Application of vascular exclusion and blood vessel repair in the resection of hepatoblastoma

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Abstract: Background: Hepatoblastoma (HB) is the most common liver cancer in children and accounts for 1% of all pediatric malignancies. We investigated the effect of different methods of vascular exclusion and blood vessel repair during HB surgery. **Methods:** We retrospectively reviewed the records of 83 children with HB who underwent tumor resection in our hospital from September 2005 to September 2012, and were given different methods of vascular exclusion and blood vessel repair or vessel ligation during surgery. **Results:** The Pringle maneuver was performed for 21 cases, the mean blood loss was 31.10 ± 3.88 mL (range: 25 to 40 mL), and the 24-month survival was 85.6%. Hemihepatic vascular clamping was performed for 20 cases, the mean blood loss was 36.65 ± 5.26 mL (range: 25 to 45 mL), and the 24-month survival was 80.0%. Total hepatic vascular exclusion was performed for 24 cases, the mean blood loss was 25.83 ± 3.75 mL (range: 20 to 36 mL), and the 24-month survival was 75.0%. Hepatic vascular exclusion with preservation of the caval flow was performed for 18 cases, the mean blood loss was 19.78 ± 3.81 mL (range: 14 to 26 mL), and the 24-month survival was 61.1%. In 48 cases, the tumor location was complicated and close to the major intrahepatic vessels. In 18 cases, the affected liver segments and blood vessels were removed simultaneously. In 30 cases, the affected blood vessels and normal liver parenchyma were preserved and the injured blood vessels were repaired. **Conclusion:** Appropriate application of hepatic vascular exclusion and intrahepatic blood vessel repair allows for more widespread use of surgery for hepatoblastoma, prevents postoperative liver failure, and ensures favorable intraoperative and postoperative outcomes.

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Introduction

Hepatoblastoma (HB) is the most common liver cancer in children and accounts for 90% of all pediatric liver malignancies and 1% of all pediatric malignancies. Surgery is the preferred and most effective treatment for HB. The suitability of *en bloc* resection is a major determinant for the prognosis of patients with HB,[1] but this surgery can be difficult and is associated with postoperative complications. There are only rare reports describing the methods of vascular exclusion and blood vessel repair during the surgical resection of pediatric HB.

We performed surgical resection of 83 children with HB from September 2005 to September 2011 and retrospectively analyzed the methods of vascular exclusion and blood vessel repair during the surgery.

Materials and Methods

Clinical data

Eighty-three children (47 males, 36 females; mean age: 56.59 ± 23.16 months; age range: 1 month to 107 months) with HB were treated in the Department of Pediatric Surgery of the First Affiliated Hospital of Zhengzhou University (Henan, China) from September 2005 to September 2012. All patients underwent surgical treatment and pathological examination for confirmation of diagnosis.

There was an abdominal mass in 43 cases, vomiting and anorexia in 15 cases, abdominal pain and distension in 8 cases, jaundice in 3 cases, and the tumor was found by physical examination in 14 cases. Computed tomography (CT) indicated that the tumor was in the left lobe or right lobe of the liver in 22 cases, in both lobes in 2 cases, close to the first porta hepatis in 11 cases (including 2 cases with tumor thrombosis), close to or invading the second porta hepatis or third porta hepatis in 26 cases, and invading the inferior vena cava and containing tumor thromboses in 4 cases. According to the International Society of Pediatric Oncology (SIOP) staging system, 9 cases were stage I, 13 cases were stage II, 28 cases were stage III, and 34 cases were stage IV. The mean tumor diameter was 12.51 ± 4.77 cm (range: 2.5 to 22 cm).

Grouping and methods

The patients were divided into four groups according to the method used for vascular exclusion (Figure 1).

Group I: Pringle maneuver. The hepatoduodenal ligament was isolated and blocked by a band. Before blocking, the presence of abnormalities in the left and right hepatic arteries was confirmed. This method is effective when the right hepatic artery comes from the superior mesenteric artery (traveling within the hepatoduodenal ligament). The left hepatic artery should be blocked separately when it comes from the left gastric artery (traveling outside the hepatoduodenal ligament).

Group II: Hemihepatic vascular clamping. The first porta hepatis was dissected and the left and right hepatic arteries and the left and right branches of the portal vein were isolated. Blood flow to the affected half of the liver was blocked selectively. The gallbladder can be removed and the gallbladder triangle can be dissected before isolating the right branch of the portal vein to expand the surgical field.

Group III: Total hepatic vascular exclusion (THVE). The first porta hepatis, the subhepatic inferior vena cava superior to the right adrenal vein, and the suprahepatic inferior vena cava were isolated and blocked sequentially. Blocking was released in the reverse order.

Group IV: Hepatic vascular exclusion with preservation of the caval flow (HVEPC). The hepatic vein was dissected and blocked at the first and second porta hepatis. The right hepatic vein and the combined trunk of the middle and left hepatic veins were blocked sequentially.

Application of blocking methods

Table 1 summarizes the different blocking methods used for the 83 cases. The Pringle maneuver was used when HB lesions were in the right lobe, left lobe, segment IV, or segment V of the liver, with no direct invasion to the first porta hepatis, and the hepatectomy was thought to be simple. Hemihepatic vascular clamping was used when large HB lesions compressed or covered the major intrahepatic vessels, the tumor lesion exceeded half of the volume of the liver (with a small residual liver), and preoperative evaluation indicated that surgery would be difficult and the need for long-duration of blood flow blocking. THVE was used when the tumor was close to or invaded the main trunk of the hepatic vein or the inferior vena cava and contained a tumor thrombosis. HVEPC was used when the tumor was close to the intrahepatic major vessels but did not directly invade and/or compress the main trunk of the hepatic vein or the inferior vena cava.

Management of intrahepatic blood vessels during the hepatectomy for stage III and IV tumors

In 48 cases (58%), the tumor compressed or covered more than two major vessels inside and outside the liver, induced deformity and displacement of the affected vessels, and the tumor lesion was larger than 50% of the liver volume. According to the SIOP staging system, these tumors were stage III or IV. During surgery, two different methods were applied to affected vessels of these patients. Routine hepatectomy was used in 18 cases (vessel-ligation group), in which blood flow to the liver was blocked, and then the affected intrahepatic major vessels were ligated and removed together with the tumor and the affected liver lobe/parenchyma. Vessel-preservation was used in 30 of these cases (vessel-repair group), in which the affected intrahepatic major vessels were dissected and preserved together with normal liver lobe/parenchyma and the injured major vessels were repaired.

Results

We performed routine laboratory examinations every two days from the first day after surgery. Blood tests, measurement of serum electrolytes, and liver function tests were performed at 6 AM. After 3 days, liver function tests were performed every 3-5 days. Recovery of liver function was defined by the presence of normal levels of aspartate transaminase, albumin, and direct bilirubin.

Table 2 compares the surgical characteristics and outcomes of patients who were given different methods of vascular exclusion during surgery. Patients in Group I (Pringle maneuver) had the shortest exclusion time (14.67 ± 3.94min), shortest surgery time (69.57 ± 10.50 min), and best 24-month survival rate (85.6%). Patients in Group IV (HVEPC) had the longest surgery time (151.11 ± 20.48 min), the least amount of intra-operative blood loss (19.78 ± 3.81 mL), the longest duration for post-operative recovery of liver function (23.50 ± 2.53 days), and the worst 24-month survival rate (61.1%).

Table 3 compares surgical characteristics and outcomes of stage III and IV HB patients who were given vessel ligation or vessel repair during surgery. In the vessel-ligation group, 8 patients who underwent palliative resection died of metastasis within 3 months after surgery. Among 10 patients who underwent *en bloc* resection, 1 patient died of postoperative liver failure, 2 patients rejected postoperative chemotherapy after discharge and died of metastasis within 6 months after surgery, and 7 patients underwent standard chemotherapy. A total of 22.2% of these patients survived for 24 months after surgery. In the vessel-repair group, all 30 patients were discharged after full recovery. Three of these patients rejected postoperative chemotherapy and died of recurrence and metastasis within 12 months after surgery. The remaining 27 patients underwent standard chemotherapy. A total of 76.7% of these patients survived for 24 months after surgery.

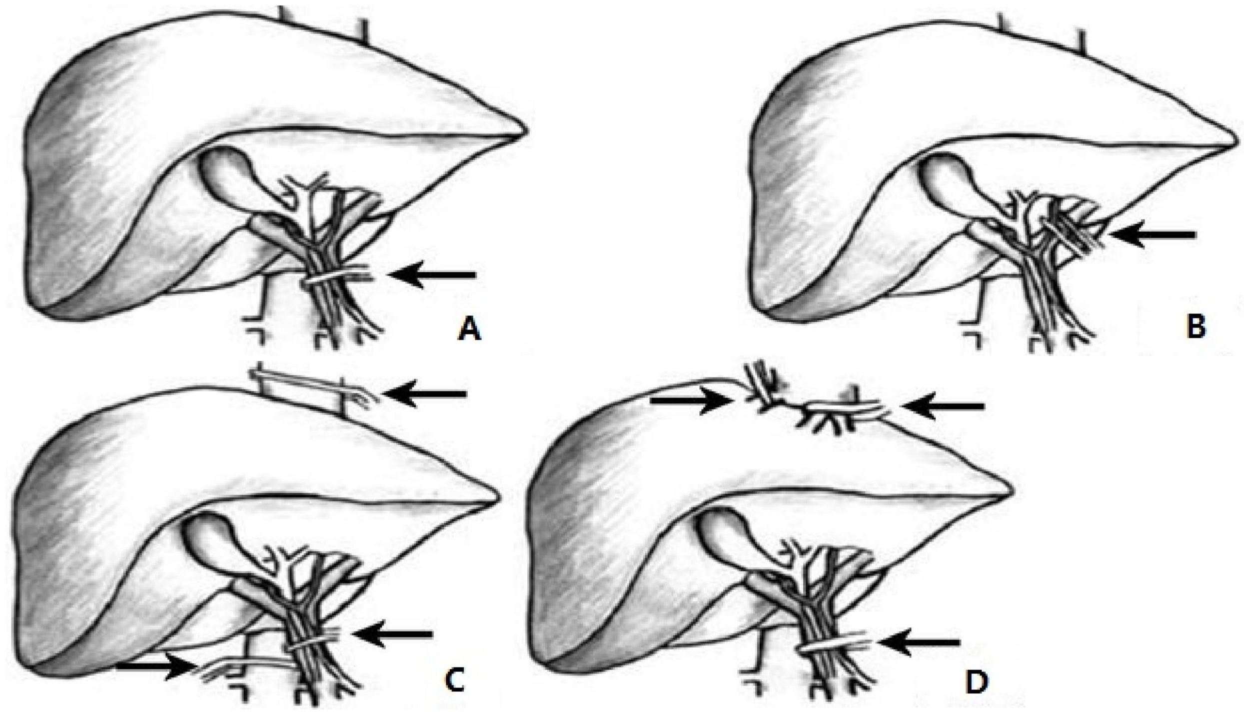

Figure 1. Methods of vascular exclusion used during surgery of hepatoblastoma patients. Arrows indicate the location of blocked vessels. A, Pringle maneuver. The portal vein and the hepatic artery are blocked in the first porta hepatis. B, Hemihepatic vascular clamping. The left hepatic artery and the left branch of the portal vein are blocked. C, Total hepatic vascular exclusion (THVE). The portal vein, the hepatic artery, the suprahepatic inferior vena cava and the subhepatic inferior vena cava are blocked. D, Hepatic vascular exclusion with preservation of the caval flow (HVEPC). The portal vein and hepatic artery in the first porta hepatis, the right hepatic vein and the combine trunk of the left and middle hepatic veins in the second porta hepatis are blocked.

Table 1. Characteristics of hepatoblastoma patients who were given different methods of vascular exclusion during surgery.

	Group I	Group II	Group III	Group IV	Total
Left or right lobes of the liver	13	9	—	—	22
Huge type	—	11	—	—	11
Close to or compressing the first porta hepatis	8	—	—	12	20
Close to or compressing the second and third porta hepatis	—	—	20	6	26
Invading the inferior vena cava and containing tumor thrombosis	—	—	4	—	4
Total	21	20	24	18	83

Table 2. Characteristics of the surgery and outcomes of HB patients who were given different methods of vascular exclusion during surgery.

	Group I	Group II	Group III	Group IV
Exclusion time (min)	14.67±3.94	32.90±6.45	20.63±4.99	24.67±4.54
Operative time (min)	69.57±10.50	102.60±13.51	120.83±17.24	151.11±20.48
Surgical blood loss (mL)	31.10±3.88	36.65±5.26	25.83±3.75	19.78±3.81
Postoperative stay (days)	17.71±3.77	15.05±2.52	24.38±3.05	19.94±3.42
Duration for postoperative recovery of liver function (days)	20.19±4.57	12.95±2.19	20.21±2.99	23.50±2.53
Survival rate at 24 months after surgery	85.6%, 18/21	80.0%, 16/20	75%, 18/24	61.1%, 11/18

Table 3. Characteristics stage III and IV HB patients who were given vessel ligation or vessel repair during surgery.

	Vessel ligation (18 cases)	Vessel repair (30 cases)	*P*
Rate of *en bloc* resection	55.6% (10/18)	100% (30/30)	—
Rate of discharge with full recovery	50% (9/18)	100% (30/30)	—
Postoperative length of stay in patients with complete recovery (days)	20.50±3.71	17.80±4.09	$p<0.05$
Duration for liver function recovery in patients with complete recovery (days)	25.72±2.47	17.23±4.42	$p<0.05$
Survival rate at 24 months in patients who underwent postoperative standard chemotherapy	57.1% (4/7)	85.2% (23/27)	—
Total survival rate at 24 months after surgery	22.2% (4/18)	76.7% (23/30)	—

Discussion

HB usually presents as a single lesion (83%), but is occasionally composed of multiple nodules. Generally, the boundary of the tumor is clear and there is a membrane covering. Previous research indicated that the lesion may occur in the right lobe (48-58%), the left lobe (15%-22%), or in both lobes simultaneously (27%-29%).[3] During tumor resection, bleeding can occur during *(i)* isolation of the liver, *(ii)* dissection of blood vessels and the biliary tract in the porta hepatis, or *(iii)* cutting off of the liver parenchyma. Reducing the central venous pressure (CVP), application of special instruments (such as an ultrasonic scalpel), and blocking liver blood flow[2] can effectively decrease blood loss. Vascular exclusion is mainly used to control bleeding during the stage when liver parenchyma are cut off.

The Pringle maneuver is the simplest and most widely used of the four methods described here[4] because the surgery time is the shortest and intraoperative bleeding can be effectively controlled. This method can be used during relatively simple hepatectomies for removal of HB lesions in the left or the right lobe of the liver, or in segment IV and V of the liver in which there is no invasion of the first porta hepatis. Ischemia-reperfusion injury is the major shortcoming of this technique, especially for patients with cirrhosis. Although HB patients generally do not have cirrhosis, the duration of blood flow blockage should be strictly controlled to reduce liver injury and failure. Previous research reported that 60 min is the safe time limit for persistent liver blocking in adults,[5] and that the safe time limit for children is 40 min[6].

In the present study, we treated 21 patients by the Pringle maneuver (Group I) and used persistent blocking for 8-35 min in 18 of these patients. The other 3 cases had tumors in segment IV and V, so surgery was more difficult and the duration of surgery was longer. Thus, in these 3 patients blocking was carried out twice at 5 min intervals and the total blocking duration was less than 40 min. Postoperative recovery of liver function was satisfactory in all 3 of these patients. The Pringle maneuver does not block all liver blood flow, and bleeding from the hepatic vein can still occur during exclusion. Therefore, low central venous pressure (LCVP) should be applied. After ensuring the absolute blood volume, intraoperative fluid infusion should be controlled strictly, patient position can be adjusted, and vasoactive drugs (nitroglycerin, dopamine, etc.) can be used to reduce the effective circulating blood volume and expand the peripheral blood vessels for reduction of bleeding when cutting off the liver parenchyma. A previous report showed that these methods were effective[7]. In the current study, we placed our patients in the Trendelenburg position (with the feet higher than the head by 15°) during surgery to reduce CVP, decrease use of vasoactive drugs, and prevent air embolism. None of our patients experienced air embolism.

Hemihepatic vascular clamping can block hepatic blood inflow to the ipsilateral side, retain arterial inflow and venous outflow of the normal liver segment/tissue, reduce blood stasis of the mesentery/bowel and high venous pressure, and sustain hemodynamic stability. Among our four groups of patients, exclusion time was the longest, postoperative recovery of liver function was faster and duration of post-surgical hospital stay was longest in this group (Group II). In the current study, 20 patients had lesions in the left or right lobe, and we determined before surgery that the surgery might be difficult and the duration of vascular exclusion would be long. Thus, we used hemihepatic vascular clamping for these patients (Group II). In this procedure, we dissected and blocked the ipsilateral arteries and branches of the portal vein and performed careful resection of the ipsilateral tumor after a clear boundary appeared on the liver surface due to ischemia. This prevented ischemic injury to normal liver tissue and maximally preserved residual liver and its peripheral major blood vessels. Surgery was successful in all 20 patients, and postoperative recovery of liver function was satisfactory. However, it can be difficult and risky to dissect blood vessel branches at the first porta hepatis, and the surgery time is longer than for the Pringle maneuver. There are communicating branches between the unblocked and blocked sides during this procedure, so this group had the greatest surgical blood loss, even though LCVP was applied during surgery. Previous publications[9-10] reported that the outcome of *en block* hemihepatectomy after simultaneous blocking of the arterial inflow and venous outflow of the ipsilateral half liver was satisfactory, consistent with our results. Further studies are needed for verification.

All blood flow to the liver is blocked during the THVE (Group III) and HVEPC (Group IV), but the vena cava is blocked only during THVE. Thus, THVE is usually used when the tumor is close to or invading the main trunk of the hepatic vein or the vena cava, and especially when the vena cava contains a tumor thrombosis. HVEPC is mainly used for tumors closely associated with the intrahepatic major vessels, especially when there is a high risk of dissecting blood vessels from the tumor.

In group III, the first porta hepatis was blocked first, the short hepatic vein was managed, blocking bands were used for the superior and inferior vena cava, and hepatectomy was then performed. The vena cava was blocked when the procedure progressed to the second porta hepatis. These tumors were all completely dissected. If a tumor thrombosis was inside the vena cava, the vena cava was cut open, the thrombus was removed, and the vena cava was then closed by continuous suture. Before tying the knot, the blocking band was relaxed to allow blood flow into the vena cava to prevent air thrombosis.

In group IV, a blocking band was placed in the first porta hepatis, the short hepatic vein was managed, and the right hepatic vein and combined trunk of the left and middle hepatic veins in the second porta hepatis were dissected. Then, the first and second porta hepatis were blocked, the tumor lesion was dissected, small vascular branches to the tumor were ligated, and the injured major blood vessels were repaired. In group III, all liver blood flow was blocked, so blood loss was less than in groups I and II. However, there was still bleeding from the vena cava. Moreover, ischemia-reperfusion injury of normal liver tissue was inevitable, so the duration of the postoperative hospital stay and time needed for recovery of liver function were relatively long in this group. In group IV, all liver blood flow was completely blocked, and the vena cava was isolated to prevent subsequent bleeding. Therefore, this group had the least amount of intraoperative bleeding. The THVE procedure restricts reflux of the inferior vena cava, greatly affects systemic hemodynamics, and controls blocking time to less than 25 min. In contrast, HVEPC requires dissection of the main trunk of the hepatic vein, and is a more difficult procedure. Thus, the duration of surgery was greatest for Group IV patients. However, in the HVEPC procedure the inferior vena cava remained unobstructed and the systemic hemodynamics was relatively unaffected, so the duration of postsurgical hospital stay and time needed for recovery of liver function were shorter for group III.

Recently, HB patients with stage III or IV disease have been treated by surgical resection following chemotherapy. For example, a previous report indicated that 2-4 courses of chemotherapy before surgical resection may improve the rate of surgical resection[11]. However, it is difficult to identify the pathological type of the tumor before chemotherapy. Liver aspiration biopsy destroys the integrity of the tumor membrane and the tumor cells can move along the punctured tract to other sites, laparoscopic or open biopsy may cause excessive trauma, and chemotherapy is not effective for all cases[12], which may delay surgery. Moreover, after chemotherapy there is severe adhesion between the lesion and peripheral tissue and there is no clear boundary between the lesion and normal tissue, so tumor recurrence can occur at the surgical margin. It is also possible that distant metastasis may occur due to the transfer of tumor cells inside the necrotic tumor thrombus formed after chemotherapy[13].

It was previously believed that huge HB lesions invading major blood vessels including the inferior vena cava, the main trunk of the hepatic vein, and the portal vein were unresectable. However, *en bloc* resection of these complicated HB lesions has become possible with the development of better surgical technique[14]. In particular, a previous report indicated successful resection in 23 children with HB tumors that involved the porta hepatis.[15] In the current study, there were 48 cases with stage III/IV lesions closely related to the intrahepatic major vessels. Among these patients, the duration of hospital stay, time needed for recovery of liver function, and postoperative survival rate were all significantly better in the vessel-repair group than the vessel-ligation group. For patients in the vessel-repair group, the injured blood vessel was repaired after *en bloc* tumor resection and the affected blood vessels were preserved to ensure blood supply to the residual liver. This allowed maximal preservation of normal liver tissue and enhancement of liver regeneration, and thereby prevented liver failure due to the presence of a small amount of functional liver during the perioperative period. For patients in the vessel-ligation group, the volume of postoperative residual liver was small and some of the normal liver parenchyma were destroyed. This caused the liver to become an “invalid residual liver” and the liver function decreased greatly, recovery was slow, and perioperative liver failure occurred in some cases.

Summing up, selective application of different hepatic vascular exclusion techniques can decrease blood loss during hepatectomy, increase the safety of surgical resection, and allow more widespread use of surgery for HB. In addition, selective application of hepatic vascular exclusion techniques can preserve the intrahepatic major vessels, prevent postoperative liver failure, and ensure satisfactory intraoperative and postoperative safety.

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