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Selective Hemihepatic Vascular Occlusion Versus Pringle Maneuver in Hepatectomy for Primary Liver Cancer

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Background: This study was conducted to compare the clinical effects of two techniques used for inflow occlusion during hepatectomy (selective hemihepatic vascular occlusion *vs.* Pringle maneuver) for the treatment of primary liver cancer.

Material/Methods: A total of 63 patients with primary hepatocellular carcinoma who underwent hepatectomy during June 2006 and June 2011 were included in this retrospective study. A total of 26 patients in group A accepted selective hemihepatic vascular occlusion, and 37 patients in group B underwent the Pringle maneuver during hepatectomy. The intraoperative conditions, postoperative liver function recovery, and complication rates were compared between these two groups.

Results: There were no significant differences in intraoperative blood loss, blood transfusion, occlusion time, and postoperative complication rates between group A and group B ($P>0.05$). However, postoperative serum levels of alanine transaminase (ALT), aspartate transaminase (AST), total bilirubin (TBIL), and albumin (ALB) in group A were significantly lower than those in group B ($P<0.05$). Moreover, there were noteworthy differences in peripheral artery pressure and sphygmus ($P<0.05$).

Conclusions: During hepatectomy, selective hemihepatic vascular occlusion benefits the patients with primary hepatocellular carcinoma by reducing the hepatic damage and improving postoperative hepatic function recovery, compared with the Pringle maneuver.

MeSH Keywords: **Hepatectomy • Liver Neoplasms • Mesenteric Vascular Occlusion**

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Background

Primary liver cancer (PLC) is one of the most common malignancies in the world with 696,000 deaths in 2008 [1]. Hepatocellular carcinoma (HCC) is the most common primary form of liver cancer [2]. To date, the first choice for the treatment of PLC is resection. Because there is plentiful blood flow in the liver, intraoperative bleeding control is a crux of successful surgery. The foremost concern in liver surgery is to minimize blood loss and avoid transfusions, which have been shown to have a deleterious impact on both short- and long-term outcomes [3–6].

In 1908, James Hogarth Pringle proposed a vascular isolation method in hepatectomy, known as the Pringle maneuver, which has a benefit of controlling bleeding during surgery [7,8]. However, it can induce ischemia-reperfusion injury in the liver, which results in metabolic, immunological, and microvascular changes [6]. Besides, it is hypothesized that the Pringle maneuver should be avoided during hepatectomy for cancer patients due to its side effects, mainly in terms of the ischemia-reperfusion injury, which would induce a worse prognosis [9]. Subsequently, hemihepatic vascular occlusion was developed by Makuuchi et al. in 1987 to control bleeding [10]. Its efficiency and safety have been confirmed by a plentiful number of scholars [11–13]. But there are still inconsistent opinions on the choice of selective hemihepatic vascular occlusion or the Pringle maneuver [14]. Some propose that there is no difference in therapeutic effects and bleeding control [15–17]. However, Fu et al. conducted a prospective randomized controlled trial to compare the Pringle maneuver, hemihepatic vascular inflow occlusion, and main portal vein inflow occlusion in partial hepatectomy [18]. They found that all 3 vascular inflow occlusion techniques were efficacious and safe in reducing blood loss, but the Pringle maneuver resulted in more postoperative liver injury and complication rates [18]. Recently, a retrospective study suggested that selective inflow occlusion was more efficient than the Pringle maneuver in terms of intraoperative blood loss and transfusion rates [19].

This retrospective study analyzed the clinical data of primary HCC patients in our department who accepted hepatectomy using 2 vascular inflow occlusion techniques, selective hemihepatic vascular occlusion or the Pringle maneuver. We anticipate that the results will contribute to the choice of PLC treatment by hepatectomy.

Material and Methods

Patients

The patients who were pathologically diagnosed with primary HCC using ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), and laboratory examination (Figure 1A, 1B, 1E, 1F) and had indications for hepatectomy were retrospectively reviewed between June 2006 and June 2011. A total of 63 patients (53 males and 10 females) were included in the present study. The age of the patients ranged from 25 to 72 years old (median 48.5 years old). In addition, 55 patients were Child-Pugh grade A and 8 patients were Child-Pugh grade B according to the preoperative liver function classifications. In total, 7 of 63 patients had more than two tumors in the liver. Diameters of tumor ranged from 2 to 16 cm (mean 6.98±3.26 cm). These 63 patients were divided into two groups according to the status of inflow occlusion during hepatectomy: group A, selective hemihepatic vascular occlusion (n=26); and group B, the Pringle maneuver (n=37). The characteristics of the patients in these two groups are listed in Table 1. Liver cirrhosis was present in 20 (77%) and 17 (46%) patients in group A and group B, respectively. However, hepatitis B and hepatitis C were the etiology of cirrhosis in these patients. The levels of alanine transaminase (ALT) and aspartate transaminase (AST) were significantly elevated beyond the normal range.

The methods of vascular occlusion

Selective hemihepatic vascular occlusion was performed through two approaches: the liver parenchymal approach and the hepatic portal panel approach. (1) In the liver parenchymal approach, a small hole in the liver capsule was made by a sharp blade along the ductuli hepaticus communis and confluence of left and right ductus hepaticus. A right-angle forceps was inserted into the hole to bluntly dissect the liver parenchyma outside Glisson's sheath. A No. 8 catheter was introduced to the hepatoduodenal ligament and drawn forth at the junction of the portal vein branch and the caudate lobe (Figure 1C, 1D). Tightening of the catheter could occlude the blood inflow of the right lobe. For devascularization of the left lobe, the catheter should be introduced through the lesser omentum and drawn forth from the ligamentum hepatogastricum and screwed (Figure 1G, 1H). (2) In the hepatic portal panel approach, as above, the right-angle forceps was inserted for blunt separation of the hepatic portal panel and the Glisson's capsule outside Glisson's sheath, and then the hemihepatic vascular occlusion could be performed by blocking the three vessels in Glisson's sheath by a No. 8 catheter.

As for the Pringle maneuver, the lesser omentum was opened at the droopy site, and a No. 8 catheter was introduced to encircle the hepatoduodenal ligament by a right-angled forceps. The hepatic blood inflow could be occluded by tightening the catheter. The devascularization time should not exceed 20 min, and intermittent occlusion was performed when the time was >20 min. Besides, the declamping time was 5 min.

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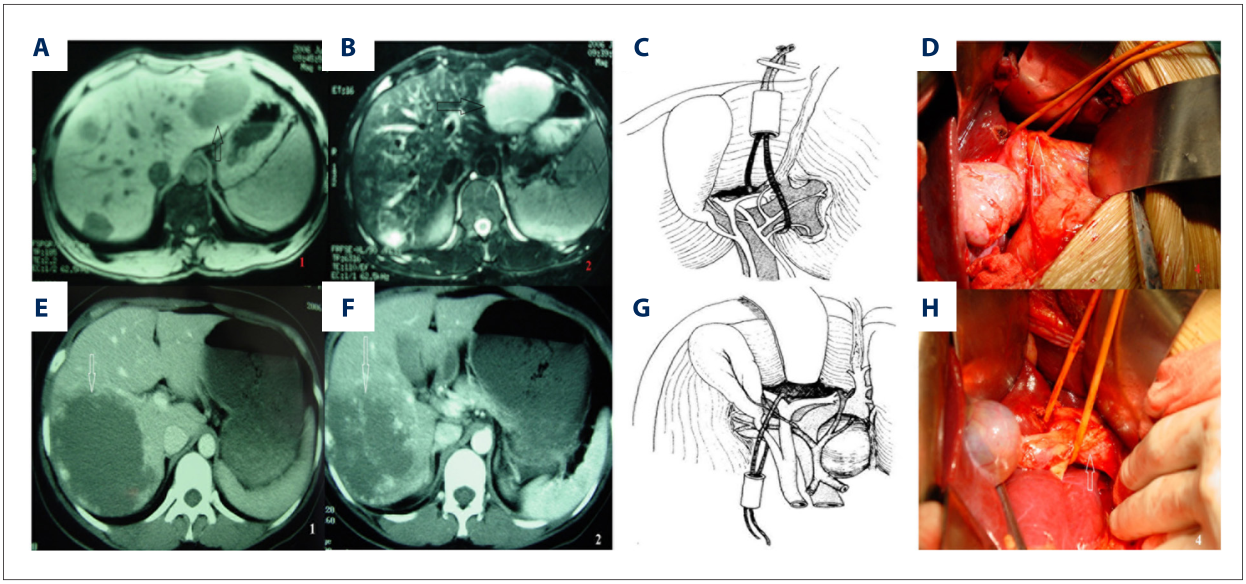

Figure 1. (**A–D**) Case one: patient with primary liver cancer of the left heel. (**E–H**) Case two: patient with primary liver cancer of the right heel. (**A, E**) T1 weighted image on MRI; (**B, F**) weighted image on MRI; (**C, G**) devascularization of the left lobe; (**D, H**) devascularization of the right lobe.

Table 1. Characteristics of the patients.

Group	Group A	Group B
Patients/n	26	37
Male/female	20/6	33/4
Age/years	34–72 (median 53)	25–70 (median 47.5)
Hepatic cirrhosis/n (%)	20 (77%)	17 (46%)
Non-cirrhosis/n (%)	6 (23%)	20 (54%)
Hepatitis/n	2	5
Child classification (A/B)	24/2	31/6
ALT/(IU·L^{-1})	50.4±45.3	48.1±32.0
AST/(IU·L^{-1})	48.3±31.9	42.6±20.7
Surgery	Selective hemihepatic vascular occlusion	Pringle maneuver

There were no any differences in terms of surgical margins between the two methods.

Observations

The intraoperative blood loss, blood transfusion, and the hepatic portal occlusion time were measured. Systolic arterial pressure, sphygmus, and oxyhemoglobin saturation were also monitored 1 min before devascularization, 1 min after devascularization, and 1 min after loosening the catheter, respectively. Liver function indicators including ALT, AST, albumin (ALB), and total bilirubin (TBIL) were determined 1 day before and 1, 3, and 7 day(s) after the surgery. The hepatic portal ventilation time and peritoneal drainage were recorded, and the complications were also observed.

Statistical analysis

All statistical analyses were performed by using SPSS 11.5 software (SPSS Inc., Champaign, Illinois, USA). The measurement data were expressed as mean±standard deviation (SD). Comparison between the two groups was performed by using student's t-test, and the comparisons among different time points were conducted by analysis of variance (ANOVA). The enumeration data were compared by using the χ^2 test. P<0.05 was considered statistically significant.

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Table 2. Intraoperative observations.

Group	Group A (n=26)	Group B (n=37)	Comparison
Blood loss/mL	1117±925.3	855.1±669.2	t=1.56, P>0.05
Blood transfusion/mL	1015±840.8	896.2±915.2	t=0.589, P>0.05
Cross-clamp time/min	29.12±10.62	24.46±10.30	t=1.99, P=0.05
Systolic arterial pressure			
1 min before occlusion	121.7±11.30	119.3±11.56	t=–0.81, P>0.05
1 min after occlusion	122.2±12.23	145.1±17.20	t=–5.85, P<0.01
1 min after open	119.0±12.78	116.3±13.37	t=0.83, P>0.05
Sphygmus			
1 min before occlusion	79.19±10.35	81.32±10.64	t=–0.79, P>0.05
1 min after occlusion	81.77±8.680	96.14±14.36	t=–4.52, P<0.05
1 min after open	79.04±13.23	82.28±12.59	t=–0.99, P>0.05
Oxyhemoglobin saturation			
1 min before occlusion	100.0±0.000	99.99±0.110	t=0.46, P>0.05
1 min after occlusion	100.0±0.000	100.0±0.000	–
1 min after open	100.0±0.000	99.98±0.230	t=0.112, P>0.05

Table 3. Postoperative observations.

Group	Group A (n=26)	Group B (n=37)	Comparison	
Hepatic portal ventilation time/d	3.15±0.54	3.14±0.42	t=0.125	P>0.05
Peritoneal drainage/mL	312.00±375.51	354.85±358.33	t=0.643	P>0.05
Diaphragmatic fluid infection (yes/no)	0/26	1/36	χ^2=0.714	P>0.05
Pleural effusion infection (yes/no)	2/24	2/35	χ^2=0.134	P>0.05
Biliary fistula (yes/no)	0/26	1/36	χ^2=0.337	P>0.05
Fever (yes/no)	1/25	2/35	χ^2=0.714	P>0.05
Hematological change (continue to rise/return to normal)	0/26	2/35	χ^2=1.451	P>0.05

Results

Intraoperative observations

Table 2 shows the intraoperative indicators of the two groups. There was no significant difference in intraoperative blood loss (1116.92±925.33 mL *vs.* 855.13±669.15 mL), blood transfusion (1015.38±840.81 mL *vs.* 896.15±915.16 mL), and occlusion time (29.12±10.62 min *vs.* 24.46±10.30 min) between the two groups ($P\geq0.05$). In addition, we found no statistical difference in the oxyhemoglobin saturation, peripheral artery pressure (121.7±11.30 *vs.* 119.3±11.56), and sphygmus between two groups before the devascularization. But there was a notable elevation in peripheral artery pressure (122.2±12.23 *vs.* 145.1±17.20) and sphygmus after the devascularization ($P<0.05$). After opening of the blood flow, the peripheral artery pressure (119.0±12.78 *vs.* 116.3±13.37) and sphygmus in both groups returned to the levels before occlusion, which were not significantly different ($P>0.05$). These results indicated that selective hemihepatic vascular occlusion had less influence on the systemic hemodynamics than the Pringle maneuver.

Complications

No patient died of liver failure after hepatectomy. The liver failure was caused by an insufficient liver remnant. Student's

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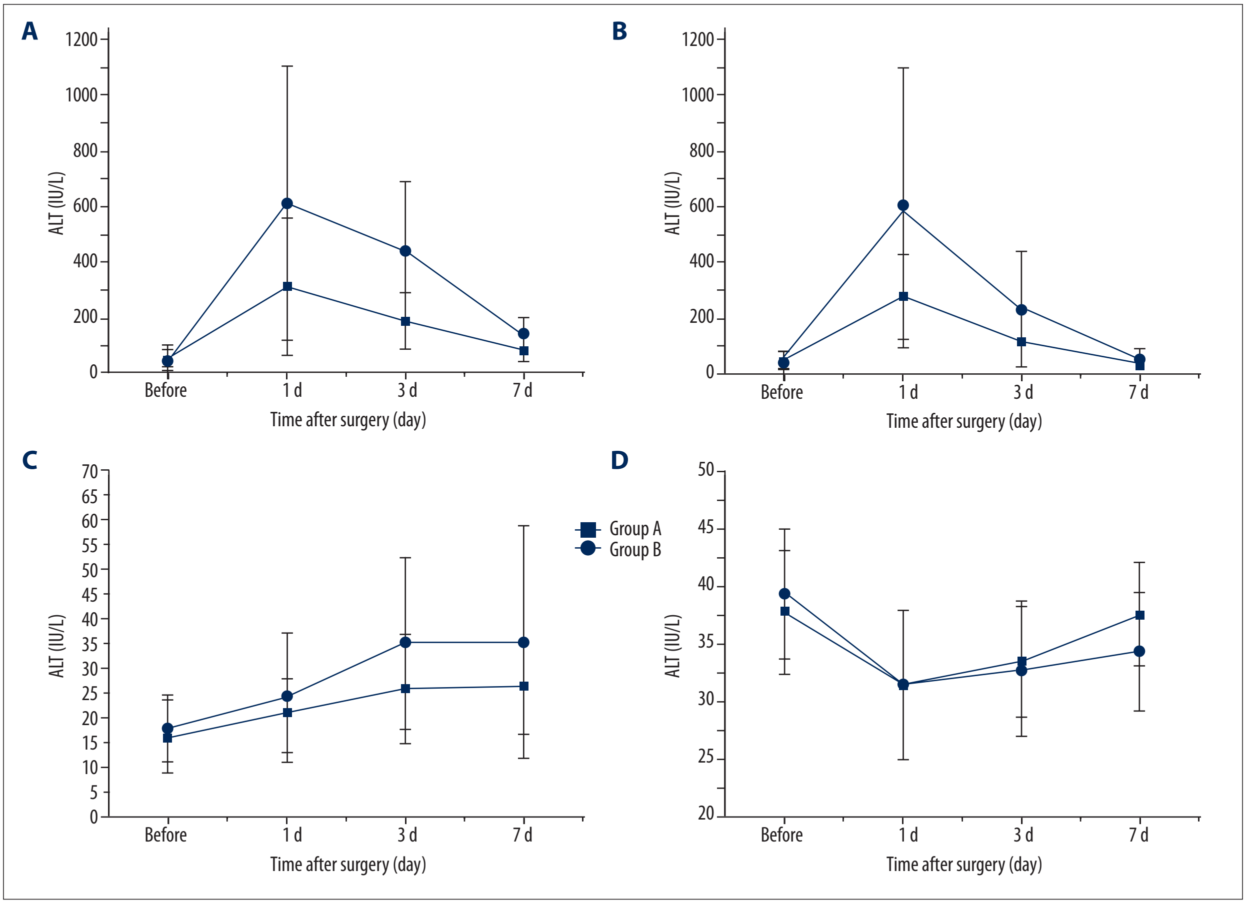

Figure 2. Postoperative recovery of liver function. ALT – alanine transaminase; AST – aspartate transaminase; ALB – albumin; TBIL – serum total bilirubin.

t-test showed no significant difference in the hepatic portal ventilation time and peritoneal drainage between the two groups. The complications are listed in Table 3. In group A, no diaphragmatic fluid infection, biliary fistula, and hematological changes were observed, but there were 2 pleural effusion infections and 1 fever, while there were more complications in group B. The χ^2 test showed no significant difference between the two groups in all complications ($P>0.05$).

Postoperative liver function recovery

The significant elevated pre-hepatectomy ALT (group A: 50.4±45.3 $U \cdot L^{-1}$; group B: 48.1±32.0 $U \cdot L^{-1}$) and AST (group A: 48.3±31.9 $U \cdot L^{-1}$; group B: 42.6±20.7 $U \cdot L^{-1}$) levels (Table 1) indicated obvious ischemia injury in all PLC patients. Post-hepatectomy liver function recovery was indicated by the changes in serum ALT and AST (Figure 2), which all decreased to levels similar to those before surgery ($P<0.01$). In addition, there was also a statistically significant change with regard to TBIL in group A compared with group B ($P<0.05$). There was a significant decrease in ALB levels one day after the hepatectomy compared with those before surgery; then, ALB increased to levels similar to the pre-hepatectomy levels at 7 days after surgery in group A. However, there was no significant difference in terms of change of ALB in group A compared with group B ($P>0.05$). This result suggested that selective hemihepatic vascular occlusion was more effective in possibly alleviating hepatic ischemia-reperfusion injury than the Pringle maneuver, benefiting liver function recovery.

Discussion

This study retrospectively compared the clinical effects of hemihepatic vascular occlusion and the Pringle maneuver during hepatectomy for the treatment of PLC. The results indicated that selective hemihepatic vascular occlusion had less influence on hemodynamics and did better in terms of earlier recovery of postoperative liver function, which could be indicated by liver enzymes. However, there was no difference in intraoperative blood loss and complications between the two methods.

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Because of the bleeding tendency of those patients who need to undergo liver resection, the blood loss can be huge, with the subsequent need for blood transfusion [14]. Additionally, postoperative liver function damage can be substantial. Avoidance of excessive bleeding and blood transfusion is mandatory in these patients [14]. Plenty of studies have been performed concerning the control of bleeding during the surgery. For instance, Chau et al. evaluated the outcomes of hepatic resection in HCC patients with impaired liver function using either no inflow occlusion, hemihepatic vascular occlusion, or the Pringle maneuver during hepatectomy, and they demonstrated that both hemihepatic vascular occlusion and the Pringle maneuver were safe and effective in reducing blood loss [14]. The Pringle maneuver, a technique of transient hepatic vascular inflow occlusion, is one surgical procedure that can decrease blood loss and the need for transfusion considerably during liver surgery [20]. The Pringle maneuver is simple and easy to apply but it has its adverse effects, and the efficacy of the Pringle maneuver still remains controversial. To avoid its adverse effects, such as ischemic-reperfusion injury and splanchnic congestion, hemihepatic inflow occlusion techniques have been advocated to control hemorrhage from the liver parenchyma in hemihepatectomies [21].With this method, visceral congestion is considered to be limited because considerable portal blood flow is preserved, and because only portions of the liver are rendered anoxic. Ni et al. compared the perioperative outcomes of partial hepatectomy for HCC with hepatitis B-related cirrhosis, and they found that hemihepatic vascular inflow occlusion was better than the Pringle maneuver in terms of better liver function recovery and lower complication rates [17]. Fu et al. also found a similar result in a prospective randomized controlled trial: there was no significant difference in intraoperative blood loss, but the Pringle maneuver resulted in a higher degree of postoperative liver injury and complication rates [18]. Zhu et al. also reported a similar finding [19]. But other scholars have not found any difference between these two methods [16]. Tanaka et al. compared the outcomes of hemihepatic vascular occlusion and the Pringle maneuver in resections limited to one hepatic section or less, and they found no significant difference between these two methods [15]. Despite the disagreement, these studies confirmed the safety (no death) and the bleeding control benefit of both methods [14,22,23].

The pre-hepatectomy liver function injury may be characterized by the significantly elevated ALT and AST levels. Occlusion of the inflow on one hand blocks bleeding and on the other hand induces ischemia and anoxia of the liver, leading to further liver tissue injury and liver function damage. On the first day after hepatectomy, the levels of ALT and AST dramatically increased, which may suggest severe damage, and then the levels of ALT and AST gradually recovered to the preoperative levels within 7 days, indicating reversible damage. In addition, the changes in liver function indicators (ALT, AST, and TBIL) in patients with hemihepatic vascular occlusion were significantly different from those in the Pringle maneuver group (P<0.05). Although the levels of ALT and AST decreased gradually after the operation, the levels of ALT and AST in groups A and B remained higher than the normal range (0–40 $U\cdot L^{-1}$) at seven days after the hepatectomy. However, the level of ALB in group A was not significantly different from that in group B, perhaps because we provided exogenous supplement after the operation. Collectively, it appears that both methods caused reversible liver function injury, and hemihepatic vascular occlusion had some advantage with regard to the recovery of liver function over the Pringle maneuver in this study.

Furthermore, it is reported that the hepatic inflow blocking, especially a long time (41 min) of continuous blocking, can cause systemic hemodynamic instability, increasing the mean arterial pressure by 10% and decreasing the cardiac index by 10% [24]. However, Capussotti et al. suggest that there is no need for intermittent portal triad clamping during hepatectomy in cirrhosis [25]. Quan et al. also indicate the safety of continuous (within 1 hour) hepatic inflow occlusion [8]. In the present study, after occlusion, the systolic arterial pressure was elevated from 119.3 to 145.1 in the Pringle maneuver group with a cross-clamp time of 29.12 min, while there was no difference in the selective hemihepatic vascular occlusion group (before 121.7 *vs.* after 122.2) with a cross-clamp time of 24.46 min. In accordance with the results of the liver enzyme tests, the influence on the hemodynamics was reversible because after opening the clamp, the systolic arterial pressure (group A 119.0 *vs.* group B 116.3) recovered to the level of pre-occlusion (group A 121.7 *vs.* group B 119.3) without a significant difference between these two groups. In addition, the sphygmus was significantly elevated after occlusion in both groups, although it was lower in the selective hemihepatic vascular occlusion group compared with the Pringle maneuver group (81.77 *vs.* 96.14, P<0.05). Similarly, after opening the clamp, the sphygmus recovered in both groups without a significant difference between them. Selective hemihepatic vascular occlusion blocks the inflow on the lesion side and avoids ischemic injury in the preserved inflow side, which allows longer inflow occlusion for operation.

The present study found no difference between the groups in intraoperative blood loss, which is consistent with the previous reports [16,18]. Post-hepatectomy complications like fever, pleural effusion, and subphrenic infection burdened hepatectomy patients with high rates of mortality [26]. Our study found that there was no significant difference between group A and group B (P>0.05) in the complications, including diaphragmatic fluid infection (0/26 *vs.* 1/37), pleural effusion infection (2/26 *vs.* 2/37), biliary fistula (0/26 *vs.* 1/37), fever (1/26 *vs.* 2/37), and hematological change (0/26 *vs.* 2/37).

In addition, with the development of the techniques and methods for parenchymal resection, other methods have been utilized [27], for instance, associating liver partition with portal vein ligation for staged hepatectomy (ALPPS) [28], laparoscopic liver resection [29], and laparoscopic-assisted open liver resection [30], as well as stapler hepatectomy [31,32]. Moreover, hepatic parenchymal preservation surgery is recommended to improve liver resection outcomes [33]. Thus, selection of a suitable method should be based on the condition of patients and surgeons' proficiency in operating. Certainly, studies on comparison and improvement of these methods are vital in the future.

However, this study still had several limitations. Firstly, it was a retrospective comparison. Prospective randomized trials are needed to definitively prove the effectiveness and safety of using hemihepatic inflow occlusion and the Pringle maneuver during hepatic resection in PLC patients. Secondly, as hepatitis B or hepatitis C were the etiology of cirrhosis in these patients and there were only 2 patients in group A and 5 patients in group B with hepatitis, we could not exclude any other demographic or clinicopathologic variables that might have contributed to the outcomes in this study. Thirdly, the number of patients included in this study was relatively small. Further investigations with a greater number of patients are needed to verify these results.

Conclusions

In summary, the present study indicated that selective hemihepatic vascular occlusion had less influence on hemodynamics and was superior to the Pringle maneuver for liver function recovery, but did not differ from the Pringle maneuver in intraoperative blood loss and incidence of complications in hepatectomy for PLC. We recommend selective hemihepatic vascular inflow occlusion in hepatectomy for PLC patients. However, because this study was a retrospective comparison, further research is required to provide a definitive conclusion.

Conflict of interests

The authors declare that they have no conflict of interests.

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