Risk Factors Associated with Major Intraoperative Blood Loss in Hepatic Resection for Hepatobiliary Tumor

Boonchoo Sirichindakul MD*, Rawisak Chanwat MD*,
Bunthoon Nonthasoot MD*, Jade Suphapol MD*, Supanit Nivatvongs MD*

** Department of Surgery, Faculty of Medicine, Chulalongkorn University*

Background and Purpose: *Hepatic resection is the mainstay treatment of hepatobiliary tumor. Nowadays, mortality is less than 6%. However, morbidity is still high. Bleeding is one of the most common problems during hepatic resection which can sometimes lead to catastrophe. The purpose of the present study was to investigate the risk factors associated with major blood loss during hepatic resection for hepatobiliary tumor.*
Material and Method: *A total of 69 consecutive patients who underwent elective hepatic resection for hepatobiliary tumor from May 2002 to April 2004 were enrolled into this retrospective study.The Patients were divided into 2 groups(group I and II) according to the intraoperative blood loss. Patients who had a blood loss of more than 1,000 ml were defined as the major blood loss group(groupI). Thirteen variable factors were analyzed to determine the risk of major intraoperative blood loss. Operative outcomes between the two groups were also compared.*
Results: *Of the sixty-nine patients, 36 patients were in group I and 33 patients were in group II. 75% of the patients in group I and 36.4% of the patients in group II were transfused. Median blood transfusion in group I and II were 3 and 0 units of packed red cell. Univariate analysis showed tumor size, extent of hepatic resection , tumor pathology and operative time were factors affecting major intraoperative blood loss. However, multivariate analysis showed only operative time and tumor size to be independent risk factors. Patients in group I had higher surgical morbidity and prolonged hospital stay compared with patients in group II.*
Conclusion: *Blood loss is still a major concern in performing hepatic resection. From the present study, tumor size and operative time are the independent factors affecting major intraoperative blood loss. Proper screening or a surveillance program may enhance the chance to find small tumors. Refined operative techniques such as anterior approach and liver hanging would facilitate resection for large right sided tumors.*

Keywords: *Liver neoplasm, Hepatectomy, Blood transfusions*

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Hepatic resection is now accepted as the standard treatment for most benign and malignant liver tumors.The mortality rate is currently less than 6%[1,2]. However, morbidity is still high. One of the major concerns in performing hepatic resection is bleeding during the operation. Hemorrhage can occur in any phase of the operation such as hilar dissection , liver mobilization and parenchyma transection. Major hemorrhage during hepatic resection not only increases morbidity which can sometimes lead to death but also reduces the patient's overall survival. To reduce the risk of operative hemorrhage is still challenging especially in complex hepatic resection. The aim of the present study was to review the factors affecting major blood loss during hepatic resection and discuss the strategy to overcome or reduce this condition.

Correspondence to : Nivatvongs S, Department of Surgery, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand. Phone: 0-2256-4117, E-mail: Supanit.N @chula.ac.th

Material and Method

The 69 consecutive patients who underwent elective hepatic resection for hepatobiliary tumors in our unit from May 2002 to April 2004 at King Chulalongkorn Memorial Hospital were enrolled into the present study. There were 31 males and 38 females. Mean (±SD) age was 56 (±14) years (range 19-78). Hepatic resection was performed for primary liver cancer in 40 cases, liver metastasis in 21 cases and benign tumors in 8 cases. Blood loss during hepatic resection was estimated as the sum of blood absorbed by surgi-

cal swabs and the amount recorded in suction units at the end of the operation. Intraoperative blood transfusion, defined as the number of units of packed red cells transfused during the operation or in the immediate postoperative period, was judged necessary by anesthesiologists according to the patients' condition as dictated by intraoperative monitoring of vital signs, hemoglobin level, urine output and blood gases. The criteria were to transfuse the amount necessary to maintain normal vital signs and to replace hematocrit up to 30%.

Hepatic resection was defined as extended when 5 or more Couinaud's segments were removed. A major resection was when 3 or 4 segments were removed and minor resection when 2 segments or less were removed[3]. The procedures were performed under Pringle's maneuver liberally and hepatic parenchymal transection was done by clamp fracture technique. Hemorrhage was controlled by electrocautery, argon beam coagulator and suture ligation.

Patients were divided according to the intraoperative blood loss into major blood loss group (group I) when the loss was more than 1000 ml and minimal blood loss group (group II) when the loss was 1000 ml or less. The following data were analyzed by univariate analysis to determine the risk factors of major intraoperative blood loss: gender, age, cirrhosis, tumor size, tumor pathology, type of resection, preoperative values of hemoglobin concentration, platelet count, prothrombin time: INR ratio, serum bilirubin concentration, intraoperative CVP level, Pringle maneuver and operative time. For patients bearing more than one tumor, the largest one was taken into account for the calculation of the mean tumor diameter. Operative outcomes between the two groups were also compared. Statistically significant factors tested by univariate analysis were studied further by multivariate analysis.
Statistical analysis

Data analysis was performed using the SPSS program. In a univariate analysis, qualitative variables were compared by the chi-square test meanwhile quantitative variables were expressed as mean ($\pm$SD) and compared by the Student's t test except bilirubin for which Mann-Whitney test was employed. The multivariate analysis used the stepwise logistic regression. $P< 0.05$ was determined as statistical significance.

Results

Of the sixty- nine patients, 36 patients (52%) were in group I and 33(48%) were in group II. Twenty-seven patients(75%) in group I and 12 patients (36.4%) in group II were transfused respectively. Median (min-max) blood loss and blood transfusion in group I were 1500 (1000-5500) ml and 3 (0-10) units of packed red cells. Meanwhile, median (min-max) blood loss and blood transfusion in group II were 400 (100-800) ml and 0 (0-3) unit. For both groups, median (min-max) blood loss was 1000 (100-5,500) ml and blood transfusion was 1 (0-10) unit. In the postoperative period, no patient was transfused.

The results of univariate analysis of risk factors associated with major intraoperative blood loss are listed in Table 1. Tumor size, extent of hepatic resection, tumor pathology and operative time were significant risk factors of major intraoperative blood loss.

Preoperative hemoglobin level, preoperative liver functions (bilirubin, prothrombin time: INR), Pringle maneuver and intraoperative CVP had no effect on major intraoperative major blood loss. The multivariate analysis showed tumor size and operative time were independently correlated with major blood loss ($P<0.05$).

Operative outcomes between the two groups were compared. In group I , 75 % of patients were transfused. Meanwhile 36% of patients in group II were transfused. ICU stay in both groups was not statistically different but hospital stay in group I was longer significantly. Patients in group I had more morbidity than patients in group II as shown in Table 2.

Discussion

Blood loss is one of the major concerns in performing hepatic resection. The adverse sequelae of transfusion in patients with liver a tumor undergoing hepatic resection are well known[5-8]. Blood transfusion has been proposed to be associated with poor disease free and shortened overall survival rate[6-8]. The presented data showed that patients with major intraoperative blood loss had more surgical morbidity and prolonged hospital stay.

In specialized centers, the rate of the blood transfusion is less than 30 %[9, 10]. In the present study, 56.5 % of patients were transfused. This high number might reflect a lower threshold to transfuse. In group II , there were 3 patients who received 3 units of packed red cells (data not shown). However, median volume of blood transfusion in both groups was 1 unit of packed red cells.

An important step to improve the outcome of hepatic resection is to minimize blood loss. Careful preoperative evaluation especially of liver functions is

Table 1. Results of univariate analysis for qualitative and quantitative variables

Variables	Group I (n=36)	Group II (n=33)	p value
Age: year (SD)	57.4 (12)	54.6 (15)	0.40[a]
Gender: n (%)			0.06[b]
Male	20 (55.6)	11 (33.3)	
Female	16 (44.4)	22 (66.7)	
Tumor size: cm (SD)	8.2 (5.4)	5.4 (3.6)	0.015[a]
Cirrhosis: n (%)	5 (13.9)	3 (9.1)	0.53[b]
Operation: n (%)			0.002[b]
Major	12 (33.3)	9 (27.3)	
Minor	11 (30.6)	22 (66.7)	
Extended	13 (36.1)	2 (6.1)	
Tumor pathology:n (%)			0.04[b]
Primary	26 (72.2)	14 (42.4)	
Metastasis	8 (22.2)	13 (39.4)	
Benign	2 (5.6)	6 (18.2)	
Hemoglobin: g/dl (SD)	12.4 (1.6)	12.3 (3.1)	0.89[a]
Platelet count: $*10^3$ /L (SD)	285 (133)	262 (95)	0.43[a]
INR (SD)	1.04 (0.2)	1.04 (0.2)	1.0[a]
Bilirubin: mg% (SD)	1.4 (2.0)	0.89 (0.66)	0.244[c]
Pringle maneuver:no. (%)	29 (81)	24 (73)	0.628[b]
CVP:cmH_2O (SD)	10.9 (3.8)	10.2 (3.4)	0.45[a]
Operative time: hour (SD)	6.7 (2.6)	4.3 (1.6)	0.0[a]

a: t test , b: chi square test , c: Mann-Whitney U test

Table 2. Comparing operative outcomes between two groups

Outcome	Group I	Group II	p value
Transfusion: n(%)	27 (75)	12 (36.4)	
Hospital stay: days (SD)	32.3 (30.2)	16.8 (9)	0.006
ICU stay: days (SD)	3.4 (7)	1.2 (0.8)	0.08
Postoperative complication[a]:n (%)			0.008
grade 0	15 (44.1)	25 (75.8)	
grade I	4 (11.8)	3 (9.1)	
grade II	7 (20.6)	2 (6.1)	
grade III	8 (23.5)	3 (9.1)	
grade IV	0 (0)	0 (0)	
grade V	0 (0)	0 (0)	

[a] : Grading system of postoperative complication[4]

Grade 0 : no complication

Grade I : requiring no intervention or minor intervention such as oral antibiotics ,bowel rest or basic monitoring

Grade II : requiring moderate intervention such as intravenous medication, TPN, prolonged tube feeding, or chest tube insertion

Grade III : requiring hospital readmission, surgical intervention or radiologic intervention

Grade IV : producing chronic disability, organ resection, or enteral diversion

Grade V : death

the first step to select the patients for surgery. The authors' policy is to improve or correct liver dysfunction before resection by all possible means such as nutrition support, biliary drainage in obstructive jaundice and infection control. This might explain why preoperative liver functions in the present study had no effect on major intraoperative blood loss. Tumor size, type of tumor pathology were the preoperative factors that influenced the major intraoperative blood loss from univariate analysis. Type of operation, operative time

were also the risk factors for major intraoperative blood loss. The relationship between the larger size of the tumor, the greater complexity of the procedure and longer operative time was confirmed by multivariate analysis which showed only tumor size and operative time as the independent risk factors associated with major intraoperative blood loss.

Bleeding can occur in any phase of hepatic resection such as hilar dissection, liver mobilization and parenchymal transection. With advances in technology many new instruments are available to help minimizing blood loss during hepatic resection. However, The authors find the technique of clamp fracture and electrocautery highly satisfactory. Data from Makuuchi et al[11] did not demonstrate any difference in blood loss using sophisticated instrument compared to clamp fracture during hepatic resection.

From the present study, it appears that the strategy to reduce blood loss during hepatic resection for the large tumor rests upon good screening or surveillance program and refined operative techniques. The first policy is to detect earlier and hence smaller tumors which can be treated by nonoperative management such as radiofrequency ablation. If surgery is indicated for these tumors, it can be performed in relative safety due to small sizes. It is prudent to follow up the chronic hepatitis B or C patients by ultrasonography and alpha-fetoprotein every 3-6 months. For metastatic tumors especially from colorectal cancer, screening ultrasonography and monitoring of CEA level may detect tumors early when surgical resection can be performed safely. The second policy concerns the operative approach for large right sided tumors. Exposure for large right sided tumor is sometimes limited. Liver mobilization for such tumors not only causes tumor rupture but also increases the chance of injury to the short hepatic vein and IVC. There are many ways to facilitate resection of a large right sided tumor. Extension of the abdominal incision into the thoracoab dominal approach[12] can lead to better exposure. Anterior approach during parenchymal transaction[13] before liver mobilization and liver hanging[14] are the alternative techniques to manage this tumor.

In conclusion, minimizing blood loss during hepatic resection is an important step to achieve better outcome. Tumor size and operative time are the independent risk factors affecting major intraoperative blood loss. Proper screening or a surveillance program for patients with chronic hepatitis B or C and for patients with colorectal cancer to detect smaller tumors and refinement of operative technique are the strategy to overcome these risks.

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ปัจจัยที่มีผลต่อการเสียเลือดในการผ่าตัดตับของเนื้องอกระบบทางเดินน้ำดีและตับ

บุญชู ศิริจินดากุล, ระวิศักดิ์ จันทร์วาสน์, บัณฑูร นนทสูติ, เจษฎ์ ศุภผล, สุภนิติ์ นิวาตวงศ์

ผู้รายงานได้ศึกษาถึงปัจจัยที่มีผลต่อการเสียเลือด และให้เลือดในผู้ป่วยที่ได้รับการผ่าตัดตับ ของเนื้องอกระบบทางเดินน้ำดีและตับ โดยแบ่งผู้ป่วยเป็น 2 กลุ่ม กลุ่มที่ 1 คือ ผู้ป่วยที่เสียเลือดในระหว่างผ่าตัดมากกว่า 1,000 มล. และกลุ่มที่ 2 คือ ผู้ป่วยที่เสียเลือดในระหว่างผ่าตัดน้อยกว่า 1,000 มล. ผลการศึกษาพบว่า ผู้ป่วยทั้งหมด 69 คน เป็นผู้ป่วยอยู่ในกลุ่มที่หนึ่ง 36 คน กลุ่มที่สอง 33 คน ผู้ป่วยกลุ่มที่ 1 มีปริมาณการเสียเลือดเฉลี่ย 1500 มล. และได้รับเลือดเฉลี่ย 3 ยูนิต ของเม็ดเลือดแดง ในขณะที่ผู้ป่วยกลุ่มที่ 2 มีปริมาณการเสียเลือดเฉลี่ย 400 มล. และได้รับเลือดเฉลี่ย 0 ยูนิตของเม็ดเลือดแดง ปัจจัยที่มีผลต่อการเสียเลือด ได้แก่ ขนาดของเนื้องอก ชนิดของเนื้องอก วิธีการผ่าตัดและระยะเวลาการผ่าตัด ผู้ป่วยกลุ่มที่ 1 มีภาวะแทรกซ้อนและอัตราการอยู่โรงพยาบาลนานกว่าผู้ป่วยกลุ่มที่ 2

การลดการเสียเลือดในการผ่าตัดตับของเนื้องอกระบบทางเดินน้ำดีและตับ เป็นวิธีการหนึ่งที่ทำให้การผ่าตัดประสบความสำเร็จ การเฝ้าติดตามผู้ป่วยที่มีความเสี่ยงในการเกิดเนื้องอก เช่น ผู้ป่วยที่มีภาวะตับแข็งจากไวรัสตับอักเสบบี หรือซี ผู้ป่วยที่เป็นมะเร็งลำไส้ใหญ่ เพื่อตรวจให้พบเนื้องอกที่มีขนาดเล็ก รวมไปถึงเทคนิคการผ่าตัดที่ดีเป็นวิธีการที่จะช่วยลดการเสียเลือดในระหว่างการทำผ่าตัดตับได้