Usefulness of Intraoperative Measurement of Portal Venous Pressure for Confirming the Most Appropriate Hepatectomy in Patients with Borderline Hepatic Functional Reserve

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Abstract

Background We investigated whether portal venous pressure (PVP) measured immediately before surgery and then immediately after clamping of the Glissonian pedicle can be used to predict postoperative complications (ascites or jaundice) and thus select the extent of resection in patients with liver disease requiring hepatectomy.

Methods Thirty-seven patients with hepatic functional reserve near the advisable limit and in whom direct measurement of PVP was done just before surgery and after clamping of the Glissonian pedicle were divided into two groups, an Event group (n = 9) and a Non-event group (n = 28), according to whether postoperative complications developed. The relation between PVP and the complication rate was analyzed, and a PVP safety margin was identified.

Results PVP obtained after the Glissonian pedicle was clamped was significantly higher in the Event group than in the Non-event group (18.8 vs. 15.7 cmH₂O; p = 0.03). The PVP gradient (defined as PVP after Glissonian clamping – PVP before surgery) tended to be greater in the Event group (5.1 versus 3.6 cmH₂O; p = 0.13). PVP after Glissonian clamping plotted against the PVP gradient revealed safety margins of PVP gradient < 5 cmH₂O and PVP < 20 cmH₂O, respectively.

Conclusion PVP after Glissonian clamping and the PVP gradient may be useful for predicting post-hepatectomy complications.

Key words portal venous pressure, major hepatectomy, liver

Introduction

Hepatectomy is one of the most effective treatments for liver tumor, including hepatocellular carcinoma (HCC), the most common primary liver cancer and one of the most frequently occurring malignancies in Asia¹. Hepatectomy is often necessary for liver diseases other than HCC, and HCC itself often develops against a background of chronic liver damage. In any case, the extent of liver resection must be determined preoperatively, and in patients with liver tumor this determination is based on hepatic functional reserve. The potential for curative hepatectomy is often limited due to poor hepatic functional reserve. Although outcomes of hepatectomy for HCC and for other conditions have improved greatly in recent years as a result of refinements in surgical technique and perioperative management, there is no way to reliably predict difficult-to-manage jaundice or ascites that can occur immediately after hepatectomy.
In general, post-surgical jaundice and ascites are caused by an elevation in portal venous pressure (PVP). To date, the extent of liver resection has been based on the volume of the remnant liver, but ideally, the predicted change in PVP after liver resection should be incorporated into the decision-making process. The aim of this retrospective study was to determine whether PVP measured directly before hepatectomy and then after clamping of the Glissonian pedicle but before its division can be used to predict postoperative outcomes in patients treated by hepatectomy. The study looked particularly at the relation between PVP and ascites and hyperbilirubinemia after surgery.

**Methods**

Study subjects were 37 patients who underwent major hepatectomy for HCC or another disease at either Tokyo Women’s Medical University Hospital or St. Marianna University School of Medicine Hospital between 1991 and 2013. Only patients in whom hepatic functional reserve was near the limit as set forth by Takasaki et al. were included. Patients in whom elective hepatectomy was initiated but then abandoned intraoperatively because of extensive liver fibrosis or because the remnant liver volume was judged to be too small were not included in the study.

Hepatectomy was performed if indicated by preoperative tumor staging and liver function tests. Tumor staging involved preoperative ultrasonography, multidetector computed tomography, or magnetic resonance imaging in all patients. We use the Takasaki criteria, based on the indocyanine green retention rate at 15 minutes (ICG-R15), to determine the maximum liver resection volume (Fig. 1). Preoperative liver function was assessed by the ICG-R15, Child-Pugh classification, and liver damage grading system of the Liver Cancer Study Group of Japan.

Intraoperative PVP measurements were performed as follows: After the ligamentum teres hepatitis was opened, a 16-gauge catheter was inserted, and the tip was positioned at the main trunk of the portal vein. Continuous direct measurement of PVP was performed with a blood pressure transducer (Becton, Dickinson and Co., Franklin Lakes, New Jersey, USA) and tracked on an INTElliVueMX700 monitor (Phillips and Co., Amsterdam, Netherlands). PVP was measured before hepatectomy by means of a water pressure gauge used with physical saline. PVP was also measured just after clamping of the Glissonian pedicle. In addition, the PVP gradient was calculated as PVP after clamping – PVP before hepatectomy.

The ICG-R15 was used as a predictive index upon which we selected the extent of hepatectomy; selection was based on the Takasaki method (Fig. 1). Hepatectomy was limited to an ICG-R15 value < 50% in cases of non-cirrhotic liver and < 40% in cases of cirrhotic liver.

The patients were divided into two groups: an Event group and a Non-event group, depending on postoperative morbidity including severe ascites (developing during the hospitalization period immediately after surgery, ≥ grade III Clavien-Dindo complication) and hyperbilirubinemia (serum bilirubin ≥ 10 mg/dL and ≥ grade II Clavien-Dindo complication).

We examined the ICG-R15 value, PVP after Glissonian pedicle clamping, and the PVP gradient, and we compared these values between the Event group and the Non-event group. We also plotted the PVP gradient against the post-clamping PVP for both groups to identify the safety margins for each of these potential predictors.

Other variables examined were patient sex and age, disease type, extent of liver resection, frequency of surgery-related deaths, and the number and types of post-surgical events.

Values are shown as mean (± SD). Between-group differences in the ICG-R15, PVP after clamping, and PVP gradient were analyzed by Student’s t test or Mann-Whitney U test, as appropriate. SPSS 17.0 statistical software (SPSS, Chicago, IL, USA) was used for all statistical analyses. A *p* value of 0.05 was accepted as statistically significant.

**Results**

The 37 study patients underwent hepatectomy for HCC (n = 32), liver metastasis (n = 3), intrahepatic cholangiocarcinoma (n = 1), or perihilar bile duct cancer (n = 1). The procedures included right trisectionectomy (n = 2), right hepatectomy (n = 22), central bisectionectomy (n = 3), anterior sectionectomy (n = 3), and posterior sectionectomy (n = 7). There were no surgery-related deaths.

Nine patients developed post-hepatectomy ascites (Clavien-Dindo grade IIIa or above) that required strict control, and 2 of these 9 patients showed severe jaundice (serum bilirubin > 10 mg/dL, Clavien-Dindo grade II or above). These patients comprised the Event group, and the remaining 28 patients comprised the Non-event group. Patients’ clinical
Preoperative ICG R15

Residual liver function (ICG R15)

Liver resection rate (%)

Fig. 1. Selection of the extent of hepatectomy by the Takasaki method. The liver resection volume is determined according to the non-tumoral liver parenchyma. The extent of hepatectomy is determined by plotting variables as shown on the graph above. The preoperative ICG-R15 is plotted on the Y axis, and residual liver function (ICG-R15) is plotted on the Z axis according to the proposed percentage of liver resection. A line is drawn between point R and point (A), and the planned extent of liver resection is determined as the value on the X-axis (A or B) at the intersection of line (a) (non-cirrhosis) or line (b) (cirrhosis) and the straight line [R to (A)].

Characteristics are shown per group in Table 1.

The predictive ICG-R15 value was 36.5 (± 10.8)% in the Non-event group, and 35.2 (± 11.9)% in the Event group (Fig. 2) and did not differ significantly between the two groups (p = 0.77).

Post-clamping PVP was 15.7 (± 3.1) cmH$_2$O in the Non-event group and 18.8 (± 4.7) cmH$_2$O in the Event group (Fig. 3), and the difference was significant (p = 0.03).

The PVP gradient tended to be higher in the Event group (3.6 ± 2.2 cmH$_2$O) than in the Non-event group (5.1 ± 3.1 cmH$_2$O), but the difference did not reach statistical significance (p = 0.13) (Fig. 4).

A scatter plot showing the post-clamping PVP values against the ICG-R15 values is shown in Fig. 5. There was no conspicuous trend respective to either study group.

A scatter plot showing the PVP gradient values against the post-clamping PVP values is shown in Fig. 6. No patient in the Event group had both a PVP gradient < 5 cmH$_2$O and a post-clamping PVP < 20 cmH$_2$O. Therefore, a PVP gradient < 5 cmH$_2$O and a post-clamping PVP < 20 cmH$_2$O were determined as the cut-off values for prediction of postoperative complications.

Discussion

Several preoperative criteria have been reported for determining the limit of liver resection$^{2, 6-8}$. The Makuuchi and Takasaki criteria are well-known liver volume-based criteria$^{2, 7}$. The Makuuchi criteria are both stepwise and strict, so we apply these criteria when judging the extent of liver resection in patients in whom hepatic functional reserve is close to the lowest advisable limit. The Takasaki criteria are sequential, but they do not compensate for the high risk of complications in patients with severe liver cirrhosis.

What is needed in surgical practice is a guide that can be used when there is any doubt whether the planned surgical procedure should be carried out. However, reports on intraoperative criteria are few$^{9-11}$. Kanematsu et al. reported an absence of a significant correlation between PVP and the preoperative ICG-R15, especially in patients with an ICG > 20%$^{9, 10}$. There were no complications when the PVP was < 20 cmH$_2$O.

Although the 2005 findings of Kanematsu et al.$^{10}$ were significant, their study was limited to prehepatectomy PVP. They found simply that complica-
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<th>Table 1  Clinical Characteristics of Patients Per Study Group*</th>
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Numbers of patients are shown unless otherwise indicated.
Non-event group: patients with post-hepatectomy complications; Event group: patients without post-hepatectomy complications; IQR: Interquartile range; LCSGJ: Liver Cancer Study Group of Japan; SD: Standard deviation; PVP: Portal venous pressure.

*Differences in clinical characteristics were not significant by Fisher’s exact test.

**Fig. 2.** ICG-R15 values obtained for prediction of post-hepatectomy liver function. Values did not differ between groups.
Fig. 3. PVP per group after clamping of the Glissonian pedicle. PVP values were significantly higher in the Event group than in the Non-event group.

Fig. 4. PVP gradient per study group. The PVP gradient was calculated as follows: PVP after Glissonian pedicle clamping − PVP before surgery. The PVP gradient tended to be higher in the Event group.

tions occur with increased frequency when the pre-hepatectomy PVP is > 20 cmH\(_2\)O. Thus, their guideline does not apply to situations in which we must re-evaluate intraoperatively whether the planned operative procedure should be implemented.

Although Katsuragawa et al.\(^{12}\) reported focusing on the changes in PVP, they described a method for estimating the ICG-R15 value from the intraoperative change in PVP. They concluded that the ICG-R15 value is a direct reflection of the change in PVP and that it can be used reliably for a final intraoperative decision regarding the extent of hepatectomy.

We investigated whether a decision can be made to implement the planned operative procedure by measuring PVP before hepatectomy and after clamping of the Glissonian pedicle and then calculating the gradient. We found a PVP gradient < 5 cmH\(_2\)O and a post-clamping PVP < 20 cmH\(_2\)O to be predictive of
only a few or even no postoperative complications. Thus, the intraoperative PVP gradient would be useful to the surgeon in making a final decision. The post-clamping PVP < 20 cmH\textsubscript{2}O points away from portal hypertension. In view of the fact that obliteration of a portosystemic shunt in cases of Child-Pugh A or B hepatic impairment increases the PVP by < 60\% \cite{13}, the criteria we are proposing are quite strict. We must bear in mind, however, that the chief consideration is avoidance of complications after surgery, especially those that can result in death. Thus, these strict criteria may be appropriate for avoiding the post-surgical complications.

Our method is limited by the fact that it is not easily applied to all hepatectomy procedures, such as right trisegmentectomy and central bisegmentectomy, in which the Glissonian pedicle will not be approached. To solve this problem, we can encircle the Glissonian pedicle of segment 4 to remove a little of the liver parenchyma tissue inside the umbilical portion.

Surgeons can view and touch the cirrhotic liver...
intraoperatively to determine whether the planned surgical resection is in fact appropriate. For most types of hepatectomy, PVP measurement is feasible after the Glisssonian pedicle is encircled but before it is divided, and therefore the PVP gradient can be calculated just before dissection of the liver. Intraoperative measurement of PVP may allow us to avoid major postoperative complications and to make a final selection of the most appropriate liver resection in patients with borderline hepatic functional reserve.

**Conclusion**

PVP obtained after clamping of the Glisssonian pedicle and the PVP gradient may be useful for predicting post-hepatectomy complications in patients with borderline hepatic functional reserve.

**References**