Selective Inflow Occlusion Technique Versus Intermittent Pringle Maneuver in Hepatectomy for Large Hepatocellular Carcinoma

A Retrospective Study

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INTRODUCTION

Hepatocellular carcinoma (HCC) is a highly prevalent and lethal cancer. It is estimated that 500,000 to 1 million annual cases are reported worldwide, especially in the Asia-Pacific region. Partial hepatectomy is a potentially curative therapy for HCC patients, but liver resection may present intraoperative bleeding. Moreover, bleeding together with the subsequent blood transfusions can increase postoperative morbidity and mortality. In addition, blood transfusions, even in small volumes, have been found to enhance tumor recurrence in patients undergoing surgical excision of the HCC.

Hepatic vascular control is effective in minimizing intraoperative bleeding during hepatectomy, especially for large tumors or those located in proximity to major vascular structures. The Pringle maneuver, a technique of transient hepatic inflow occlusion by clamping the portal triad, is the simplest and most established method for controlling afferent blood flow. However, the Pringle maneuver carries the risk of ischemia-reperfusion injury to liver, particularly in patients with chronic hepatic cirrhosis. Ischemia-reperfusion injury caused by temporarily interrupted blood inflow to liver is a complex, multifactorial pathophysiologic process that includes intrahepatic adenosine-5′-triphosphate (ATP) depletion, oxidative stress, and generation of inflammatory mediators.

Selective inflow occlusion (SIO) techniques, with continuous occlusion of hepatic artery and intermittent occlusion of the portal vein supplying the tumor-containing portion of the liver, have been applied to reduce blood loss and injury to the liver function. In this study, this maneuver was applied to decrease ischemia-reperfusion injury of the remnant liver, especially for patients with cirrhosis. The advantage of this maneuver is to provide continuous arterial inflow of nontumorous liver by the hepatic artery during surgery.

Until now, the clinical advantage of using either the SIO or intermittent Pringle maneuvers (IPs) remained unclear. To address this issue, a retrospective study was designed to evaluate these 2 vascular control methods during large HCC resections.

PATIENTS AND METHODS

Patients

From January 2008 to May 2012, we evaluated 656 large HCC cases in our department. This study was approved by the Ethics Committee for Clinical Pharmacology in Tongji Medical College, and all the information of patients were kept private. Large HCC was defined with a tumor diameter ≥ 5 cm. Based on the maneuvers of hepatic vascular occlusion, these patients were divided into 2 groups: IP group (n = 336) and SIO group.
The diagnoses of cirrhosis and HCC were confirmed by histological studies of the surgical specimens. The following patients were excluded from this study: patients with a history of previous liver resection, patients with other concomitant major surgical procedures, such as splenectomy, bowel resection, bile duct resection, and esophageal devascularization. Data were recruited consecutively to address potential sources of bias.

**Preoperative Evaluation**

All patients had a chest X-ray, abdominal ultrasonography, and computer tomography portography vascular imaging. Preoperative laboratory blood tests included hemoglobin, platelet count, alanine aminotransferase (ALT), aspartate amino transferase (AST), serum total bilirubin, alkaline phosphatase, γ-glutamyl transferase, cholesterol, indocyanine green retention at 15 minutes after intravenous injection, creatinine, prothrombin time (PT), fibrinogen, hepatitis B surface antigen, hepatitis C antibody, and serum alpha-fetoprotein. Child–Pugh score was used to assess hepatic function for each patient. No patient received preoperative transcatheter hepatic arterial chemoembolization treatment.

**Surgical Procedure**

All surgical procedures were accomplished by 4 experienced liver surgeons from the same department, ensuring procedures performed in a standardized manner. Intraoperative ultrasonography was routinely used in all patients to assess the number and size of the tumors, and their relation to nearby vascular structures. The hepatic parenchyma was transected using an ultrasonic scalpel. Liver resections based on segmental anatomy were performed in all patients.

In SIO group, the portal vein, proper hepatic artery, right and left hepatic arteries, and bile ducts were dissected. The hepatic artery in the tumor bearing lobe was continuously blocked with a bulldog clamp. The portal vein was encircled with a rubber tourniquet in advance. During the parenchymal transection, all vessels and bile ducts were ligated on the preserved side. Small hepatic venous bleeding was ligated or coagulated. Intermittent portal vein occlusion was tightened when more bleeding from portal vein system was encountered during transection. Finally major hepatic vein was doubly ligated and divided.

In IP group, hepatic vascular control was performed through encircling the hepatoduodenal ligament with an umbilical tape and then applying a tourniquet until the pulse in the hepatic artery disappears distally. The porta hepatis was intermittently clamped with cycles of 15 minutes of inflow occlusion followed by 5 minutes of reperfusion.

Anesthetic management was accomplished by general anesthesia, and blood loss was estimated by taking into account suction volume minus rinsing fluids. Indications for red blood

| TABLE 1. Clinical Characteristics of HCC Patients |
|-----------------------------------------------|
| Variable | Intermittent Pringle Maneuver (n = 336) | Selective Inflow Occlusion (n = 320) | P* |
|---------|-----------------------------------------|----------------------------------|----|
| Age, year | 46.4 (28–62) | 45.2 (27–61) | 0.381 |
| Sex (male%) | 285 (85%) | 284 (89%) | 0.487 |
| Hepatitis B carrier, % | 292 (87%) | 268 (84%) | 0.660 |
| HBV, log10copy/mL | 5.51 (3.13–6.82) | 4.76 (2.75–7.33) | 0.001 |
| Liver function status | | | 0.865 |
| Child–Pugh A | 240 | 224 | |
| Child–Pugh B | 96 | 96 | |
| Cirrhosis, % | 256 (76%) | 256 (80%) | 0.577 |
| Preoperative laboratory tests | | | |
| Hemoglobin, g/L | 139.0 (111–170) | 137.8 (97–167) | 0.646 |
| Platelet count, 109/L | 199.8 (11–353) | 178.4 (36–343) | 0.075 |
| ALT, U/L | 39.4 (19–87) | 43.1 (11–128) | 0.360 |
| AST, U/L | 44.4 (18–111) | 45.3 (12–96) | 0.810 |
| Albumin, g/L | 36.2 (27.7–42.1) | 37.1 (29.7–45.9) | 0.185 |
| Bilirubin, μmol/L | 14.4 (8.4–57.6) | 15.4 (5.3–27.9) | 0.509 |
| Prealbumin, mg/L | 67.2 (18–271) | 63.6 (51–298) | 0.285 |
| ALP, U/L | 105.5 (62–211) | 101.8 (40–205) | 0.541 |
| GGT, U/L | 150.3 (25–825) | 111.8 (14–576) | 0.114 |
| Cholesterol, mmol/L | 4.01 (2.44–11.56) | 3.98 (2.72–5.48) | 0.882 |
| ICG-15, % | 13.9 (5.4–26.0) | 14.3 (4.9–24.0) | 0.681 |
| Creatinine, μmol/L | 63.5 (47–81) | 61.4 (44–86) | 0.206 |
| PT, s | 11.8 (9.4–15.0) | 11.8 (10.2–13.7) | 0.894 |
| PTA, % | 102.8 (12–158) | 95.7 (67–127) | 0.054 |
| Fibrinogen, g/L | 3.72 (2.34–4.81) | 3.65 (2.57–4.81) | 0.435 |
| AFP, log10ng/mL | 2.2 (0–5) | 2.3 (0–5) | 0.797 |

Values are mean (range). AFP = alpha-fetoprotein, ALP = alkaline phosphatase, ALT = alanine aminotransferase, AST = aspartate aminotransferase, GGT = gamma glutamyl transferase, HCC = hepatocellular carcinoma, HBV = hepatitis B virus, ICG = indocyanine green retention, PT = prothrombin time, PTA = prothrombin activity.

* Student’s t-test.
† Except χ² test.
In total, 336 patients were included in IP group and 320 patients in SIO group. There was no significant difference between the 2 groups in rates of age, sex ratio, cirrhosis ratio, types of hepatectomy, and preoperative laboratory test, except hepatitis B virus (HBV) DNA level (Table 1). Hepatitis B patients were distributed homogeneously between groups.

ALT, AST, and alpha-fetoprotein were higher than normal value in both groups (Table 1).

### Clinopathological Characteristics and Type of Hepatectomy

There were no significant differences between the 2 groups regarding tumor size, patients with multiple tumors, grade of tumor differentiation, and American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC) staging system (Table 2). More than half of the patients belonged to medium differentiation and AJCC/UICC stage I. None of the patients exhibited distant metastasis. There was no significant difference in type of hepatectomy between 2 groups (Table 2).

### Influence of Type of Clamping on Postoperative Laboratory Test Results

Peak values of ALT and AST occurred on the 1st day after surgery (Figure 1). Total ALT, AST, and total bilirubin levels in IP group were significantly higher than those in SIO group, while cholesterol and fibrinogen levels in IP group were lower (Table 3). The dynamic change of transaminase, albumin, bilirubin, cholesterol, and prealbumin level on postoperative days 1, 3, 5, and 7 are shown in Figure 1. For SIO group, the cholesterol level showed an earlier increase to normal value, and the albumin level returned to baseline level on postoperative day 7. There was a significant difference in the change of prealbumin on postoperative day 5 and day 7 between 2 groups.

### Influence of Type of Clamping on Operative Parameter

The intraoperative data including operative time, ischemic duration, intraoperative blood loss, and blood transfusion are
shown in Table 4. Several patients suffered from different complications (61.9% vs 57.5%, Table 4). No patients died after the operation in any group. No patients were found to have early postoperative bleeding requiring reexploration in any of 2 groups. More than half of the patients had abdominal/subphrenic collection or pleural effusion, and only few patients suffered complications of bile leak, wound infection, or chest infection. There was no significant difference in hospital stay between 2 groups.

**Risk Factors Related to Major Complications**

Multivariate analysis confirmed that albumin, total bilirubin, HBV DNA, cirrhosis were related to postoperative complications morbidity (Table 5). The logistic regression analysis showed that 4 parameters were independent predictive factors for the development of complications (Table 6). The subgroup analysis showed that patients with moderate or severe cirrhosis, total bilirubin $>17\,\text{mmol/L}$, or HBV DNA $>10^4\,\text{copy/mL}$ in SIO group resulted in less major complication, when compared with the IP group (Table 7). However, the type of hepatic vascular occlusion had no influence on morbidity in albumin ($<35\,\text{g/L}$), albumin ($>35\,\text{g/L}$), and total bilirubin ($<17\,\text{mmol/L}$) subgroups.

**DISCUSSION**

Excessive blood loss during hepatectomy requiring perioperative blood transfusion has a negative impact on morbidity and mortality,\textsuperscript{6,20,21} particularly in patients with cirrhosis. Using modern technology, hepatic parenchymal transection can be carried out with little blood loss. A Japanese survey revealed that only a minority (7%) of surgeons never use inflow occlusion, whereas 25% apply a Pringle maneuver on a routine basis even in cirrhotic patients.\textsuperscript{22} Although inflow occlusion is not necessarily accepted as routine practice, many surgeons still prefer to use hepatic vascular inflow occlusion with, or without outflow occlusion during parenchymal transection,\textsuperscript{3,12,23,24} especially in those cirrhotic patients with irregular branches and collateral circulations of vessels.

The Pringle maneuver is sufficient in most situations to control bleeding from the hepatic artery or portal vein during hepatectomy. However, it is hard to avoid ischemic injury in the remnant liver after Pringle maneuver and may result in postoperative liver dysfunction.\textsuperscript{3,12,15,16} The degree of ischemic injury to the hepatocytes may be accentuated in the presence of underlying liver disease.\textsuperscript{25} Therefore, several strategies have been used to minimize ischemic injury during liver surgery. Makuuchi et al\textsuperscript{26} first interrupted long ischemic intervals during

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**TABLE 3. Postoperative Laboratory Test Results and Outcome Data**

| Variable | Intermittent Pringle Maneuver (n = 336) | Selective Inflow Occlusion (n = 320) | P$^*$ |
|----------|-------------------------------------|-------------------------------------|-------|
| Nadir hemoglobin, g/dL | 115.6 (21.2) | 114.9 (20.4) | 0.824 |
| Nadir platelet count, $\times 10^{3}/\mu\text{L}$ | 116.9 (51.3) | 120.2 (54.6) | 0.695 |
| ALT, U/L | Peak | 1101 (649) | 419 (262) | <0.001 |
| | AUC, per day | 539 (309) | 205 (115) | <0.001 |
| AST, U/L | Peak | 1141 (671) | 374 (204) | <0.001 |
| | AUC, per day | 410 (262) | 144 (83) | <0.001 |
| Albumin, g/L | Nadir | 28.2 (3.4) | 29.5 (5.9) | 0.097 |
| | AUC, (per day) | 31.1 (3.2) | 32.2 (4.4) | 0.064 |
| Total bilirubin, $\mu\text{mol/L}$ | Peak | 26.0 (23.7) | 17.8 (6.5) | 0.002 |
| | AUC, per day | 22.6 (16.6) | 16.5 (6.6) | 0.003 |
| Cholesterol, mmol/L | Nadir | 2.1 (0.4) | 2.6 (0.8) | <0.001 |
| | AUC, (per day) | 2.5 (0.7) | 3.0 (0.8) | <0.001 |
| Prealbumin, mg/L | Nadir | 56.4 (28.6) | 71.2 (45.0) | 0.013 |
| | AUC, per day | 90.1 (38.0) | 97.5 (47.6) | 0.270 |
| PT, s | Peak | 14.2 (1.8) | 13.7 (1.8) | 0.099 |
| | AUC, per day | 13.4 (1.7) | 13.3 (1.5) | 0.842 |
| PTA, % | Nadir | 76.7 (15.0) | 75.5 (12.6) | 0.562 |
| | AUC, per day | 82.8 (17.2) | 80.6 (13.5) | 0.364 |
| Fibrinogen, g/L | Nadir | 3.1 (1.1) | 3.3 (1.1) | 0.179 |
| | AUC per day | 3.4 (0.9) | 3.7 (1.0) | 0.035 |

Values are mean (SEM). Nadir or peak values were minimum or maximum values measured within the first 7 days after surgery. AFP = alpha-fetoprotein, ALT = alanine aminotransferase, AST = aspartate aminotransferase, AUC = area under the curve for the first 7 days after surgery, PT = prothrombin time, PTA = prothrombin activity.

$^*$ Student’s t-test.
liver resection with short periods of reperfusion in 1980s. Belghiti et al.27 RCT provided evidence that intermittent clamping of portal triad was superior to protect liver function when compared with continuous clamping. Thereafter, ischemic preconditioning was considered as an alternative to intermittent clamping and was proved to protect liver from injury.28 In addition, more than 80% of HCC patients suffer from HBV infection in China,3,4,10,11 which also contributes to a different degree of cirrhosis. For these patients, choosing an inflow occlusive maneuver during liver resection still warrants further study.

Since 1963, continuous selective inflow occlusion of the hepatic artery supplying the tumor-containing segments of liver plus intermittent occlusion of the portal vein has been applied to reduce blood loss and injury to the liver function.17 The main concern over the SIO maneuver is whether there is an increase in ischemic complications, especially when the occlusion is required for a long time. In the Cochrane review by Gurusamy et al.29 there was no evidence to support SIO over portal triad clamping. However, all trials in this review were of high risk of bias. Our data showed that intraoperative blood loss (473 vs 691 mL) and perioperative blood transfusion (11.3% vs 28.6%) in SIO group were significantly less than those in the IP group, although the ischemic duration was longer (25.2 vs 17.9 minutes). The difference might be caused, in part, by different parenchymal transection speed. Further the work of hemostasis may not be performed until the transection is finished. This was confirmed by results of blood loss and blood transfusion rates. Based on our data, liver function was less intensely influenced and recovered more quickly in SIO group when compared with IP group. This could be explained by less impairment of hepatic metabolism and synthesis function as a consequence of continuous arterial infusion of remnant liver in the SIO group.

In 2006, Clavien28 reported that the rate of overall and major (grade 3–5) postoperative complications with IP maneuver was 37.8% and 27%. In 2010, Fu et al.23 reported that overall postoperative complication and operative mortality rates for liver resection under total hepatic vascular exclusion were 53% and 2%. In this study, only 60 patients (18.8%) with SIO maneuver suffered from major postoperative complications, and no patient died in the SIO group. Four patients with hepatic insufficiency recovered and were discharged. All of these findings confirm that the SIO maneuver is safe and well-tolerated compared with the IP maneuver and total hepatic vascular exclusion.

Multiple European-based studies6,30 have confirmed that hepatitis C virus related cirrhosis, intraoperative bleeding volume, high central venous pressure, low lactate clearance, and hepatic venous pressure gradient > 10 mmHg are the main predictors for hepatic decompensation after hepatectomy, especially in patients with liver cirrhosis. Further multivariate analyses demonstrated that initial central venous pressure higher than 9 mmHg, initial HVPG higher than 10 mmHg, and intraoperative bleeding volume were independent predictors related to postoperative morbidity.6,30,31 However, there is controversy about the clinical importance of these factors in Asian countries. For instance, most HCC patients in oriental countries are HBV-infected.3,32 As Makuuchi33 and Fan34,35 revealed, selection of candidates for liver resection relies on Child–Pugh classification and indocyanine green retention at...
15 minutes retention test, while hepatic venous pressure gradient is not routinely measured and used to decide whether it is appropriate for operation or not. Therefore, we could not use these factors to evaluate the risk of postoperative complication, which is also one of the main limitations of this retrospective study. Based on our results, cirrhosis (moderate and severe), total bilirubin (>17 mol/L), albumin (<35 g/L), and HBV DNA (>10^4 copy/mL) are independent predictive factors for the development of postoperative complications. Albumin not only plays an important role in maintaining the fluid balance between the intravascular and extravascular compartments, but can also

### TABLE 4. Comparison of Operative Parameters and Outcomes of Hepatocellular Carcinoma (HCC) Patients

| Variables               | Intermittent Pringle Maneuver (n = 336) | Selective Inflow Occlusion (n = 320) | P*  |
|-------------------------|----------------------------------------|-------------------------------------|-----|
| Operative time, min     | 282 (190–410)                          | 277 (170–450)                      | 0.618 |
| Ischemic duration, min  | 17.9 (11–32)                           | 25.2 (13–50)                       | <0.001 |
| Intraoperative blood loss, mL | 691 (50–2030)                        | 473 (100–1250)                     | 0.001 |
| Transfusion requirements |                                       |                                     |     |
| Patients transfused, %  | 96 (28.6%)                             | 36 (11.3%)                          | 0.006 |
| Packets red cell, mL    | 750 (400–1200)                         | 711 (600–800)                       | 0.671 |
| Overall complications   | 208 (61.9%)                            | 184 (57.5%)                         | 0.634 |
| Grade 1                 |                                         |                                     |     |
| Wound infection         | 12                                     | 8                                   |     |
| Grade 2                 |                                         |                                     |     |
| Pleural effusions (not requiring aspiration) | 100                               | 108                                 |     |
| Peritoneal effusions    | 84                                     | 100                                 |     |
| Pulmonary problems      | 12                                     | 12                                  |     |
| Total minor complications (Grade 1 + 2) | 132 (39.3%)                         | 124 (38.8%)                         | 0.944 |
| Grade 3                 |                                         |                                     |     |
| Pleural effusions (requiring aspiration) | 64                                | 52                                  |     |
| Bilioma bile leak       | 12                                     | 8                                   |     |
| Intra-abdominal bleeding| 0                                      | 0                                   |     |
| Grade 4                 |                                         |                                     |     |
| Grade 4a (single organ dysfunction) | 4                                 | 4                                   |     |
| Grade 4b (multiorgan failure) | 0                                 | 0                                   |     |
| Grade 5                 |                                         |                                     |     |
| Death                   | 0                                      | 0                                   |     |
| Total major complications (Grade 3 + 4 + 5) | 76 (22.6%)                       | 60 (18.8%)                          | 0.541 |
| Hospital stay (day)     | 25 (18–44)                             | 25 (16–57)                          | 1.000 |

Values are mean (range or percentage).

* Student’s t-test.

† except χ² test.

### TABLE 5. Risk Factors for Major Complications According to Multivariate Analysis

| Variables               | Unstandardized Coefficients | P   |
|-------------------------|----------------------------|-----|
| Age, year               | 0.010                      | 0.865 |
| Preoperative laboratory tests |                                 |     |
| Platelet count, 10^9/L  | 0.048                      | 0.151 |
| ALT, U/L                | −0.110                     | 0.180 |
| AST, U/L                | 0.064                      | 0.459 |
| Albumin, g/L            | −0.134                     | 0.018 |
| Total bilirubin, µmol/L | 0.449                      | 0.001 |
| Cholesterol, µmol/L     | −0.008                     | 0.866 |
| Prothrombin activity, % | −0.133                     | 0.155 |
| HBV-DNA, log_{10}copy/mL | −0.140                   | 0.000 |
| TNM                     | −0.033                     | 0.565 |
| Blood loss, mL          | 0.000                      | 0.134 |
| Blood occlusion maneuvers | 0.185                   | 0.123 |
| Cirrhosis               | 0.523                      | 0.000 |

ALT = alanine aminotransferase, AST = aspartate aminotransferase, HBV-DNA = hepatitis B virus deoxyribonucleic acid.

**TABLE 6. Risk Estimate of Factors Related With Major Complications**

| Variables               | OR (95% CI)   | P   |
|-------------------------|---------------|-----|
| Cirrhosis (moderate or severe) | 67.167(21.485–209.973) | <0.001 |
| Albumin (>35 g/L)        | 0.137(0.060–0.315) | <0.001 |
| Total bilirubin (>17 µmol/L) | 6.575(2.889–14.964) | <0.001 |
| HBV-DNA (>10^6 copy/mL)  | 0.255(0.114–0.570) | 0.001 |

CI = confidence interval, HBV-DNA = hepatitis B virus deoxyribonucleic acid, OR = odds ratio.
modulate hyperinflammatory responses after surgery through scavenging free radicals and reactive inflammatory mediators in the intravascular compartment.\textsuperscript{37} Many studies\textsuperscript{38,39} have confirmed that albumin administration may improve outcomes with respect to morbidity and mortality in liver disease or hypoalbuminemia patients. So, we routinely recommend the administration of 20% albumin to correct serum levels up to 30 g/L during perioperative period.

As we know, each hepatic vascular occlusion technique has its place in liver surgery. Tumor location, underlying liver disease, the experience of the surgical, and anesthetic team should be taken into account to select the appropriate method for achieving hepatic vascular control in a given patient. Based on the findings of this study, we recommend that the SIO maneuver has superiority over the IP maneuver in terms of parenchymal tolerance to ischemia for patients with moderate or severe cirrhosis, total bilirubin (>35 g/L), albumin (<35 g/L), and HBV DNA (>10^4 copy/mL). We also recommend antiviral therapy for those patients with HBV DNA more than 500 copy/mL if needed. Recent study\textsuperscript{32} confirmed that partial hepatectomy for HBV-related HCC induced HBV reactivation in a proportion of patients. We recommend antiviral therapy for those patients with HBV DNA more than 500 copy/mL and close monitoring with HBV DNA in the perioperative period for all patients with HBV-related HCC.

As far as the limitation is concerned, it is a retrospective study with limited number of patients in a single center. Risk of bias still existed, although it was performed in a consecutively manner. A randomized clinical trial comparing infrahepatic inferior vena cava clamping with low central venous pressure in complex liver resections involving the Pringle manoeuvre. Br J Surg. 2012;99:781–788. are independent predictive factors for morbidity. For patients with moderate or severe cirrhosis, total bilirubin >17 \mu mol/L, or HBV DNA >10^4 copy/mL, SIO maneuver is preferentially recommended. We think that these conclusions may help hepato-biliary surgeons decide which maneuver to choose during hepatectomy, if occlusion is necessary.

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**REFERENCES**

1. El-Serag HB, Rudolph KL. Hepatocellular carcinoma: epidemiology and molecular carcinogenesis. Gastroenterology. 2007;132:2557–2576.
2. Arii S, Yamaoka Y, Futagawa S, et al. Results of surgical and nonsurgical treatment for small-sized hepatocellular carcinomas: a retrospective and nationwide survey in Japan. The Liver Cancer Study Group of Japan. Hepatology. 2000;32:1224–1229.
3. Zhu P, Lau WY, Chen YF, et al. Randomized clinical trial comparing infradiaphragmatic inferior vena cava clamping with low central venous pressure in complex liver resections involving the Pringle manoeuvre. Br J Surg. 2012;99:781–788.
4. Chen XP, Qiu FZ, Wu ZD, et al. Chinese experience with hepatectomy for huge hepatocellular carcinoma. Br J Surg. 2004;91:322–326.
5. Kooby DA, Stockman J, Ben-Porat L, et al. Influence of transfusions on perioperative and long-term outcome in patients following hepatic resection for colorectal metastases. Ann Surg. 2003;237:860–869discussion 869–870.
6. Jarnagin WR, Gonen M, Fong Y, et al. Improvement in perioperative and long-term outcome in patients following hepatic resection: analysis of 1,803 consecutive cases over the past decade. Ann Surg. 2002;236:397–406discussion 406–407.
7. Shiba H, Ishida Y, Wakiyama S, et al. Negative impact of blood transfusion on recurrence and prognosis of hepatocellular carcinoma after hepatic resection. J Gastrointest Surg. 2009;13:1636–1642.

**TABLE 7. Comparison of Postoperative Complications According to Different Risk Factors**

|               | Intermitent Pringle Maneuver | Selective Inflow Occlusion | χ² | P* |
|---------------|-------------------------------|----------------------------|----|----|
|               | Minor | Major | n | Minor | Major | n |    |
| Cirrhosis     |       |       |   |       |       |   |    |
| No or slight  | 128(50%) | 0(0%) | 256 | 108(39.7%) | 32(11.8%) | 272 | 0.016 |
| Moderate or severe | 4(5%) | 76(95%) | 80 | 16(33.3%) | 28(58.3%) | 48 | 0.034 |
| Albumin <35 g/L | 32(33.3%) | 48(50%) | 96 | 28(25%) | 44(39.3%) | 112 | 0.303 |
| >=35 g/L      | 100(41.7%) | 28(11.7%) | 240 | 96(46.2%) | 16(7.7%) | 208 | 0.749 |
| Total bilirubin <=17 \mu mol/L | 132(43.4%) | 44(14.5%) | 304 | 72(37.5%) | 16(8.3%) | 192 | 0.353 |
| >17 \mu mol/L | 0(0%) | 32(100%) | 32 | 52(40.6%) | 44(34.4%) | 128 | 0.004 |
| HBV-DNA <10^4 copy/mL | 0(0%) | 16(33.3%) | 48 | 48(42.9%) | 48(42.9%) | 112 | 0.001 |
| >=10^4 copy/mL | 132(45.8%) | 60(20.8%) | 288 | 76(36.5%) | 12(5.77%) | 208 | 0.009 |

\* χ² test.

HBV-DNA = hepatitis B virus deoxyribonucleic acid.
8. Kwon AH, Matsui Y, Kamiyama Y. Perioperative blood transfusion in hepatocellular carcinomas: influence of immunologic profile and recurrence free survival. Cancer. 2001;91:771–778.

9. Yamamoto J, Kosuge T, Takayama T, et al. Perioperative blood transfusion promotes recurrence of hepatocellular carcinoma after hepatectomy. Surgery. 1994;115:303–309.

10. Chen XP, Qiu FZ. A simple technique ligating the corresponding inflow and outflow vessels during anatomical left hepatectomy. Langenbecks Arch Surg. 2008;393:227–230 discussion 231–234.

11. Chen XP, Zhang ZW, Zhang BX, et al. Modified technique of hepatic vascular exclusion: effect on blood loss during complex mesohepatectomy in hepatocellular carcinoma patients with cirrhosis. Langenbecks Arch Surg. 2006;391:209–215.

12. Fu SY, Lau WY, Li GG, et al. A prospective randomized controlled trial to compare Pringle maneuver, hemihepatic vascular inflow occlusion, and main portal vein inflow occlusion in partial hepatectomy. Ann Surg. 2011;201:62–69.

13. Malassagne B, Cherqui D, Alon R, et al. Safety of selective vascular clamping for major hepatectomies. J Am Coll Surg. 1998;187:482–486.

14. Lau WY. A review on the operative techniques in liver resection. Chin Med J (Engl). 1997;110:567–570.

15. Selzner N, Rudiger H, Graf R, et al. Protective strategies against ischemic injury of the liver. Gastroenterology. 2003;125:917–936.

16. Serracino-Inglott F, Habib NA, Mathie RT. Hepatic ischemia-reperfusion injury. Am J Surg. 2001;181:160–166.

17. Xia S. An approach to the typical liver resection. J Huazhong Univ Sci Technol. 1984;13:384–387.

18. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240:205–213.

19. Rahbani NN, Mehrabi A, Mollberg NM, et al. Hepatocellular carcinoma: current management and perspectives for the future. Ann Surg. 2011;253:453–469.

20. Rahbani NN, Koch M, Mehrabi A, et al. Portal triad clamping versus vascular exclusion for vascular control during hepatic resection: a systematic review and meta-analysis. J Gastrointest Surg. 2009;13:558–568.

21. Smyrniotis V, Farantonis C, Kostopanagiotou G, et al. Vascular control during hepatectomy: review of methods and results. World J Surg. 2005;29:1384–1396.

22. Nakajima Y, Shimamura T, Kamiyama T, et al. Control of intraoperative bleeding during liver resection: analysis of a questionnaire sent to 231 Japanese hospitals. Surg Today. 2002;32:48–52.

23. Fu SY, Lau WY, Li AJ, et al. Liver resection under total vascular exclusion with or without preceding Pringle manoeuvre. Br J Surg. 2010;97:50–55.

24. Zhang J, Lai EC, Zhou WP, et al. Selective hepatic vascular exclusion versus Pringle manoeuvre in liver resection for tumours encroaching on major hepatic veins. Br J Surg. 2012;99:973–977.

25. Grace PA. Ischaemia-reperfusion injury. Br J Surg. 1994;81:637–647.

26. Makuch H, Mori T, Gunpen P, et al. Safety of hemihepatic vascular occlusion during resection of the liver. Surg Gynecol Obstet. 1987;164:155–158.

27. Belghiti J, Noun R, Malafosse R, et al. Continuous versus intermittent portal triad clamping for liver resection: a controlled study. Ann Surg. 1999;229:369–375.

28. Petrowsky H, McCormack L, Trujillo M, et al. A prospective, randomized, controlled trial comparing intermittent portal triad clamping versus ischemic preconditioning with continuous clamping for major liver resection. Ann Surg. 2006;244:921–928 discussion 928–930.

29. Gurusamy KS, Sheth H, Kumar Y, et al. Methods of vascular occlusion for elective liver resections. Cochrane Database Syst Rev. 2009:CD007632.

30. Bruix J, Castells A, Bosch J, et al. Surgical resection of hepatocellular carcinoma in cirrhotic patients: prognostic value of preoperative portal pressure. Gastroenterology. 1996;111:1018–1022.

31. Melendez JA, Arslan V, Fischer ME, et al. Perioperative outcomes of major hepatic resections under low central venous pressure anesthesia: blood loss, blood transfusion, and the risk of post-operative renal dysfunction. J Am Coll Surg. 1998;187:620–625.

32. Huang G, Lai EC, Lau WY, et al. Posthepatectomy HBV reactivation in hepatitis B-related hepatocellular carcinoma influences post-operative survival in patients with preoperative low HBV-DNA levels. Ann Surg. 2013;257:490–505.

33. Orii R, Sugawara Y, Hayashida M, et al. Effects of amrinone on ischaemia-reperfusion injury in cirrhotic patients undergoing hepatectomy: a comparative study with prostaglandin E1. Br J Anaesth. 2000;85:389–395.

34. Fan ST, Mau Lo C, Poon RT, et al. Continuous improvement of survival outcomes of resection of hepatocellular carcinoma: a 20-year experience. Ann Surg. 2011;253:745–758.

35. Fan ST, Lo CM, Liu CL, et al. Hepatocytectomy for hepatocellular carcinoma: toward zero hospital deaths. Ann Surg. 1999;229:322–330.

36. Yang J, Wang WT, Yan LN, et al. Alternatives to albumin administration in hepatocellular carcinoma patients undergoing hepatectomy: an open, randomized clinical trial of efficacy and safety. Chin Med J (Engl). 2011;124:1458–1464.

37. Wiedermann CJ. Colloidal and pharmacological activity of albumin in clinical fluid management: recent developments. Curr Drug Ther. 2006;1:319–328.

38. Vincent JL, Dubois MJ, Navickis RJ, et al. Hypoalbuminemia in acute illness: is there a rationale for intervention? A meta-analysis of cohort studies and controlled trials. Ann Surg. 2003;237:319–334.

39. Haynes GR, Navickis RJ, Wilkes MM. Albumin administration—what is the evidence of clinical benefit? A systematic review of randomized controlled trials. Eur J Anaesthesiol. 2003;20:771–793.