

Effects of the Supine and Reverse Trendelenburg Positions on Central Venous Pressure During Hepatectomy: A Prospective Randomized Controlled Trial

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Background: Hepatectomy is an operation that has potentially significant blood loss. The low central venous pressure (CVP) technique has been accepted as a method to minimize blood loss during hepatectomy. From previous studies, reverse Trendelenburg position (rTP) decreased CVP, however, no randomized control study has compared the effectiveness of these techniques in terms of reducing CVP and decreasing blood loss.

Objective: To demonstrate the benefit of rTP in lowering the CVP and blood loss compared to the supine position (SP) during hepatectomy.

Materials and Methods: The present randomized, controlled two-arm trial was conducted between March 2021 and October 2023. The patients who underwent open hepatectomy were randomized into two groups, the SP and the rTP groups. The primary outcome was CVP during liver resection and secondary outcome was blood loss and rate of blood transfusion.

Results: One hundred and twelve patients undergoing open hepatectomy were randomized into two groups. Fifty-seven patients were allocated to the SP group while rTP group was applied to 55 patients. The baseline CVP in the SP group was 6.9 ± 3.0 centimeters of water column (cmH₂O), and in the rTP group was 6.5 ± 2.9 cmH₂O. The average CVP from 0 to 60 minutes was significantly decreased from 7.0 ± 2.7 in SP group to 5.3 ± 2.7 in rTP group ($p=0.001$). The spot CVP was significantly lower at 5, 15, 45, and 60 minutes after adjusting position. There was no significant difference in total blood loss and rate of blood transfusion during liver resection between the two groups. However, in the rTP group, blood loss during the transection of the liver may be reduced and the transection time may be less.

Conclusion: The present study demonstrated that the rTP is effective in lowering CVP. It can reduce CVP after position adjustment for 60 minutes, but it could not reduce blood loss.

Trial registration: Thai Clinical Trials Registry, TCTR20210614001

Keywords: Low central venous pressure; Position; Hepatectomy, Reverse Trendelenburg; Blood loss; Blood transfusion

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Hepatectomy is performed to treat hepatobiliary carcinoma, benign liver tumors, and liver metastasis lesions, and is a major operation that has the potential causing substantial blood loss. Bleeding during hepatectomy involves the Glisson's system, or the inflow system, and the hepatic venous system, or the

outflow system⁽¹⁾. Strategies have been developed to decrease blood loss during hepatectomy, such as the Pringle's maneuver, which is used to control bleeding from the Glisson's system, energy devices, and the anesthetic low central venous pressure (CVP) technique. It has been established that a CVP of below 5 mmHg minimizes blood loss during hepatectomy by decreasing bleeding from the hepatic venous system⁽²⁻¹²⁾. Furthermore, a retrospective study reported that the reverse Trendelenburg position (rTP) significantly decreases the CVP^(1,13,14). However, no randomized controlled study has compared the effectiveness of these techniques in reducing the CVP and controlling bleeding and complications during hepatectomy.

The present randomized controlled trial aimed to demonstrate the benefits of the rTP during liver resection in terms of reducing the CVP, blood loss,

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requirement for vasopressors, volume of blood transfusion, length of hospital stay, and incidence of complications compared with the conventional supine position.

Materials and Methods

Study design and participants

The authors estimated the sample size by calculating to evaluate significant differences in CVP between the two randomized groups at the 5% significant level (two-side), with a power of 80%. The CVP for the sample size calculation was obtained from previous, non-randomized controlled trials and assumed to apply to the present randomized controlled trial. Yoneda et al. reported that the mean CVP values in the SP and rTP groups were 8 and 5.6 cmH₂O, respectively⁽¹⁾. Based on the standard deviation, the common variances from the same previous study were 7.7 and 7 cmH₂O, respectively⁽¹⁾, was used to calculate the sample size. After accounting for a 10% expected dropout rate in each group, the final number of participants required per group was 154.

Randomization and blinding

The present study was a prospective, single-center, randomized, two-arm trial conducted between March 2021 and October 2023. The present study was approved by the Institutional Ethics Committee (approval No. MURA2017/402) and registered with the Thai Clinical Trials Registry, TCTR20210614001.

Computer-generated block randomization was used to allocate the participants into two groups, the conventional supine position, as SP group, during liver resection, and those at a 5-degree inclination in the rTP during parenchymal transection, as the rTP group.

The random numbers were written on pieces of paper and placed in opaque, sealed envelopes that were opened in the operating room by the nurses after intraoperative staging had been performed and the surgeons had decided to proceed with the hepatectomy. The participants were blinded to their group allocation, and the individuals who opened the envelopes did not participate in the operation. The surgeons and anesthesiologists were not blinded to the participants' group allocations (Figure 1).

Participants

Patients scheduled for elective open hepatectomy were eligible for inclusion in the present study. The inclusion criteria were patients aged older than 18 years scheduled for open hepatectomy for any

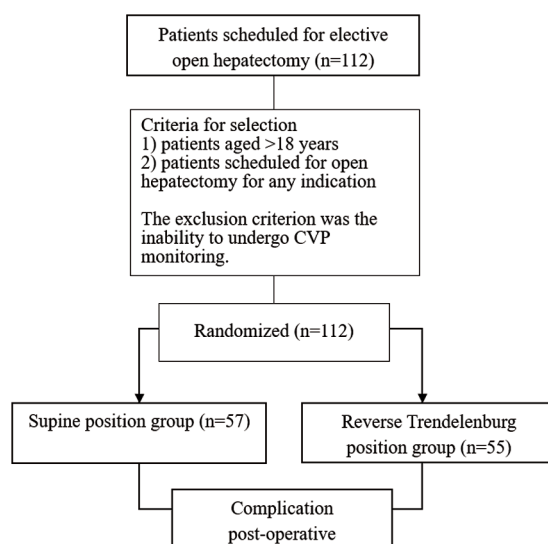


Figure 1. Flow chart group allocations and criteria for selection. Supine position group and Reverse Trendelenburg position group.

indication. The exclusion criterion was the inability to undergo CVP monitoring. The participants provided written informed consent on their admission date before undergoing surgery.

Surgical protocol

All patients were routinely admitted to the hospital one day before the operation and underwent preoperative laboratory testing comprised of a complete blood count, coagulogram, and liver function tests. Surgery was performed either under general anesthesia alone or under general anesthesia combined with thoracic epidural anesthesia. After tracheal intubation and the induction of epidural anesthesia, an anesthesiologist inserted a central venous catheter into the right internal jugular vein under ultrasound guidance and fixed it in place at 10 to 13 cm so that the tip of the catheter was in the superior vena cava.

The suction measurement was separated into two systems, the first was applied during liver resection, while the second was applied in other parts of the surgery. The gauzes and swabs were also separated into two systems, during parenchymal transection, and during other parts of the surgery. Blood loss was calculated by measuring the weight of gauzes and swabs after the operation (Figure 2).

The Cavitron ultrasonic surgical aspirator (CUSA), clamp crushing, ultrasonic scalpel, and vessel sealing devices were used depending on the surgeon's preference. Norepinephrine infusion,

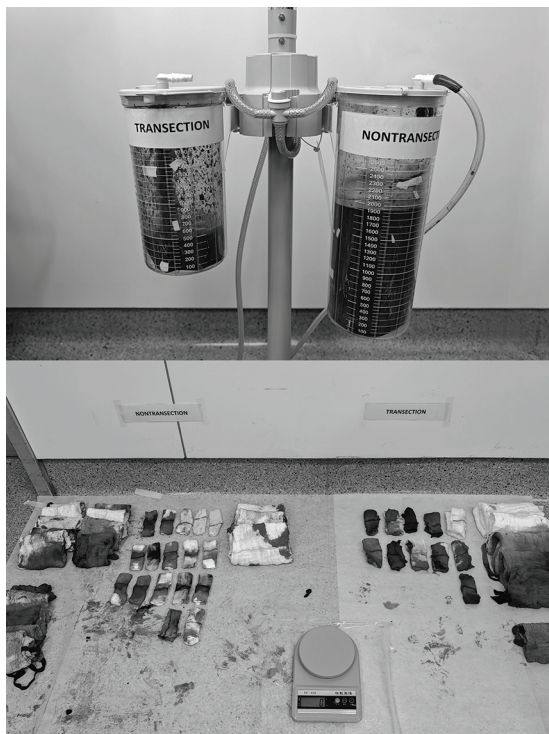


Figure 2. The suction measurement, gauze, and swab were separated into two systems.

nitroglycerine infusion, and positive end-expiratory pressure were used based on the anesthesiologist's preference to maintain normotension of systolic blood pressure at greater than 90 mmHg and a mean arterial pressure of more than 65 mmHg. The indication for an intraoperative blood transfusion was decided by the anesthesiologist when the maximum allowable blood loss was reached. The indication for postoperative blood transfusion was a hemoglobin level of less than 8 g/dL.

The CVP measurements were recorded by an anesthesiologist before the positional adjustment as the baseline CVP, 5 minutes after the positional adjustment, and every 15 minutes after the start of parenchymal transection.

The complete blood count, coagulation results, liver function test results, and bilirubin concentration of the drainage fluid were measured on postoperative days 0, 1, 3, and 5. All patients were routinely followed up at the outpatient clinic at 1 week, 2 weeks, and 1 month after surgery. The 30-day mortality and morbidity rates were recorded. Complications such as abdominal fluid collection, postoperative bile leak, postoperative liver failure, pulmonary embolism, postoperative pneumonia, reoperation, organ injury,

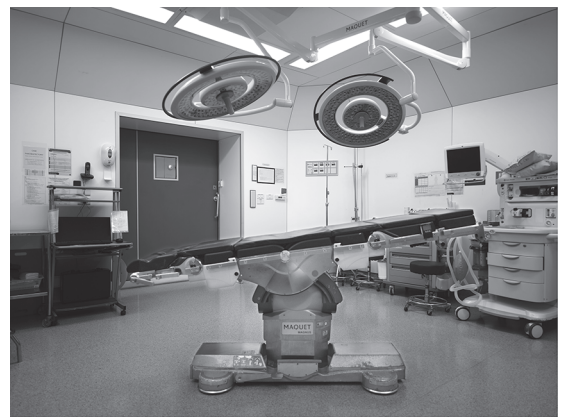


Figure 3. The 5-degree inclination of the body position was measured by a miter angle digital gauge in the reverse Trendelenburg position group.

and surgical site infection were recorded.

Intervention

After opening the abdomen and performing intraoperative staging, the sealed envelope was opened to dictate the position of the patient. In the rTP group, the body position was inclined by 5 degrees as measured by a miter angle digital gauge (Figure 3). The rTP was only used during parenchymal transection, after that, the patient was returned to the supine position.

Endpoints

The primary endpoint was the CVP. The secondary endpoints were blood loss, complications, 30-day morbidity, and mortality.

Statistical analysis

Statistical analysis was done using Stata Statistical Software, version 17 (StataCorp LLC, College Station, TX, USA). Continuous data were compared using the independent samples t-test or Mann-Whitney U test. Categorical variables were expressed as frequencies and percentages and analyzed using the chi-square test or Fisher's exact test. Differences were considered significant at a p-value of less than 0.05. The CVP was compared between the two groups using the paired t-test.

Results

One hundred and twelve patients who underwent open hepatectomy were included in the present study. The patients undergoing open hepatectomy between March 2021 to October 2023 were randomized into two groups with 57 patients assigned to the SP group,

Table 1. Patients' characteristics

	Total (n=112)	Supine position (n=57)	Reverse Trendelenburg position (n=55)	p-value
Age (years); mean±SD	63.6±9.6	63.4±10.3	63.9±9.0	0.829
Weight (kg); mean±SD	64.8±11.8	64.8±11.7	64.5±11.9	0.894
Height (cm); mean±SD	161.7±8.2	161.5±7.7	162.9±8.8	0.752
Body mass index (kg/m ²); mean±SD	24.6±3.6	24.8±3.9	24.5±3.4	0.629
Sex; n (%)				0.814
Male	68 (60.7)	34 (59.6)	34 (61.8)	
Female	44 (39.3)	23 (40.4)	21 (38.2)	
ASA classification; n (%)				0.567
I	1 (0.9)	1 (1.8)	0 (0.0)	
II	36 (32.1)	19 (33.3)	17 (30.9)	
III	73 (65.2)	37 (64.9)	36 (65.5)	
IV	2 (1.8)	0 (0.0)	2 (3.6)	
Child-Pugh score; n (%)				0.085
Score 5	106 (94.6)	56 (98.3)	50 (90.9)	
Score 6	6 (5.4)	1 (1.7)	5 (9.1)	
Preoperative laboratory; mean±SD				
Hb (g/dL)	12.9±1.7	12.9±1.7	12.8±1.7	0.841
Platelet (×10 ³ /μL)	226±80	235±86	218±72	0.274
INR	0.98±0.07	0.98±0.08	0.97±0.06	0.484

ASA=American Society of Anesthesiologists; Hb=Hemoglobin; INR=International normalized ratio; SD=standard deviation

while rTP group was applied to 55 patients. The patients' demographics are summarized in Table 1. There were no differences between the SP and the rTP groups in age, gender, body mass index, American Society of Anesthesiologists classification, diagnosis, and operative procedure. The two groups also had similar incidences of redo hepatectomy, Child-Pugh score, and preoperative laboratory data, including hemoglobin level, coagulation, platelet count, and bleeding risk (Table 1).

Operative information

The operative information and monitoring results are summarized in Table 2. The diagnoses were hepatocellular carcinoma and colorectal liver metastasis in 35 patients, cholangiocarcinoma in 35 patients, and others in 11 patients. There was no significant difference between the SP and the rTP groups in the distribution of patients based on the extent of resection such as minor or major ($p=0.263$). The CUSA was frequently used in both groups. There were no significant differences between the two groups in the use of these energy devices. Pringle's maneuver was applied to almost all participants in both groups. The mean duration of the Pringle's maneuver was similar in the SP and the rTP groups at 72.6 ± 37.5 and 72.7 ± 40.2 minutes, respectively ($p=0.984$). There were no significant differences

between the two groups in the percentages of patients receiving positive end-expiratory pressure, norepinephrine infusion, and nitroglycerine infusion. The operative and parenchymal transection times did not significantly differ between the two groups. The baseline CVP was 6.9 ± 3.0 cmH₂O in the SP group and 6.5 ± 2.9 cmH₂O in the rTP group. The average CVP from 0 to 60 minutes was significantly lower in the rTP group than in the SP group at 5.3 ± 2.7 versus 7.0 ± 2.7 cmH₂O ($p<0.001$). The spot CVP values at 5, 15, 45, and 60 minutes after the position was adjusted were significantly lower in the rTP group. However, from 60 minutes after adjusting the position onwards, the CVP did not significantly differ between the rTP group and the SP group (Figure 4).

Surgical outcomes

The surgical outcomes are summarized in Table 3. Two patients died in the hospital due to coronavirus disease (COVID-19) pneumonia, one in the SP group and one in the rTP group. The median and interquartile range blood loss during parenchymal transection did not significantly differ between the two groups ($p=0.284$). There were also no significant differences between the SP and rTP groups in the percentages of patients receiving intraoperative and postoperative packed red cell transfusions, the incidence of complications at 31.6%

Table 2. Operative information

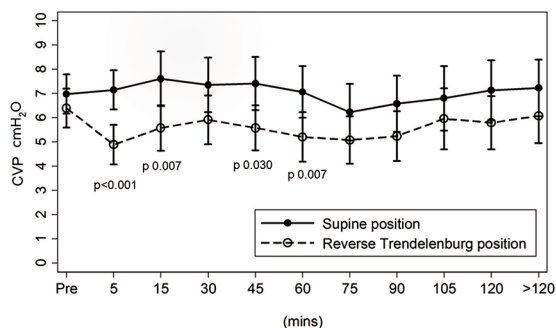
	Total (n=112)	Supine position (n=57)	Reverse Trendelenburg position (n=55)	p-value
Epidural anesthesia; n (%)	84 (75.0)	47 (82.5)	37 (67.3)	0.071
Redo hepatectomy; n (%)	29 (25.9)	15 (26.3)	14 (25.4)	0.917
Diagnosis; n (%)				0.442
Hepatocellular carcinoma	43 (38.4)	23 (40.3)	20 (36.4)	
Colorectal liver metastasis	43 (38.4)	20 (35.1)	23 (41.8)	
Cholangiocarcinoma	15 (13.4)	6 (10.5)	9 (16.4)	
Others	11 (9.8)	8 (14.1)	3 (5.4)	
Surgical procedure; n (%)				0.972
Limited resection	59 (52.6)	31 (54.3)	28 (50.9)	
• 1	30 (50.9)	20 (64.6)	10 (35.7)	
• 2	16 (27.1)	5 (16.1)	11 (39.3)	
• 3	11 (18.6)	4 (12.9)	7 (25.0)	
• 4	1 (1.7)	1 (3.2)	0 (0.0)	
• 5	1 (1.7)	1 (3.2)	0 (0.0)	
Right posterior sectionectomy	9 (8.0)	5 (8.8)	4 (7.3)	
Extended right hepatectomy	7 (6.3)	3 (5.3)	4 (7.3)	
Left lateral sectionectomy	5 (4.5)	3 (5.3)	2 (3.6)	
Left hepatectomy	5 (4.5)	3 (5.3)	2 (3.6)	
Right anterior sectionectomy	3 (2.7)	2 (3.5)	1 (1.8)	
Extended left hepatectomy	2 (1.8)	1 (1.7)	1 (1.8)	
Extent of resection; n (%)				0.263
Minor	63 (56.3)	35 (61.4)	28 (50.9)	
Major	49 (43.7)	22 (38.6)	27 (49.1)	
Energy devices; n (%)				
CUSA	112 (100)	57 (100)	55 (100)	-
Ultrasonic scalpel	15 (13.4)	7 (12.3)	8 (14.6)	0.725
Clamp crushing	84 (75.0)	46 (80.7)	38 (69.1)	0.156
Vessel sealing device	55 (49.1)	30 (52.6)	25 (45.5)	0.448
Pringle's maneuver; n (%)	110 (98.2)	57 (100)	53 (96.4)	0.239
Duration Pringle's maneuver (minutes), mean±SD	72.6±38.7	72.6±37.5	72.7±40.2	0.984
Operating time (minutes); mean±SD	313±105	309±110	319±101	0.612
Transection time (minutes); mean±SD	170±74	178±79	162±68	0.273
Norepinephrine infusions; n (%)	52 (46.4)	28 (49.1)	24 (43.6)	0.561
Norepinephrine dose (mg); median (IQR)	0.24 (0.15, 0.53)	0.2 (0.13, 0.6)	0.3 (0.16, 0.48)	0.706
Nitroglycerine infusions; n (%)	10 (8.9)	6 (10.5)	4 (7.3)	0.546
Nitroglycerine dose (mg); median (IQR)	3.92 (1.2, 10)	8 (1.2, 10)	1.72 (1.2, 9.92)	0.521
PEEP (cmH ₂ O); n (%)	86 (76.8)	44 (77.2)	42 (76.4)	0.917
Average CVP from 0 to 60 minute (cmH ₂ O); mean±SD	6.1±2.8	7.0±2.7	5.3±2.7	0.001
Spot CVP (cmH ₂ O); mean±SD				
Pre (n=108)	6.7±2.9	6.9±3.0	6.4±2.9	0.312
After 5 minutes (n=106)	6.0±3.0	7.1±3.0	4.9±2.5	<0.001
After 15 minutes (n=68)	6.4±3.1	7.6±2.9	5.6±3.0	0.007
After 30 minutes (n=63)	6.6±3.3	7.3±2.3	5.9±3.8	0.067
After 45 minutes (n=70)	6.3±3.5	7.4±3.3	5.6±3.5	0.030
After 60 minutes (n=65)	6.1±2.8	7.1±2.7	5.2±2.7	0.007
After 75 minutes (n=63)	5.5±2.8	6.2±2.9	5.1±2.6	0.109
After 90 minutes (n=59)	5.8±2.6	6.6±2.9	5.2±2.3	0.054
After 105 minutes (n=42)	6.3±3.0	6.8±3.3	5.9±2.7	0.369
After 120 minutes (n=52)	6.4±3.3	7.1±3.0	5.8±3.5	0.151
After >120 minutes (n=54)	6.2±3.7	7.0±3.9	5.5±3.3	0.147

CUSA=Cavitron ultrasonic surgical aspirator; PEEP=positive end expiratory pressure; CVP=central venous pressure; SD=standard deviation; IQR=interquartile range

Table 3. Surgical outcomes

	Total (n=112)	Supine position (n=57)	Reverse Trendelenburg position (n=55)	p-value
Blood loss (mL); median (IQR)				
During parenchymal transection	383 (170, 765)	404 (215, 814)	345 (146, 724)	0.284
Others	379 (178, 647)	365 (172, 647)	404 (203, 645)	0.780
Total blood loss (mL); median (IQR)	840 (515, 1,383)	949 (533, 1,392)	824 (497, 1,291)	0.590
Total volume of fluid infusion (mL/kg/minute); mean±SD	0.16±0.08	0.15±0.07	0.17±0.08	0.289
Intraoperative PRC transfusion; n (%)	26 (23.2)	14 (24.6)	12 (21.8)	0.731
Total intraoperative PRC transfusion (mL); mean±SD	456±329	364±172	567±438	0.193
Postoperative PRC transfusion in 24 hours; n (%)	8 (7.14)	2 (3.5)	6 (10.9)	0.158
Total postoperative PRC transfusion in 24 hours (mL); mean±SD	393±265	356±214	411±305	0.795
Overall complication; n (%)	41 (36.6)	18 (31.6)	23 (41.8)	0.261
Major complication; n (%)	10 (9.0)	4 (7.1)	6 (10.9)	0.448
Clavien-Dindo classification; n (%)				0.459
Grade 1	1 (0.9)	1 (1.8)	0 (0.0)	
Grade 2	29 (26.1)	13 (23.2)	16 (29.1)	
Grade 3a	5 (4.5)	3 (5.3)	2 (3.6)	
Grade 3b	3 (2.7)	0 (0.0)	3 (5.5)	
Grade 5	2 (1.8)	1 (1.8)	1 (1.8)	
Pulmonary embolism; n (%)	2 (1.8)	2 (3.5)	0 (0.0)	-
Postoperative liver failure; n (%)				
Grade A	1 (0.9)	0 (0.0)	1 (1.8)	-
Bile leak; n (%)				0.999
Grade A	24 (77.4)	12 (80.0)	12 (75.0)	
Grade B	6 (19.4)	3 (20.0)	3 (18.8)	
Grade C	1 (3.2)	0 (0.0)	1 (6.2)	
Hospital stays (days); median (IQR)	8 (6, 11)	7 (6, 11)	8 (7, 12)	0.135

PRC=packed red cell; SD=standard deviation; IQR=interquartile range

**Figure 4.** The central venous pressure values during liver resection.

and 41.8%, respectively ($p=0.261$), the incidences of postoperative liver failure and bile leak, and the length of hospital stay. Two patients developed postoperative pulmonary embolisms, however, no patient developed intraoperative air embolism.

Discussion

Bleeding during hepatectomy involves the Glisson's system and the hepatic venous system⁽¹⁾.

Techniques used to control bleeding from the Glisson's system include the Pringle maneuver, hemihepatic vascular occlusion, or selective Glisson's sheath occlusion⁽¹⁾. Additionally, the low CVP technique has been accepted as a method to minimize blood loss during hepatectomy by decreasing bleeding from the hepatic venous system.

Many techniques have been developed to control the CVP, including low CVP anesthesia strategies based on fluid restriction, epidural blockage, diuretic administration, nitroglycerine infiltration⁽¹⁵⁾, hypoventilation anesthesia^(16,17), infra-hepatic inferior vena cava clamping^(18,19), total vascular exclusion⁽²⁰⁾, intraoperative blood salvage procedures⁽²¹⁾, and the surgical position of the patient^(1,13,14,16,20). A previous study reported that the CVP was 10, 7.8, and 6 mmHg in patients in the 20-degrees head-down, supine, and 20-degrees head-up positions, respectively⁽¹⁴⁾. Another study reported that the mean CVP decreased by 1.7 mmHg after performing a 5- to 15-degree head-up tilt before transecting the liver parenchyma⁽¹³⁾. The authors also reported that the rTP is a safer technique for lowering the CVP than clamping the inferior vena

cava⁽¹³⁾. However, a limitation of this previous study was that the anesthesia modalities and vasopressor dosage were inconsistent⁽¹³⁾. The other benefits of the rTP are easy to use and provides good exposure to the hepatic veins and hepatic hilum⁽²²⁾.

In previous studies, the head-up tilted position ranges from 5 to 20 degrees of inclination^(13,14). However, not all hepatobiliary surgeons can complete the parenchymal resection with the patient in the 5 to 20-degree rTP. Therefore, a 5-degree inclination in the rTP is the maximum inclination that is comfortable for every surgeon to perform the parenchymal resection during hepatectomy in the authors' hospital.

The present study was the first randomized study to demonstrate that the rTP can decrease the CVP after positional adjustment from the supine position under the same conditions regarding patients' demographic data and anesthesia conditions. However, the duration of the decreased CVP was 60 minutes after changing the position and the CVP was only decreased by 1.7 cmH₂O, from 7.0±2.7 to 5.3±2.7 cmH₂O, which was insufficient to reduce the intraoperative blood loss. The present results suggest that there is no relationship between the surgical position and the development of intraoperative air embolisms, and there were no significant complications in the rTP group, which is in line with the findings of previous studies^(14,22).

The present study has limitations. There were patients who could not be included as scheduled because they chose to undergo laparoscopic rather than open hepatectomy. Owing to the COVID-19 crisis, elective open hepatectomies were postponed due to the limitations of medical resources. Therefore, the number of patients who underwent open hepatectomy decreased during the study period. Moreover, the water and blood vaporization in gauzes and swabs could not be calculated and controlled.

Conclusion

The present study demonstrated that the rTP is effective in lowering the CVP, as it reduced the CVP for 60 minutes after positional adjustment from the supine position to the rTP. However, the use of the rTP did not reduce blood loss compared with the supine position. There were no increases in vasopressor requirements or complications when using the rTP compared with the conventional supine position during hepatectomy.

What is already known about this topic?

It has been established that a CVP of below 5 mmHg minimizes blood loss during hepatectomy by decreasing bleeding from the hepatic venous system. Furthermore, a retrospective study reported that the rTP significantly decreases the CVP. However, no randomized controlled study has compared the effectiveness of these techniques in reducing the CVP and controlling bleeding and complications during hepatectomy.

What does this study add?

This was the first randomized study to demonstrate that the rTP can decrease the CVP after positional adjustment from the supine. However, the duration of the decreased CVP was 60 minutes after changing the position and the CVP was only decreased by 1.7 cmH₂O, which was insufficient to reduce the intraoperative blood loss.

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Conflicts of interest

The authors declare no conflict of interest.

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