy for hepatocellular carcinoma. A: Jejunal vein at 100-120cm from Treitz ligament was cannulated immediately after celiotomy. B: Direct measurement using manometer with normal saline at the right atrium level.

Fig. 2. Correlated factors with portal venous pressure (n=177)

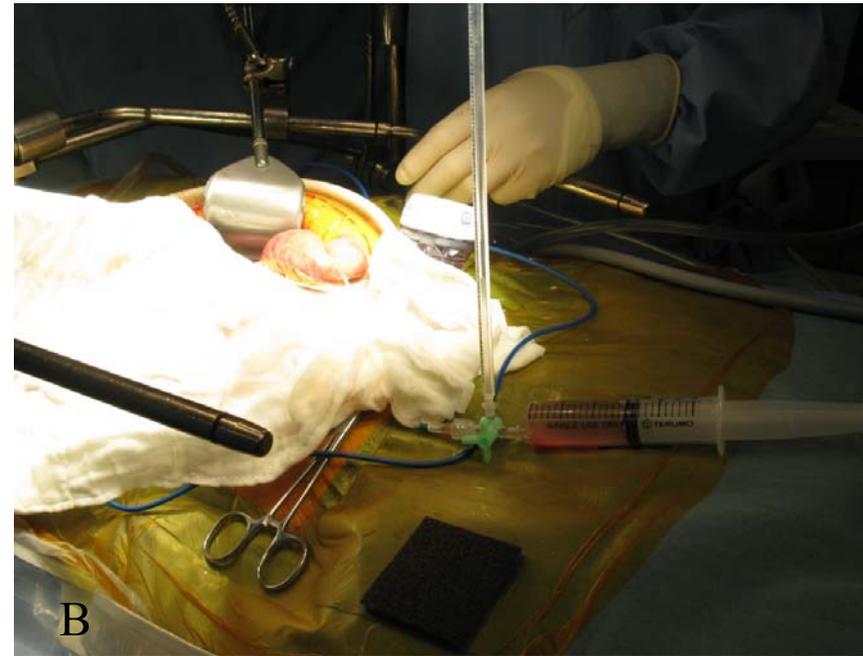
Table 1. Characteristics of the patients (n=177)

Variable			
Ages(years)	65 (20-81)	Tumor diameter (cm)	3.5 (0.5-17.0)
Gender(M:F)	147 : 30	Solitary tumor	130 (73.5%)
Etiology		Type of hepatectomy	
Hepatitis B	47 (26.5%)	Partial and	
Hepatitis C	84 (47.5%)	Segmentectomy	117 (66.1%)
Hepatitis B + C	3 (1.7%)	Major hepatectomy	60 (33.9%)
nonBnonC	43 (24.3%)	Vascular invasion	50 (28.2%)
Platelet (x10 ⁴ /mm ³)	15.1 (2.6-47)	HAI	
Prothrombin time (%)	89.0 (54-122)	Grading	5.0 (1-13)
Albumin (g/dl)	3.9 (2.6-4.8)	Staging	3 (0-4)
Total bilirubin (mg/dl)	0.75 (0.3-4.8)	APRI(AST/Platelet)	0.76 (0.08-8.01)
AST (IU/L)	38 (12-337)	IGG R15(%)	13.0 (1-40)
ALT (IU/L)	40.5 (7-222)	LHL15	0.93 (0.61-0.97)
AFP (ng/ml)	18.7 (1.2-454,300)	Child Pugh classification	
DCP (mAU/ml)	67 (1.2-151,367)	Class A	160 (90.4%)
		Class B	17 (9.6%)
PVP (cmH₂O)	16.5 (5.5-37.0)	Liver damage	
PVP >= 20 cmH₂O	48 (27.1%)	Class A	139 (78.5%)
PVP < 20 cmH₂O	129 (72.9%)	Class B	35 (19.7%)

Fig. 1 Direct measurement of PVP

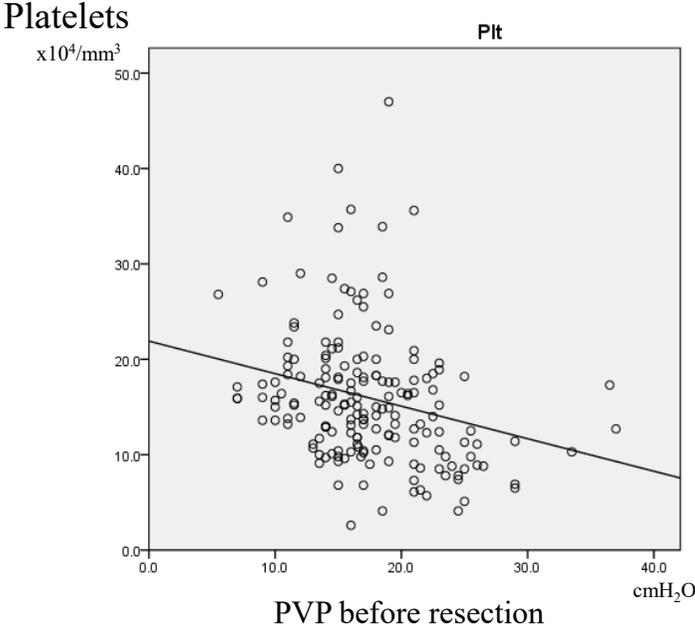


Jejunal vein at 100-120cm from treiz ligament was cannulated immediately after celiotomy

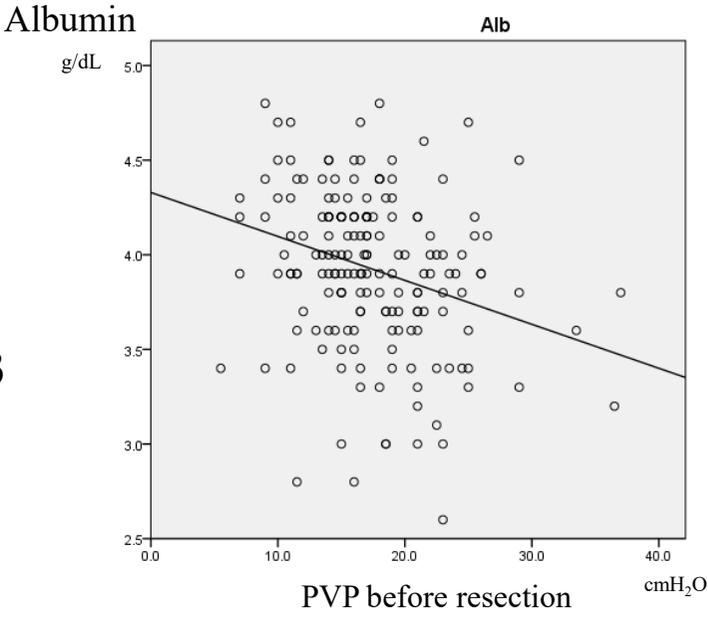


Direct measurement using manometer with normal saline at the right atrium level. The zero points were set at the level of anterior axillary line.

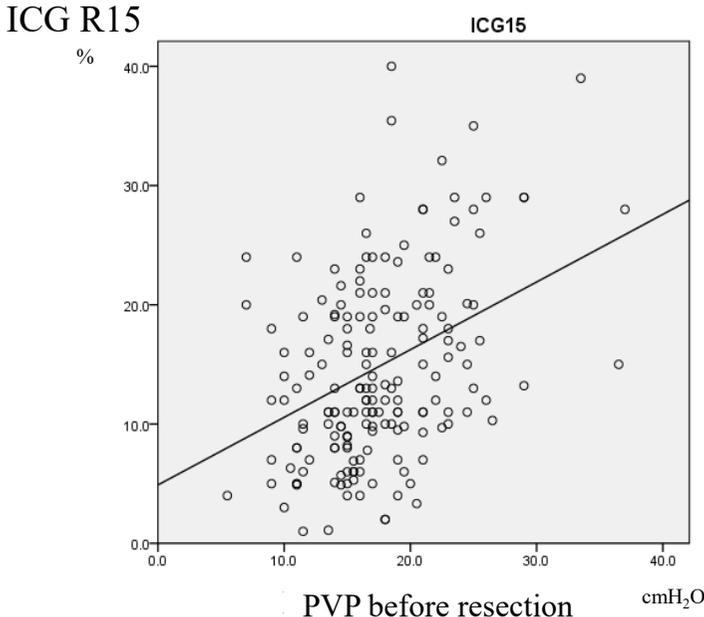
Fig. 2 Correlated factors with portal venous pressure (n=177)



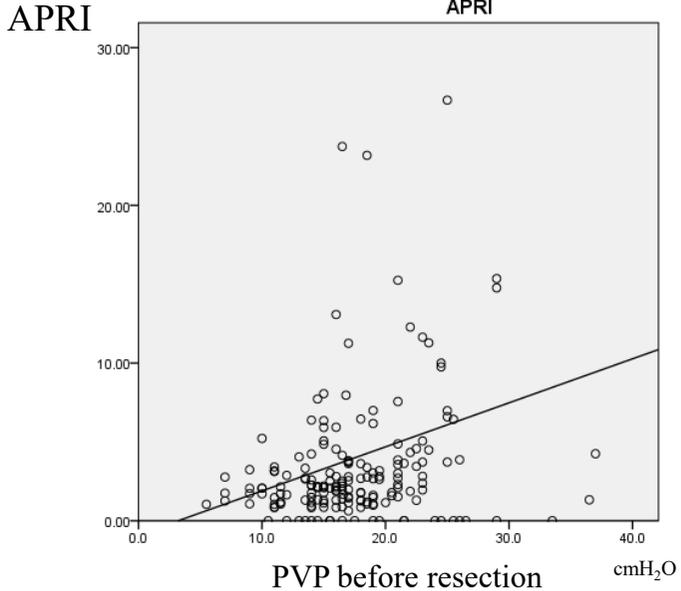
$p < 0.01$
 $r = -.293$



$p = 0.01$
 $r = -.293$



$p < 0.01$
 $r = .413$



$p = 0.001$
 $r = .332$