PO Box 2345, Beijing 100023, China
www.wjgnet.com
wjg@wjgnet.com

World J Gastroenterol 2006 February 14; 12(6): 935-939
World Journal of Gastroenterology ISSN 1007-9327

CLINICAL RESEARCH

Low central venous pressure reduces blood loss in hepatectomy

Wei-Dong Wang, Li-Jian Liang, Xiong-Qing Huang, Xiao-Yu Yin

Wei-Dong Wang, Department of General Surgery, The First People's Hospital of Shun De, Foshan, 528300, Guangdong Province, China
Li-Jian Liang, Xiao-Yu Yin, Department of Hepatobiliary Surgery, The First Affiliated Hospital, Sun Yat-Sen University, Guangzhou 510080, Guangdong Province, China
Xiong-Qing Huang, Department of Anaesthesia, The First Affiliated Hospital, Sun Yat-Sen University, Guangzhou 510080, Guangdong Province, China
Correspondence to: Li-Jian Liang, Department of Hepatobiliary Surgery, The First Affiliated Hospital, Sun Yat-Sen University, Guangzhou 510080, Guangdong Province, China. lianglj@medmail.com.cn
Telephone: +86-757-22318706 Fax: +86-757-22223899
Received: 2005-05-12 Accepted: 2005-06-6

Abstract

AIM: To investigate the effect of low central venous pressure (LCVP) on blood loss during hepatectomy for hepatocellular carcinoma (HCC).

METHODS: By the method of sealed envelope, 50 HCC patients were randomized into LCVP group ($n = 25$) and control group ($n = 25$). In LCVP group, CVP was maintained at 2-4 mmHg and systolic blood pressure (SBP) above 90 mmHg by manipulation of the patient's posture and administration of drugs during hepatectomy, while in control group hepatectomy was performed routinely without lowering CVP. The patients' preoperative conditions, volume of blood loss during hepatectomy, volume of blood transfusion, length of hospital stay, changes in hepatic and renal functions were compared between the two groups.

RESULTS: There were no significant differences in patients' preoperative conditions, maximal tumor dimension, pattern of hepatectomy, duration of vascular occlusion, operation time, weight of resected liver tissues, incidence of post-operative complications, hepatic and renal functions between the two groups. LCVP group had a markedly lower volume of total intraoperative blood loss and blood loss during hepatectomy than the control group, being 903.9 ± 180.8 mL *vs* 2 329.4 ± 2 538.4 ($W = 495.5$, $P < 0.01$) and 672.4 ± 429.9 mL *vs* 1 662.6 ± 1 932.1 ($W = 543.5$, $P < 0.01$). There were no remarkable differences in the pre-resection and post-resection blood losses between the two groups. The length of hospital stay was significantly shortened in LCVP group as compared with the control group, being 16.3 ± 6.8 d *vs* 21.5 ± 8.6 d ($W = 532.5$, $P < 0.05$).

CONCLUSION: LCVP is easily achievable in technique. Maintenance of CVP ≤ 4 mmHg can help reduce blood loss during hepatectomy, shorten the length of hospital stay, and has no detrimental effects on hepatic or renal function.

Key words: Hepatectomy; Hepatocellular carcinoma; Central venous pressure; Blood loss

Wang WD, Liang LJ, Huang XQ, Yin XY. Low central venous pressure reduces blood loss in hepatectomy. *World J Gastroenterol* 2006; 12(6): 935-939

http://www.wjgnet.com/1007-9327/12/935.asp

INTRODUCTION

Hepatectomy remains as the treatment of choice for hepatocellular carcinoma (HCC). Intra-operative blood loss is one of the major causes for post-operative morbidity and mortality. Various techniques, such as Pringle's maneuver and unilateral hepatic hilum occlusion, have been used to control bleeding from hepatic arterial and portal venous systems during hepatectomy in clinical settings. However, for excision of HCC adjacent to major blood vessels, hepatic system could be the major source of hemorrhage, especially after the application of Pringle's maneuver. Hence, effective control of hepatic venous hemorrhage is crucial to minimize intraoperative blood loss. This prospective randomized clinical trial aims at evaluating the role of low central venous pressure (LCVP) in reducing blood loss during hepatectomy for HCC.

MATERIALS AND METHODS

Patients'data and grouping

From June 2002 to December 2003, a total of 50 consecutive patients with HCC (40 men and 10 women) underwent hepatectomy by the same group of surgeons at our hospital. By the sealed envelope method, the patients were blindly randomized into LCVP group ($n = 25$) and control group ($n = 27$) at the beginning of the operation. Two patients in the control group were excluded from the study because hepatectomy was given up due to cardiac arrest in one and unclear tumor demarcation in the other. Eventually, there were 25 patients in each group. The demographic data of the patients are shown in Table 1,

Table 1 Comparison of patient's clinical data between two groups

Groups	Gender (male/female)[1]	Age (yr)[2]	Body weight (kg)[3]	Liver cirrhosis (*n*)[4]	Liver function (Child-Pugh class)[5]		
					A	B	C
LCVP	19/6	45.33±14.59	60.11±12.14	14	21	3	1
Control	21/4	46.00±12.14	59.91±10.84	15	21	4	0

[1]χ^2=0.500, [2]t=0.174, [3]t=0.055, [4]χ^2=0.082, [5]χ^2=1.143.

Table 2 Comparison of blood routine examination, hepatic and renal functions, and coagulation function between two groups

Groups	Blood routine examination			Hepatic function			Coagulation function	Renal function	
	Hb(g/L)	RBC(×10^{12}/L)	HCT	ALT(μ/L)	TBIL(μmol/L)	ALB(g/L)	PT(s)	BUN[a](mmol/L)	Cr(μmol/L)
LCVP	134.08±19.17	4.632±0.83	0.41±0.058	51.24±29.91	29.04±42.71	41.29±6.13	12.56±1.12	4.75±1.24	69.04±15.72
Control	136.48±13.51	4.58±0.55	0.41±0.039	61.36±47.51	22.64±11.27	41.12±4.79	12.53±1.16	5.48±1.12	70.76±17.99
t	0.512	0.292	0.233	0.901	0.724	573.00	0.087	2.096	0.360

[a]$P<0.05$, BUN values in both groups were within normal range (2.5-6.4 mmol/L).

and the preoperative laboratory findings are demonstrated and listed in Table 2.

Intraoperative management

In the LCVP group, patient's right internal jugular vein was cannulated by a dual-channel catheter following anesthesia, with one channel being connected to the transducer for continuously monitoring CVPs. Arterial pressure was measured by puncture of radial artery. Systolic blood pressure (SBP) was maintained above 90 mmHg by intravenous infusion of dopamine (4-6 μg/kg). During hepatectomy, CVP was maintained at 2-4 mmHg by adopting Trendelenburg's posture (with head 15° lower than low extremities), limiting the volume of infusion and intravenously administering nitroglycerine (0.5-2 mg/time), and furosemide (10-20 mg) was used if necessary. From the beginning of anesthesia to the completion of liver resection, the infusion was maintained at a speed of <75 mL/h, urine output >25 mL/h, and SBP >90 mmHg. If hypotension occurred, the dose of dopamine and the speed and volume of infusion were adjusted. If hemoglobin (Hb) was <80 g/L during the operation, packed red cells were transfused. After liver resection and hemostasis were completed, the blood volume was restored with crystalloid and colloid solutions. Post-operative Hb value should be kept at above 100 g/L. In the control group, patients were managed in the same way as those in LCVP group, except for manipulation of patient's posture and administration of nitroglycerine and furosemide to lower CVP.

Hepatectomic technique

The liver was completely separated. The extent of hepatectomy and whether or not applying hepatic blood inflow occlusion were determined based on the tumor situation and severity of liver cirrhosis. For the patients with severe cirrhosis or peripheral tumors, hepatic blood inflow occlusion was not used. For patients with tumor located at one lobe of the liver, unilateral hepatic hilum occlusion was employed. In hepatic parenchymal transection, method of blunt division but not cavitron ultrasonic surgical aspirator (CUSA) was used. The ductal structures were first ligated and then divided, with reinforced suture for larger blood vessels. The cutting surface of the liver was sprayed with biological glue. The patterns of hepatectomy between the two groups were compared as shown in Table 3.

Measurement of blood loss during hepatectomy

Total intra-operative blood loss consisted of the following three parts: (1) from the start of the operation to complete separation of the liver (pre-hepatectomic blood loss); (2) during division of hepatic parenchyma (intra-hepatectomic blood loss); (3) from completion of hepatic parenchymal division to the closure of the abdominal wall (post-hepatectomic blood loss). Operation was continued to the next step only after complete hemostasis was achieved. The blood-collection bottle was changed in each step and the volume of the collected blood was measured. All blood-stained gauzes were harvested and weighed. The difference between the weight of the blood-stained gauzes and their initial weight was considered as the weight of blood in the gauze, which was then converted into the volume of blood (the blood specific gravity: 1.054-1.062 g/mL in men with an average of 1.058 g/mL; 1.048-1.062 g/mL in women with an average of 1.055 g/mL).

Evaluation parameters

The following pre-, intra-, and post-operative data were collected: (1) patient's gender, age, body weight, red blood cell (RBC) count, hematocrit (HCT), hemoglobin (Hb), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), serum albumin (ALB), blood urea nitrogen (BUN), creatinine (Cr), prothrombin

Table 3 Comparison of operative pattern between two groups

Groups	Types of hepatectomy[1]				Types of vascular occlusions (n)[2]		time (min)[3]	Maximal tumor dimension (cm)[4]	Weight of the resected liver tissues (g)
	Right	Left	≥2 hepatic segments	Single hepatic segments	Unilateral	Portal hepatitis			
LCVP	5	3	13	4	4	7	20.00±12.17	10.7±4.9	633.80±567.38
Control	4	5	10	6	2	11	17.27±6.56	9.88±4.2	603.20±497.62

[1]χ^2=1.402, [2]χ^2=1.709, [3]t=0.621, [4]t=0.633, [5]t=0.203.

Table 4 Comparison of intra-operative blood loss between two groups

Group	Pre-hepatectomy	Intra-hepatectomy	Post-hepatectomy[2]	Total
LCVP	318.2±605.6	672.4±429.9[b]	42±35.4	903.9±180.8[d]
Control	603.4±973.7	1 662.6±1 932.1	63.4±52.9	2 329.4±2 538.4
W^1	495	543.5	538	495.5

[1]Rank sum test; [2]P = 0.05, [b]P < 0.01, [d]P < 0.01 *vs* control.

time (PT), presence or absence of liver cirrhosis and liver function grading; (2) pre-hepatectomic, intra-hepatectomic and post-hepatectomic blood loss and total intra-operative blood loss; (3) operation time, pattern of hepatic hilum occlusion and duration, maximal tumor dimension, weight of the excised liver tissue and extent of hepatectomy, transfusion volume of packed RBCs and fresh frozen plasma (FFP); (4) liver and renal functions on post-operative d 1, 3, and 7; (5) post-operative morbidity and length of hospital stay.

Statistical analysis

The results were expressed as mean ± SD. SPSS software package version 10.0 was used to run the statistical analysis. For continuous variables, Student's t test, rank test or ANOVA was employed to compare the inter-group difference, and χ^2 test was adopted for categorical variables. Statistical significance was considered at two-tailed $P < 0.05$.

RESULTS

Patient's general clinical data

There were no significant differences in gender, age, body weight, severity of liver cirrhosis and grades of liver function between LCVP and control groups (Table 1).

Preoperative laboratory data

Table 2 shows that preoperative RBC count, HCT, Hb, ALT, AST, TBIL, ALB, PT and Cr in LCVP group was not markedly different from those in the control group. Preoperative BUN in both the groups was within the normal range, being higher in control group than in LCVP group ($P < 0.05$).

Operative pattern

All patients had large tumors. There were no remarkable differences in patterns of operation, modes of hepatic blood inflow occlusion and duration, maximal tumor dimension, weight of the excised hepatic tissue between the two groups (Table 3).

Operative time, intra-hepatectomic blood loss, blood transfusion, post-operative complications and length of hospital stay

Total intra-operative blood loss and intra-hepatectomy blood loss were dramatically less in LCVP group than in the control group ($P < 0.01$, Table 4). There were no significant differences in pre- and post-hepatectomic blood losses between the two groups (Table 4). Eight of twenty-five patients in LCVP group and 14 of 25 patients in control group needed blood transfusion, with a significantly lower volume of transfusion in LCVP than in the control group ($P < 0.05$, Table 5). There was no significant difference in operative time between the two groups (Table 5). Post-operative complications included biliary fistula, gastrointestinal bleeding, pleural effusion and subphrenic fluid collection, with an incidence of 20% (5/25) in LCVP group and 24% (6/25) in control group ($P > 0.05$). LCVP group had a remarkably shorter hospital stay than the control group, being 16.3±6.8 d *vs* 21.5 ± 8.6 d ($P < 0.05$).

Post-operative hepatic and renal functions

There were no significant differences in ALT, TBIL, and Cr on post-operative d 1, 3, and 7 between the two groups (Table 6, $P > 0.05$). BUN was significantly higher in control group than in the LCVP group, but it was within the normal range in both groups (Table 6, $P > 0.05$).

DISCUSSION

Blood loss during hepatectomy has an adverse effect on the post-operative outcome and increases post-operative morbidity. Intra- or post-operative massive blood transfusion carries risks of causing infectious diseases,

Table 5 Comparison of operation time and incidence of post-operative complications

Groups	Operation time (min)[1]	Intra- and post-operative transfusion (mL)		Incidence of post-operative complications (n)[4]
		Packed RBC[2]	FFP[3]	
LCVP	229.60±67.33	525.00±237.57[a]	437.50±250.36[c]	5
Control	246.00±112.36	1 285.71±1 162.13	1 057.14±658.33	6

[1]t=0.626; [2]W=63.00, [3]t=2.537, [4]χ^2=9.778, [a]P<0.05, [c]P<0.05 *vs* control.

Table 6 Comparison of post-operative hepatic and renal functions between two groups

Parameters	Postoperative day	LCVP	Control
ALT (μ/L)[1]	1	561.00±409.23	700.76±610.77
	3	286.4±204.09	396.60±423.86
	7	104.60±56.18	173.04±268.17
TBIL (μmol/L)[2]	1	29.04±42.71	22.64±11.27
	3	39.34±47.08	40.46±28.33
	7	23.69±26.40	28.95±30.82
BUN (mmol/L)[3]	1	4.75±1.24	5.48±1.12
	3	4.87±2.59	5.72±1.84
	7	5.10±1.75	6.03±2.23
Cr (μmol/L)[4]	1	69.04±15.72	70.76±17.99
	3	58.04±15.68	65.28±17.67
	7	59.12±11.57	60.96±15.60

[1]F=72.955, [2]F=0.185, [3]F=0.860, [4]F=6.462.

coagulatory disorder, acute respiratory distress syndrome, multiple organ failure, and also promotes tumor recurrence due to its inhibitory effects on immunologic function[1,2]. Hence, various methods, including Pringle's maneuver, unilateral hepatic hilum occlusion and normothermic total hepatic vascular exclusion[3], have been adopted to reduce intra-operative blood loss. In recent years, application of CUSA in liver resection under hepatic hilum occlusion has been reported to significantly lessen the intra-operative blood loss[4]. Some studies reported that LCVP during liver resection could significantly cut down the intra-operative blood loss, decrease the incidence of post-operative complications and shorten the hospital stay[5,6]. Under hepatic hilum occlusion, blood loss during liver resection mainly derives from hepatic vein and hepatic short vein. Hepatic sinusoidal pressure is directly related to CVP. With lowering of the pressure in inferior vena cava, the hepatic venous pressure and then hepatic sinusoidal pressure would decline. Blood loss during liver resection is proportional to the pressure gradient of vascular walls and the diameter of the injured vessels. Though total hepatic vascular exclusion or clamping inferior vena cava can reduce blood loss from hepatic venous system during hepatectomy[7], they are associated with remarkable injury and technically difficult.

LCVP in hepatectomy was generally referred to as CVP lower than 5 mmHg[6]. Maintenance of LCVP should not lower the arterial pressure. In the present study, by maintaining CVP below 5 mmHg during liver resection with manipulation of patient's posture, administration of drugs and control of infusion speed, the arterial pressure was effectively sustained and blood loss was markedly cut down. Our results suggested that Trendelenburg's posture was helpful to prevent LCVP-induced air embolism. With the maintenance of the arterial pressure, the perfusion of organs was ensured. The post-operative evaluation showed that LCVP would not deteriorate hepatic and renal functions. LCVP group had shorter hospital stay than the control group. It is suggested that LCVP was helpful for post-operative recovery. The LCVP technique was not complicated and achievable even in middle-class hospitals. Hence, it is of clinical value.

Many studies reported that various methods reduced intra-operative transfusion volume[8]. However, transfusion volume sometimes could not correctly reflect intra-operative blood loss, since the former was related to the patient's preoperative conditions, tolerance to ischemia, control of intraoperative infusion volume and speed, and anesthetist's mastery of indication for transfusion. Intra-operative blood loss included bleeding not only from hepatic parenchymal division, but also from dissection of perihepatic ligaments, separation of tumors from adjacent tissues, the cutting surface of liver after resection and the accidental tumor rupture. The latter was also affected by the surgeon's experiences and techniques, and patient's coagulation function. Hence, strictly speaking, only bleeding from hepatic parenchymal division accounts for the real blood loss of hepatectomy. In the present study, we have divided the procedure of hepatectomy into three steps, i.e.,: pre-, intra-, and post-hepatectomic, and blood loss in each step was completely collected and accurately measured. Our results showed that total intra-operative blood loss was markedly less in LCVP group than that in the control group. There were no significant differences in pre-hepatectomic and post-hepatectomic blood losses between the two groups, but intra-hepatectomic blood loss was remarkably lower in LCVP group than in the control group.

It suggested that lowering CVP during hepatectomy could effectively reduce blood loss. Additionally, transfusion volume was markedly cut down in LCVP as compared with the control group. It indicated that decline in intra-hepatectomic blood loss could reduce the transfusion volume, which is helpful for the recovery of patient's immunological function and prevention of tumor recurrence. The present study is a prospective randomized clinical trial. The number of cases is not big enough, and the effect of decline in intra-operative blood loss on prognosis still awaits further observations.

REFERENCES

1 **Yamamoto J**, Kosuge T, Takayama T, Shimada K, Yamasaki S,

Ozaki H, Yamaguchi N, Mizuno S, Makuuchi M. Perioperative blood transfusion promotes recurrence of hepatocellular carcinoma after hepatectomy. *Surgery* 1994; **115**: 303-309
2 **Li CH**, Chau GY, Lui WY, Tsay SH, King KL, Hsia CY, Wu CW. Risk factors associated with intra-operative major blood loss in patients with hepatocellular carcinoma who underwent hepatic resection. *J Chin Med Assoc* 2003; **66**: 669-675
3 **Lai J M**, Liang L J, Li D M. Application of hepatovascular occlusion in hepatocellular carcinoma recection. *Chin J Bases Clin General Surg* 1999; **6**: 217-219
4 **Wu W**, Lin XB, Qian JM, Ji ZL, Jiang Z. Ultrasonic aspiration hepatectomy for 136 patients with hepatocellular carcinoma. *World J Gastroenterol* 2002; **8**: 763-765
5 **Johnson M**, Mannar R, Wu AV. Correlation between blood loss and inferior vena caval pressure during liver resection. *Br J Surg* 1998; **85**: 188-190
6 **Smyrniotis V**, Kostopanagiotou G, Theodoraki K, Tsantoulas D, Contis JC. The role of central venous pressure and type of vascular control in blood loss during major liver resections. *Am J Surg* 2004; **187**: 398-402
7 **Otsubo T**, Takasaki K, Yamamoto M, Katsuragawa H, Katagiri S, Yoshitoshi K, Hamano M, Ariizumi S, Kotera Y. Bleeding during hepatectomy can be reduced by clamping the inferior vena cava below the liver. *Surgery* 2004; **135**: 67-73
8 **Peng SY**, Liu YB, Xu B, Cai XJ, Mu YP, Wu YL, Cao LP, Fang HQ, Wang JW, Li HJ, Li JT, Wang XB, Deng GL. Role and significance of extrahepatic control of hepatic vein and inferior vena cava in difficult hepatectomies for patients with liver tumors. *Zhonghua Waike Zazhi* 2004; **42**: 260-264

S- Editor Ma JY **L- Editor** Elsevier HK **E- Editor** Kong LH