Factors Affecting Intraoperative Blood Loss during Liver Resection

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Objective: *Liver resection might be associated with significant blood loss and required blood transfusion. Many strategies were introduced to reduce blood loss during liver resection. Central venous pressure (CVP) was considered one of the factors affecting blood loss. The objective of the present study was to evaluate the factors correlated with blood loss during liver resection surgery including CVP.*

Material and Method: *Between July 2008 and July 2010, medical and anesthetic records of patients who were admitted to King Chulalongkorn Memorial Hospital for more than one segment resection of the liver were retrospectively reviewed. Factors potentially affecting blood loss including patient characteristics, surgical aspects, and anesthetic aspects in particular CVP were analyzed by regression analysis to explore the correlation with intraoperative blood loss.*

Results: *One hundred thirteen patients were included and analyzed. The mean intraoperative blood loss was 836.46±762.85 ml. The mean, maximum, and minimum values of CVP measured during liver resection were 7.36±3.26, 11.17±3.81, and 5.10±2.81 mmHg, respectively. On multiple regression analysis, the operative time and male patients were associated with blood loss. The other factors and CVP were not significantly correlated.*

Conclusion: *The present study suggested that operation time and gender were the predictors of intraoperative blood loss in more than one segment resection of the liver. In addition, CVP was not the important factor in predicting blood loss.*

Keywords: *Liver resection, Blood loss, Factor, CVP*

J Med Assoc Thai 2013; 96 (1): 58-63
Full text. e-Journal: *http://jmat.mat.or.th*

Liver resection was the curative treatment for hepatocellular carcinoma[1] and liver metastasis from colorectal cancer[2-4]. With the advances in surgical techniques, this operation was sometimes associated with significant blood loss and requires blood transfusion[5-9]. Consequently, complications of blood transfusion arose including transmission of infection and tumor recurrence with reduction of the survival rate[10-13].

Many strategies were introduced to reduce blood loss during liver resection such as portal occlusion, venovenous bypass, clamping of the structures in the lesser omentum, total vascular exclusion (TVE)[14-21]. However, with these measures, the hepatic veins remained patent and there was some bleeding from sinusoids, which the central venous pressure (CVP) may play the important role. Before parenchymal transection, the intravascular volume was expanded with crystalloid or blood products to compensate for anticipated blood loss. This added volume increased the central venous pressure (CVP) and distended the central veins. As a result, this condition augmented the difficulty in controlling blood loss from major hepatic veins[22]. Therefore, low central venous pressure was claimed to be associated with lowering blood loss and the requirement of blood transfusion as well as preservation of the renal function during liver resection[23-25]. However, this concept was controversial since a study found no significant correlation between CVP and blood loss[26]. The aim of the presented study was to find factors, including CVP, that were correlated with blood loss during liver resection surgery.

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Material and Method

After the ethics committee approval, the medical and anesthetic records of the patients who underwent more-than-1-segment resection of the liver between July 2008 and July 2010 at King Chulalongkorn Memorial Hospital were retrospectively reviewed. Eligible participants were elective surgery, aged 18 to

75 years, and ASA physical status class I-III. Exclusion criteria were thrombocytopenia (platelet count <100,000/mm^3), coagulopathy (INR >1.5), liver resection from trauma and liver resection combined with other surgery.

The medical and anesthetic records were analyzed retrospectively. Patients' characteristics, surgical-related variables and anesthetic-related variables of each patient were collected. Patients' characteristics included gender, age, weight, height, underlying disease(s), current medications, and preoperative laboratory data (CBC, coagulogram, liver function test, serum creatinine). Surgical-related variables consisted of tumor type, tumor size, operation, the Pringle maneuver, ischemic time, and operative time. Anesthetic related variables were ASA physical status, combined epidural anesthesia, CVP values (mean, maximum, and minimum), invasive arterial pressure monitoring, fluid transfusion including crystalloid, colloid and blood products, urine output, and intraoperative blood loss. Post-operative laboratory data were hemoglobin, hematocrit, and serum creatinine were also recorded.

Statistical analysis

The sample size was calculated by power analysis using G*Power Program (Erdfelder, Faul and Buchner, 1996). The mean was proved with t-test. (Alpha = 0.05, Power = 80%, medium effect size (d = 0.5) with one-tailed analysis). The calculated sample size was 102. Descriptive statistics was used for demographic data. Pearson correlation and multiple regression analyses were used to detect the correlation between intraoperative blood loss and factors including gender, body weight, ASA physical status, combined epidural anesthesia, tumor types, tumor size, type of operation, operative time, and CVP (mean, maximum, and minimum). All statistical analyses were performed using SPSS 16.0 computer software.

Results

One hundred fifty four cases of liver resection were included in this study. Forty-one patients were excluded from the review because the patients' age was over 75 years old (18 cases), only one segment resection (11 cases), liver resection combined with colonic surgery (9 cases), and thrombocytopenia (1 case). Another two cases were excluded due to extreme blood loss (>10,000 ml) from major vascular injury. The remaining 113 cases were reviewed and analyzed. The patients' characteristics are shown in Table 1. The mean blood loss was 836.5±762.9 ml. No mortality was observed during admission.

Table 1. Patients's characteristics

Age (years)	57 (14)
Gender (male:female)	76 (67.3%):37 (32.7%)
Weight (kg)	61 (18.1)
Height (cm)	163 (14)
DM	17 (15.0%)
Hypertension	32 (28.3%)
Ischemic heart disease	2 (1.8%)
Hepatitis B	38 (33.6%)
Hepatitis C	8 (7.1%)
Cirrhosis (child A)	21 (18.6%)

Data are shown as median [IQR] or number of cases (% of all cases).

The surgical and anesthetic variables are shown in Table 2. By the use of Pearson's correlation analysis and stepwise multiple regression analysis, the significant determinants predicting intraoperative blood loss were male gender ($r = 0.214$, $p = 0.004$) and operative time ($r = 0.619$, $p<0.001$), but there was no significant correlation with ASA physical status, tumor size, type(s) of operation, presence of cirrhosis, the Pringle maneuver and ischemic time, combined epidural anesthesia, mean intraoperative CVP, or hypotension. (Table 3, 4) The mean blood loss in male patients was 949.6±872.0 ml, whereas that of the female was 604.1±379.2 ml. The mean intraoperative blood loss difference between the male and female was 345.6±117.9 ml.

Discussion

In the present study, the authors retrospectively collected factors that may be associated with blood loss during hepatectomy. The authors found that the association between CVP, even mean, maximum or minimum, and intraoperative blood loss was not significant, but the operative time and the male gender were significantly correlated.

The effect of low CVP on blood loss during major hepatic surgery has been repeatedly studied with conflicting results. Jones, et al demonstrated that the volume of blood loss during liver resection was correlated with CVP[24]. Lowering the CVP to less than 5 cmH_2O was a simple and effective way to reduce blood loss during liver surgery. This effect was presumed to be due to a decrease in the sinusoidal and

Table 2. Surgical and anesthetic variables

Surgical variables	
Tumor type	
Hepatocellular carcinoma	53 (46.9%)
Cholangiocarcinoma	30 (26.5%)
Metastatic	26 (23.0%)
Other	4 (3.5%)
Tumor size (cm)	4 (3.75)
Operation	
Left hepatectomy	27 (23.9%)
Right hepatectomy	43 (38.1%)
Extended hepatectomy	8 (7.1%)
Wedge resection	35 (31.0%)
Pringle maneuver	61 (54.0%)
Ischemic time (min)	35 (21.5)
Anesthetic variables	
ASA physical status	
I	28 (24.8%)
II	81 (76.7%)
III	4 (3.5%)
Combined epidural anesthesia	42 (37.2%)
CVP monitoring	92 (81.4%)
Mean CVP (mmHg)	7 (3)
Fluid transfusion	
Crystalloid (ml)	2,500 (1,200)
Colloid (ml)	500 (1,000)
Packed red cells (unit)	0 (1)
Fresh frozen plasma (unit)	0 (0)
Platelet (unit)	0 (0)
Urine output (ml/kg/hr)	1.07 (1.19)
Intraoperative hypotension	36 (31.9%)

Data are shown as median [IQR] or number of cases (% of all cases).

Table 3. Pearson's correlation between variables and blood loss

Variables	R	p-value
Age (yr)	-0.117	0.219
Body weight (kg)	0.190	0.054
Gender (male)	0.214	0.004*
ASA physical status	-0.042	0.656
Tumor size	0.011	0.907
Combining epidural anesthesia	-0.137	0.148
Operative time	0.619	0.000*
Mean CVP	0.129	0.293
Maximum CVP	0.168	0.096
Minimum CVP	0.159	0.116

* Statistically significant ($p < 0.05$)

hepatic vein pressures. Chen et al investigated the effects of low CVP in combination with intermittent vascular occlusion during resection. They found a significant decrease in blood loss and postoperative morbidity and mortality[27]. Another study by Smyrniotis, et al demonstrated that a CVP of 5 mm Hg or less reduced blood loss in major liver resections by using the Pringle maneuver[28].

On the other hand, a recent study by Chhibber et al, done in living donor liver transplantations shows that the CVP's were maintained of less than 5 mmHg intraoperatively, but it did not show any significant reduction of blood loss in patients with relatively low CVP[29]. Lutz et al also demonstrated blood loss was not correlated with the mean CVP at any time during surgery in living liver donors[30]. Kim et al reported in 2009, CVP during hepatic resection was not associated with intraoperative blood loss in living liver donors[26]. The present study also agreed that CVP was not correlated with intraoperative bleeding during liver resection.

The male gender was one of the correlated factors that increased intraoperative blood loss in the present study. The incidence of hepatocellular

Table 4. Stepwise multiple regression analysis for operative time and male gender

Variables	Step 1			Step 2		
	B	SE B	ß	B	SE B	ß
(constant)	-558.90**	193.94		-800.79**	209.74	
Operative time	274.95**	35.00	0.624	274.73**	33.97	0.62
Male gender				351.54**	133.30	0.20
R^2		0.39			0.43	
ΔR^2, $F\Delta R^2$		0.39, 61.72**			0.04, 6.95**	

** Statistically significant ($p < 0.05$)

carcinoma was higher in male patients: the male-to-female ratio of all the recruited HCC patients was 4.5:1[31,32]. In the province of Khon Kaen of Thailand, the incidence of cholangiocarcinoma also reported higher in male (84.6: 100,000 in male vs. 36.8:100,000 in female)[33]. Approximately, two-thirds of the cases were males. However, there was no evidence to explain this correlation between the male gender and more blood loss.

In addition, the present study also found that longer operative time was associated with more intraoperative blood loss. The mean operative time in the present study was 5.14±1.82 hours, which was not different to prior studies[26,28] However, a longer operative time may imply more difficult surgical technique and consequently more blood loss.

The Pringle maneuver is the most favorite technique to control blood loss at our center. Several studies reported various techniques of vascular control and the Pringle maneuver was claimed to be effective in reducing blood loss. Nagasue et al compared the outcome of surgery between 73 patients with the Pringle maneuver and 20 patients without this technique[34]. They reported that the use of the Pringle maneuver was associated with less blood loss. Man et al. found the Pringle maneuver beneficial in reducing blood loss and in shortening the time to complete the liver transection[35]. Furthermore, it resulted in a reduction of blood transfusion. However, in the present study, the Pringle maneuver could not be analyzed because of missing data from the surgical records (documented 54%, missing data 46%).

The mean blood loss in the present study was 836.46±762.8 ml (range 100-4,000 ml), which was comparable to previous studies(23,28,36). There were two cases excluded from the statistical analysis due to extreme blood loss (10,000 ml) that might cause erroneous results. The records of these two cases were explored that there were major vascular injuries with active bleeding. There was no association between blood loss and renal injury in the present study.

Limitation

The present study was a retrospective design. The surgical techniques and anesthetic techniques were not standardized. The completeness of the records was another concern. There were some missing or loss of data from admission, anesthetic and operative records, which meant some variables could not been analyzed. In addition, this was a single-center study, the experiences of the surgeons and the anesthesiologists came from the institute only. Therefore, the results may differ from the larger or smaller institutions.

Potential conflicts of interest

None.

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ปัจจัยที่มีผลต่อการเสียเลือดระหว่างการตัดตับ

รื่นเริง ลีลานุกรม, บรรจบพร ทรงธรรมวัฒน์, อติคุณ ธนกิจ, สุธีรญา นาคบุรินทร์

วัตถุประสงค์: *การตัดตับเป็นการผ่าตัดที่อาจเสียเลือดมากและต้องให้เลือดทดแทน มีผู้นำวิธีต่าง ๆ มาใช้เพื่อลดการเสียเลือดระหว่างการตัดตับ ความดันเลือดดำส่วนกลางเป็นปัจจัยประการหนึ่งที่มีผลต่อการเสียเลือด การศึกษาครั้งนี้มีวัตถุประสงค์เพื่อศึกษาถึงปัจจัยต่าง ๆ และความดันเลือดดำส่วนกลางที่มีผลต่อการเสียเลือดระหว่างการตัดตับ*

วัสดุและวิธีการ: *ทำการศึกษาทบทวนเวชระเบียนและใบบันทึกการระงับความรู้สึกของผู้ป่วยที่มารับการตัดตับโรงพยาบาลจุฬาลงกรณ์ตั้งแต่ กรกฎาคม พ.ศ. 2551 ถึง กรกฎาคม พ.ศ. 2553 โดยการผ่าตัดนั้นต้องเป็นการตัดตับมากกว่า 1 segment นำปัจจัยที่อาจมีผลต่อการเสียเลือดระหว่างผ่าตัดมาวิเคราะห์โดยใช้การวิเคราะห์การถดถอย ปัจจัยเหล่านี้ได้แก่ ลักษณะผู้ป่วย การผ่าตัด การระงับความรู้สึก และความดันเลือดดำส่วนกลาง*

ผลการศึกษา: *ทำการวิเคราะห์ในผู้ป่วย 113 ราย การเสียเลือดเฉลี่ย คือ 836.46±762.85 มล. ความดันเลือดดำส่วนกลางเฉลี่ย สูงสุด และต่ำสุด คือ 7.36±3.26, 11.17±3.81 และ 5.10±2.81 มม.ปรอท ตามลำดับ การวิเคราะห์ถดถอยพหุพบว่า ระยะเวลาการผ่าตัด และเพศชายมีความสัมพันธ์กับการเสียเลือดอย่างมีนัยสำคัญ ปัจจัยอื่น ๆ และความดันเลือดดำส่วนกลางไม่สัมพันธ์กับการเสียเลือดอย่างมีนัยสำคัญ*

สรุป: *การศึกษาครั้งนี้บอกได้ว่า สำหรับการตัดตับที่มากกว่า 1 segment นั้น ปัจจัยที่มีผลต่อการเสียเลือดคือ ระยะเวลาการผ่าตัดและเพศ ส่วนความดันเลือดดำส่วนกลางไม่ใช่ปัจจัยสำคัญในการบอกถึงการเสียเลือด*