

## Review Article

# Pringle maneuver versus hemihepatic blood flow occlusion during hepatectomy: a systematic review and meta-analysis

Guangtong Deng<sup>1,5\*</sup>, Hui Li<sup>2,4,5\*</sup>, Furong Zeng<sup>3,4,5</sup>, Lang Chen<sup>4,5</sup>, Hongru Li<sup>5</sup>, Dongwen Wu<sup>5</sup>, Jing Liu<sup>5</sup>, Zhiming Wang<sup>1</sup>

Departments of <sup>1</sup>General Surgery, <sup>2</sup>Reproductive, <sup>3</sup>Rheumatology and Immunology, Xiangya Hospital, Central South University, Changsha, China; <sup>4</sup>The Third Xiangya Hospital, <sup>5</sup>Xiangya School of Medicine, Central South University, Changsha, China. \*Equal contributors.

Received February 21, 2017; Accepted October 10, 2018; Epub January 15, 2019; Published January 30, 2019

**Abstract:** The Pringle maneuver (PM) and hemihepatic blood flow occlusion (HHO) are used worldwide to reduce blood loss during liver resection surgery; however, it is unknown which is the optimal technique for vascular occlusion during hepatectomy. Thus, a systematic review and meta-analysis was performed to evaluate the clinical outcomes in patients undergoing hepatectomy using the PM compared to those using the HHO technique. Methods: Two authors independently assessed trials for inclusion and independently extracted the data. Risk ratio with its 95% confidence intervals (CI) were calculated for the extracted data. Results: Eight randomized controlled trials (RCTs) involving 688 patients met the predefined inclusion criteria. A total of 343 patients were treated with PM and 345 with HHO. Meta-analysis showed HHO is better than PM groups during hepatectomy on total peri-operative morbidity (RR = 1.52, 95% CI = [1.17, 1.96], P = 0.001), qualitative transfusion (ml) (standard mean difference [SMD] = 0.45, 95% CI = [0.07, 0.83], P = 0.02), total bilirubin (TBIL) levels on the postoperative days three and seven (the third day, SMD = 0.33, 95% CI = [0.13, 0.52], P = 0.001; the seventh day, SMD = 0.31, 95% CI = [0.08, 0.54], P = 0.009), albumin (ALB) levels on the postoperative day three (SMD = -0.38, 95% CI = [-0.57, -0.18], P < 0.001), pre-albumin (PAB) levels on the postoperative days three and seven (the third day, SMD = -0.34, 95% CI = [-0.57, -0.12], P = 0.003; the seventh day, SMD = -0.39, 95% CI = [-0.68, -0.10], P = 0.008), alanine aminotransferase (ALT) on the postoperative days one, three, and seven (the first day, SMD = 0.69, 95% CI = [0.31, 1.07], P < 0.001; the third day, SMD = 0.83, 95% CI = [0.47, 1.20], P < 0.001; the seventh day, SMD = 0.74, 95% CI = [0.50, 0.98], P < 0.001), and aspartate aminotransferase (AST) levels on the postoperative days one, three, and seven (the first day, SMD = 0.66, 95% CI = [0.46, 0.86], P < 0.001; the third day, SMD = 0.75, 95% CI = [0.42, 1.08], P < 0.001; the seventh day, SMD = 0.81, 95% CI = [0.32, 29], P = 0.001). No significant differences were found between the two groups in mortality, hepatic insufficiency, infection, bile leakage, splanchnocoel effusion, postoperative hemorrhage, qualitative transfusion (person), hospital stay, operating time, ischemic duration and operative blood loss. Conclusion: Our results suggested that the HHO technique is more efficacious compared to PM during hepatic resection surgery.

**Keywords:** Pringle maneuver, hemihepatic blood flow occlusion, hepatectomy

## Introduction

Selective liver resection is performed mainly for liver tumors, hepatic trauma, and hepatolith, especially for early stage hepatocellular carcinoma [1, 2]. Despite abundant experience and advanced techniques for hepatectomy, bleeding remains the main concern during parenchymal transection [3, 4]. Bleeding has been found to increase tumor recurrence and reduce the survival rate in patients undergoing partial hep-

atectomy for liver malignancy [5, 6]. Besides, Blood loss and transfusions have been shown to have a deleterious impact on short- and long-term outcomes [7, 8]. Therefore, many methods of hepatic vascular control have been developed in the past decades to control intraoperative blood loss. In 1908, Pringle described the efficacy of total hepatic inflow occlusion (THO) in cases of liver trauma for the first time. The Pringle method (PM) is a technique of encircling the hepatoduodenal ligament with a tape, and

then applying a tourniquet or a vascular clamp until the hepatic arterial pulse disappears distally [9]. It has been the standard for hepatic resection surgery for a long time. The major flaw of this procedure is resultant ischemic damage of the liver and intestinal congestion, especially in patients with chronic liver diseases [10, 11]. To avoid the ischemia reperfusion injury, Makuuchi, in 1987, proposed the hemihepatic vascular occlusion (HHO) technique, which allows for normal blood supply to the contralateral hemi-liver [12]. The advantages of the HHO maneuver are no ischemic reperfusion injury to the remnant liver, avoidance of splanchnic congestion and better hemodynamic tolerability, because considerable portal blood flow is preserved and only portions of the liver are rendered ischemic and anoxic [13]. However, portal vein and artery dissection to perform selective clamping is time consuming and may result in more blood loss from the other hemi-liver, thus causing serious complications [14].

Though there are many studies and meta-analyses comparing the safety and efficacy of the PM and HHO methods [15-17], due to their small sample size, it is difficult to draw a definitive conclusion on the best technique of hepatic vascular control. The optimal method of vascular control during hepatic resection continues to be debated. The objective of this meta-analysis study was to establish the relative safety and efficacy of the HHO versus PM, or total hepatic inflow occlusion, during hepatectomy.

### Material and methods

#### *Literature and search strategy*

Two authors independently searched Pubmed, Embase, Cochrane Library, Ovid, Web of Science Scopus, WANFANG, China National Knowledge Internet, and China Biology Medicine disc until December 2015. Details of the search strategies can be found in [Supplementary Table 1](#). The searches were conducted in English and Chinese.

#### *Inclusion and exclusion criteria*

The following inclusion and exclusion criteria were applied: (a) Types of studies: only randomized clinical trials (RCTs) were considered for

this review. Animal studies, observational studies, basic research, retrospective studies, case-control studies, semi-random control, case reports, and cohort studies were excluded. (b) Types of participants: We focused on adults (> 18 years) who needed selective hepatectomy due primarily to liver cancer, hepatolith, or hepatic trauma, which are the most common diseases requiring hepatectomy irrespective of age, gender, cirrhosis, tumor size, and nodule numbers. (c) Types of interventions: We included trials comparing the PM versus HHO during hepatectomy irrespective of ischemic preconditioning before vascular occlusion. (d) Types of outcome measures: (a) Primary outcomes: Mortality, hepatic insufficiency, peri-operative morbidity (total infection, wound infection, bile leakage, splanchnoel effusion, cardiac insufficiency, postoperative hemorrhage) and transfusion requirements (number of patients, volume). (b) Secondary outcomes: Hospital stay, operating time, ischemic duration, operative blood loss, markers of liver function (total bilirubin [TBIL], albumin [ALB], and prealbumin [PAB] levels) and biochemical markers of liver injury (aspartate aminotransferase [AST] and alanine aminotransferase [ALT] levels).

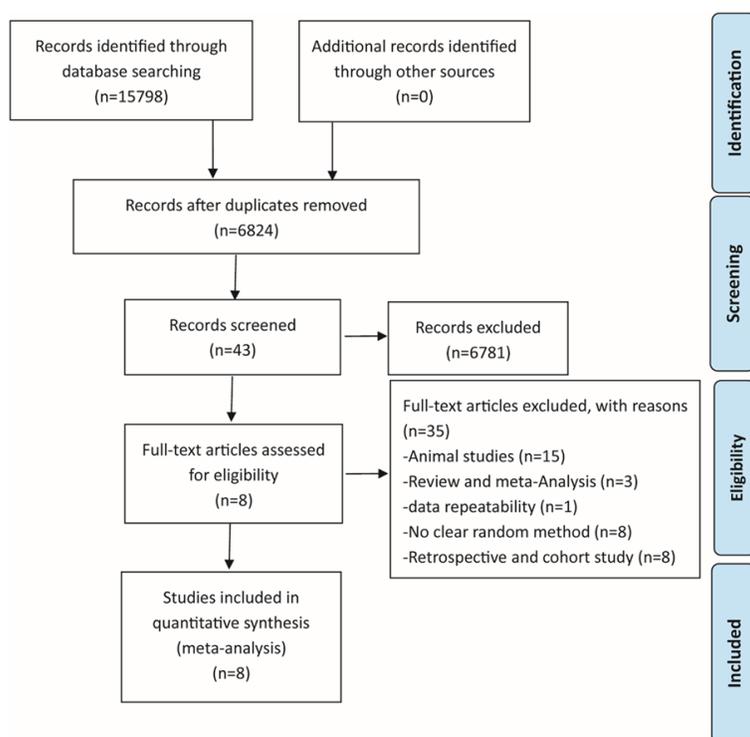
#### *Data collection and quality assessment*

The records from the initial search were scanned by two authors to exclude any irrelevant studies. Two authors subsequently performed a full-text review to apply the inclusion and exclusion criteria; discrepancies were resolved by the third author. All data were independently extracted by two authors, and each study's corresponding author was contacted to obtain additional information when missing or incomplete data were encountered. Study quality was estimated using an adaptation of the Cochrane Handbook for Systematic Reviews of Interventions [18] via the following characteristics: method of randomization, allocation concealment, patients' baseline characteristics, blinding, intention-to-treat analysis, and loss to follow-up.

#### *Statistical analysis*

Statistical heterogeneity was assessed using  $I^2$  [19] and  $P$ -value statistics, and consideration was given for appropriateness of the pooling and meta-analysis. A fixed effects model [20] was adopted if there was no evidence of signifi-

## Pringle maneuver versus hemihepatic blood flow occlusion



**Figure 1.** Flowchart of filtering of studies.

cant heterogeneity ( $I^2 \leq 50\%$  and  $P \geq 0.1$ ), and a random effects model [21] was used in all other instances ( $I^2 > 50\%$  or  $P < 0.1$ ). If possible, we explored the heterogeneity, and performed subgroup analyses based on patients' age, study area, and disease. Different models were used to detect sensitivity and evaluate the stability of the result. For dichotomous data, relative risk (RR) was adopted, while continuation outcomes were converted to the mean difference (MD) through the inverse variance method. Potential publication bias was evaluated by Egger's test. The meta-analysis was considered to have significant publication bias if the  $P$ -value was less than 0.05. All statistical calculations were performed by Review Manager 5.3 (Cochrane collaboration, Copenhagen). The Egger's tests were conducted using the STATA software (Version 12.0; STATA Corporation, College Station, TX, USA).

### Results

#### Literature search

Our search initially reached 15798 studies, although 8974 studies were subsequently

excluded due to duplication. After a review of the titles and abstracts, we excluded an additional 6781 studies. Then, by scanning the full-text (as necessary), we further excluded 35 studies (15 animal studies, three reviews and meta-analyses, one with data repeatability, eight with no clear randomization method, and eight retrospective and cohort studies). Therefore, eight RCTs [22-29] were included in our analysis (**Figure 1**).

#### Characteristics of included studies

Features of the eligible RCTs [22-29] are presented in **Table 1**. The RCTs were published between 2002 and 2015, involving 688 patients. All the trials compared HHO ( $n = 345$ ) with PM ( $n = 343$ ). Five papers

[22-24, 26, 27] were written in English while the other three [25, 28, 29] were in Chinese. Seven [22-27, 29] concluded that HHO is better than PM during hepatectomy except one trial [28] that did not provide a conclusion either way. Patients were generally well-matched in the studies according to sex, age and the tumor size.

#### Risk of bias in included studies

The risk of bias in the included studies is summarized in **Figure 2** and **Table 2**. They include randomization, allocation concealment, patients' baseline characteristics, blinding, intention-to-treat analysis and loss to follow-up.

#### Primary outcomes

##### Mortality

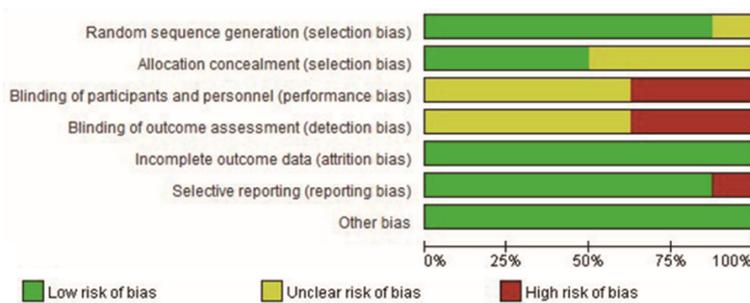
Mortality was defined as death that occurred within 30 days after the operation or during the same hospitalization. Four studies [22-24, 28] including 350 patients reported mortality. The fixed model showed no difference between groups (RR = 1.02, 95% confidence interval [CI]

# Pringle maneuver versus hemihepatic blood flow occlusion

**Table 1.** Characteristics of included studies

First author (yrs.)	Journal	Sample size (n)	PM/ HHO (n)	Age (mean yrs.) PM/ HHO	Sex (male: female) PM/ HHO	Tumor size (mean yrs.) PM/HHO	Outcome
Figueras J (2005)	Ann Surg	80	39/41	61.8/62	31:8/28:13	ND	HHO > PM
Wu CC (2002)	Arch Surg	58	28/30	53.2/57.5	23:5/25:5	9.3/8.8	HHO > PM
Fu SY (2011)	Am J Surg	120	60/60	48.6/49.3	46:14/41:19	6.8/6	HHO > PM
Liang G (2009)	Hepatogastroenterology	80	40/40	49.55/49.40	27:13/31:9	6.93/7.58	HHO > PM
Ni JS (2013)	J Gastrointest Surg	120	60/60	55.2/56.1	45:15/47:13	5.4/4.7	HHO > PM
Xiao J (2015)	Chin J Clinical Rational Drug Use	100	50/50	51.8/50.8	28:22/29:21	ND	HHO > PM
Luo Y (2011)	Chin J postgrad Med	60	31/29	50.5/51.3	ND	ND	HHO > PM
Wu ZY (2014)	Chin J Hepatopancreatobiliary Surgery	70	35/35	ND	ND	ND	ND
Total	-	688	343/345	-	-	-	-

PM: Pringle maneuver; HHO: Hemihepatic vascular occlusion; ND: The study did not describe.



**Figure 2.** Flowchart of risks of bias.

= [0.14, 7.25],  $P = 0.98$ ) without significant heterogeneity ( $P = 0.35$ ,  $I^2 = 0\%$ ) (**Figure 3A**).

### Hepatic insufficiency

Hepatic insufficiency was defined as the presence of serum bilirubin levels greater than 50  $\mu\text{mol/L}$  on postoperative day seven or thereafter or prothrombin time less than 50% of normal, or encephalopathy. Six studies [22-26, 28] including 530 patients reported severe liver dysfunction. The fixed model showed there was no difference between groups (RR = 2.11, 95% CI = [0.84, 5.31],  $P = 0.11$ ) without significant heterogeneity ( $P = 0.33$ ,  $I^2 = 14\%$ ) (**Figure 3B**).

### Peri-operative morbidity

Peri-operative morbidity was defined as complications that occurred within thirty days after the operation or during the same hospitalization. Seven trials [22-24, 26-29] including 628 patients reported peri-operative morbidity. The fixed model showed, without significant heterogeneity ( $P = 0.37$ ,  $I^2 = 7\%$ ), that the PM group had a statistically significant, higher rate of peri-operative morbidity than the HHO group

(RR = 1.52, 95% CI = [1.17, 1.96],  $P = 0.001$ ) (**Figure 3C**).

**Infection:** Infection referred to any infection documented in the postoperative period, including wound infection, which means an infection in the tissues of the incision and operative area. Four trials [23, 26, 27, 29] including 398 patients reported total infection, and three studies [23, 26, 27] with

298 patients reported wound infection. There was no significant heterogeneity (total infection:  $P = 0.19$ ,  $I^2 = 36\%$ , wound infection:  $P = 0.44$ ,  $I^2 = 0\%$ ). And the fixed model showed both parameters were not significantly different between the two groups (total infection: RR = 1.12, 95% CI = [0.53, 2.37],  $P = 0.77$ ; wound infection: RR = 1.02, 95% CI = [0.28, 3.75],  $P = 0.97$ ) (**Figure 3D, 3E**).

**Bile leakage:** Bile leakage was defined as any drainage through the catheter with a bilirubin content higher than that in the plasma. Seven studies [22-24, 26-29] including 628 patients reported bile leakage. The fixed model showed there was no difference between the two groups (RR = 1.22, 95% CI = [0.64, 2.34],  $P = 0.55$ ) without significant heterogeneity ( $P = 0.87$ ,  $I^2 = 0\%$ ) (**Figure 3F**).

**Splanchnocoel effusion:** Pleural effusion was defined as a fluid collection that required pleuracentesis to be controlled. Postoperative ascites was defined as an abdominal output greater than 500 ml/d or ascites that required treatment to be controlled. Five trials [23, 24,

## Pringle maneuver versus hemihepatic blood flow occlusion

**Table 2.** Risk of bias of included studies

First author (yrs.)	Randomization	Random sequence	Allocation concealment	Patient baseline characteristics	Blinding	Intention-to-treat analysis	Follow-up
Figueras J (2005)	Yes	Sortition and stratification	Yes	Yes	Single	Yes	100%
Wu CC (2002)	Yes	Sortition	Yes	Yes	ND	Yes	100%
Fu SY (2011)	Yes	Sortition	Yes	Yes	ND	Yes	100%
Liang G (2009)	Yes	ND	ND	Yes	ND	Yes	100%
Ni JS (2013)	Yes	Sortition	Yes	Yes	ND	Yes	100%
Xiao J (2015)	Yes	Dice rolling	ND	Yes	ND	Yes	100%
Luo Y (2011)	Yes	Randomized number table	ND	Yes	ND	Yes	100%
Wu ZY (2014)	Yes	Computer randomization	ND	Yes	ND	Yes	100%

ND: The study did not describe.

26, 27, 29] including 478 patients reported pleural effusion, and six trials [22-24, 26, 27, 29] including 558 patients reported ascites. There was no significant heterogeneity (pleural effusion:  $P = 0.87$ ,  $I^2 = 0\%$ ; ascites:  $P = 0.82$ ,  $I^2 = 0\%$ ) and the fixed model showed both of the parameters were not significantly different between the two groups (pleural effusion:  $RR = 1.42$ ,  $95\% CI = [0.79, 2.55]$ ,  $P = 0.24$ ; ascites:  $RR = 1.31$ ,  $95\% CI = [0.67, 2.58]$ ,  $P = 0.43$ ) (**Figure 4A, 4B**).

**Postoperative hemorrhage:** Postoperative hemorrhage was defined as bleeding after a surgical procedure. Five trials [23, 25-28] including 428 patients reported total bleeding, and two trials [27, 28] including 128 patients reported gastrointestinal bleeding. There was no significant heterogeneity (total bleeding:  $P = 0.96$ ,  $I^2 = 0\%$ ; gastrointestinal bleeding:  $P = 0.58$ ,  $I^2 = 0\%$ ) and the fixed model showed both of the parameters were not significantly different between the two groups (total bleeding:  $RR = 2.17$ ,  $95\% CI = [0.63, 7.50]$ ,  $P = 0.22$ ; gastrointestinal bleeding:  $RR = 1.72$ ,  $95\% CI = [0.24, 12.55]$ ,  $P = 0.59$ ) (**Figure 4C, 4D**).

**Qualitative transfusion (person):** Blood transfusion was performed when intraoperative hematocrit was less than 0.24 in patients with normal cardiopulmonary function or below 0.27 in patients aged 70 years or older or with correctable heart or lung diseases. This was continued until the early postoperative period, when fresh frozen plasma, albumin, or both were infused to keep the serum albumin level at 30 g/L or higher. Five studies [22-24, 26, 27] including 458 patients reported this parameter. The fixed model showed no difference between the two groups ( $RR = 1.14$ ,  $95\% CI =$

$[0.77, 1.68]$ ,  $P = 0.53$ ) without significant heterogeneity ( $P = 0.27$ ,  $I^2 = 22\%$ ) (**Figure 4E**).

**Quantitative Transfusion (ml):** Five studies [22-24, 26, 29] including 500 patients reported this parameter. The random model showed the PM group had statistically significant more blood transfusions than the HHO group (standard mean difference [SMD] = 0.45,  $95\% CI = [0.07, 0.83]$ ,  $P = 0.02$ ) with significant heterogeneity ( $P = 0.001$ ,  $I^2 = 78\%$ ) (**Figure 4F**).

### Secondary outcomes

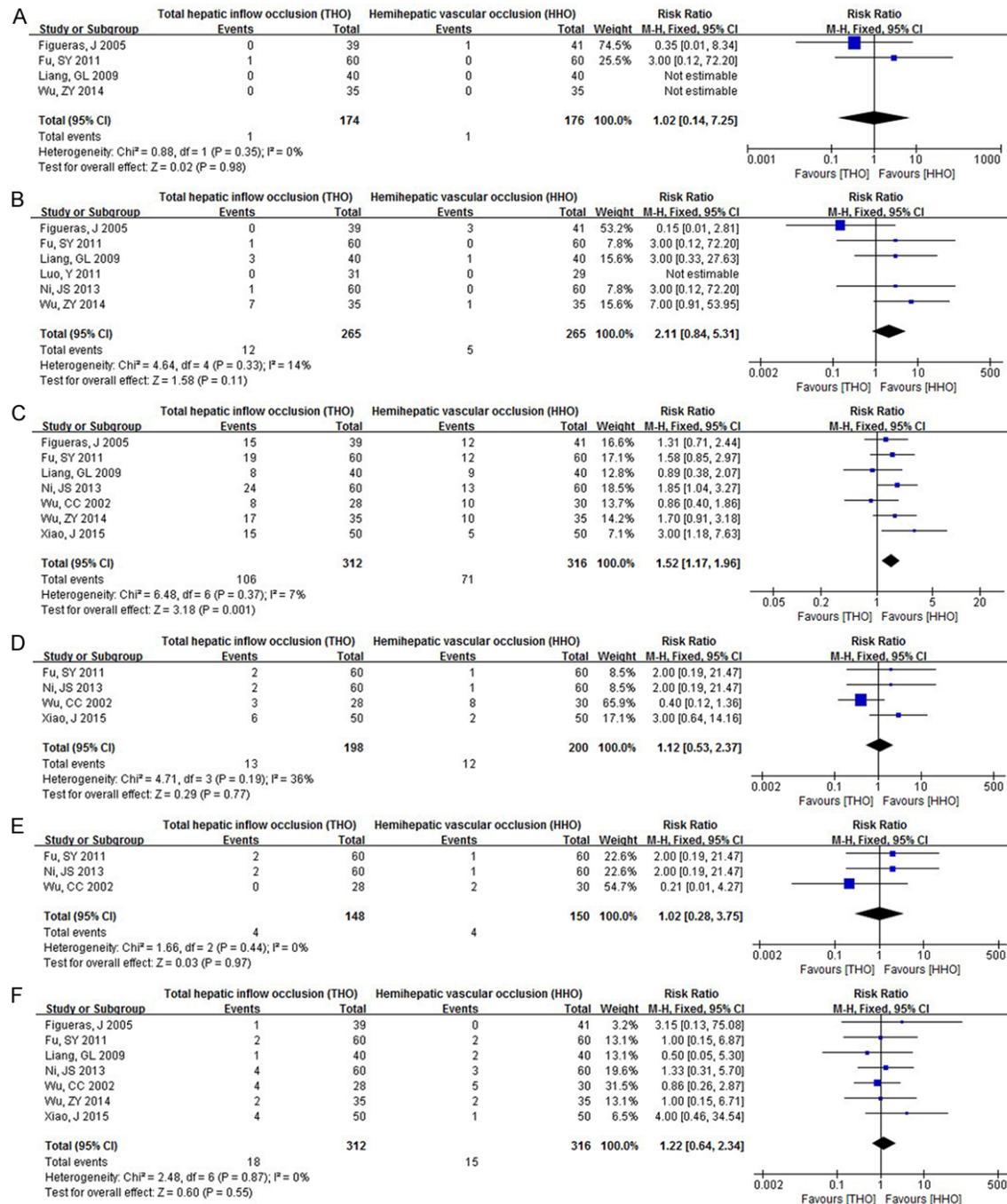
#### Hospital stay (day)

Hospital stay was defined as the length of stay of the patient at the hospital. Four studies [22-24, 27] including 338 patients reported this parameter. The random model showed no difference between the two groups (SMD = -0.03,  $95\% CI = [-0.75, 0.69]$ ,  $P = 0.94$ ) with significant heterogeneity ( $P < 0.001$ ,  $I^2 = 90\%$ ) (**Figure 5A**).

#### Operation time (min) and ischemic duration (min)

Operation time was measured from the beginning to the end of liver transection. Seven trials [22-24, 26-29] with 628 patients reported the operation time. Due to significant heterogeneity ( $P < 0.001$ ,  $I^2 = 79\%$ ), the random model was applied, and no significant difference was found between the two groups (SMD = -0.21,  $95\% CI = [-0.57, 0.14]$ ,  $P = 0.24$ ) (**Figure 5**). Ischemic duration was defined as the total time required for the administration of the PM for the PM group, from the beginning of the ipsilateral portal vein and the artery occlusion to the release of the portal vein and the artery for the

## Pringle maneuver versus hemihepatic blood flow occlusion



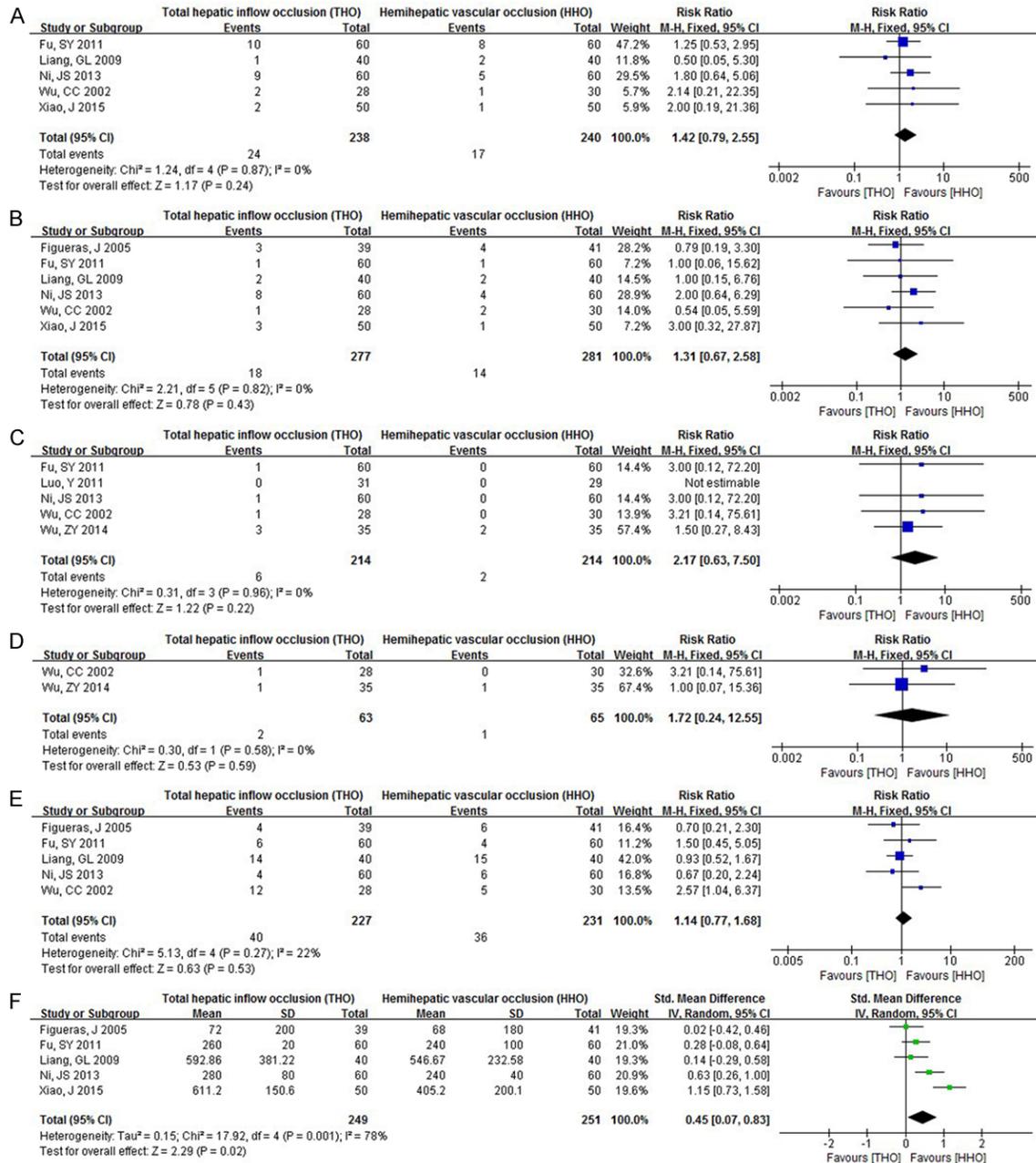
**Figure 3.** Forest plots of the Pringle maneuver (PM) versus hemihepatic blood flow occlusion (HHO) during hepatectomy. They are mortality (A), hepatic insufficiency (B), peri-operative morbidity (C), total infection (D), wound infection (E) and bile leakage (F) respectively.

HHO group. Eight studies [22-29] with 688 patients reported the ischemic duration. The random model showed no difference between the two groups (SMD = 0.09, 95% CI = [-0.15, 0.32], P = 0.46) with significant heterogeneity (P = 0.02, I<sup>2</sup> = 58%) (Figure 5B, 5C).

### Operative blood loss (ml)

Blood loss was measured by estimating the weight of the soaked gauze and the blood collected in the suction apparatus containers. Five studies [22-24, 28, 29] including 450 patients

# Pringle maneuver versus hemihepatic blood flow occlusion



**Figure 4.** Forest plots of the Pringle maneuver (PM) versus hemihepatic blood flow occlusion (HHO) during hepatectomy. They are pleural effusion (A), ascites (B), total bleeding (C), gastrointestinal bleeding (D), qualitative transfusion (person) (E), quantitative transfusion (ml) (F) respectively.

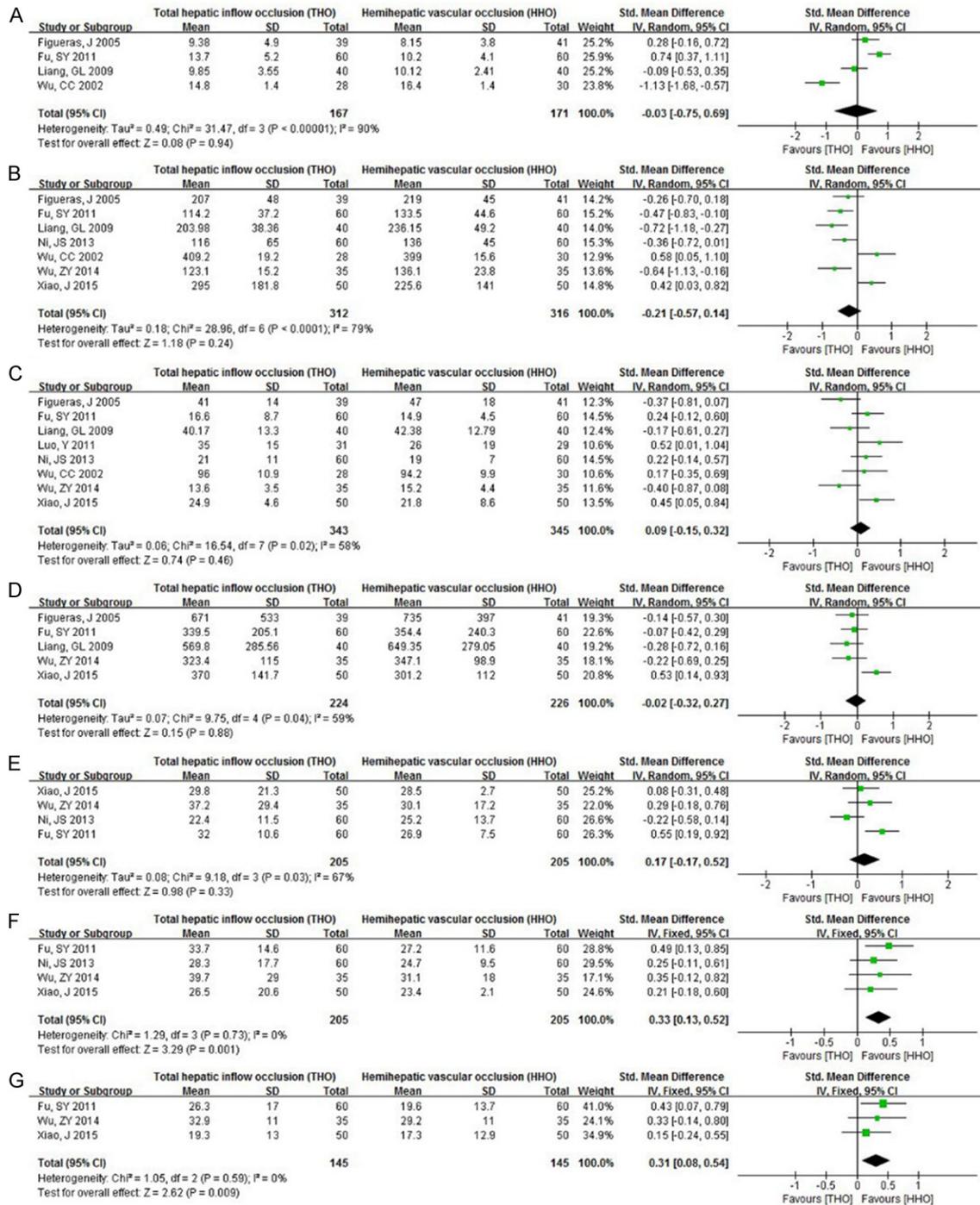
reported this parameter. The data showed no difference between the two groups (SMD = -0.02, 95% CI = [-0.32, 0.27], P = 0.88) with significant heterogeneity (P = 0.04, I<sup>2</sup> = 59%) (Figure 5D).

Markers of liver function: TBIL (μmol/L), ALB (g/L), PAB (g/L)

Four studies [23, 26, 28, 29] including 410 patients reported TBIL of the first and third

days after operation, and three trials [23, 28, 29] with 290 patients reported TBIL of the seventh day post-operation. TBIL level on the first day showed significant heterogeneity (P = 0.03, I<sup>2</sup> = 67%), and the random model showed no significant difference between the two groups (SMD = 0.17, 95% CI = [-0.17, 0.52], P = 0.33). There was no significant heterogeneity about the parameters of the third (P = 0.73, I<sup>2</sup> = 0%) and seventh (P = 0.59, I<sup>2</sup> = 0%) days after oper-

# Pringle maneuver versus hemihepatic blood flow occlusion

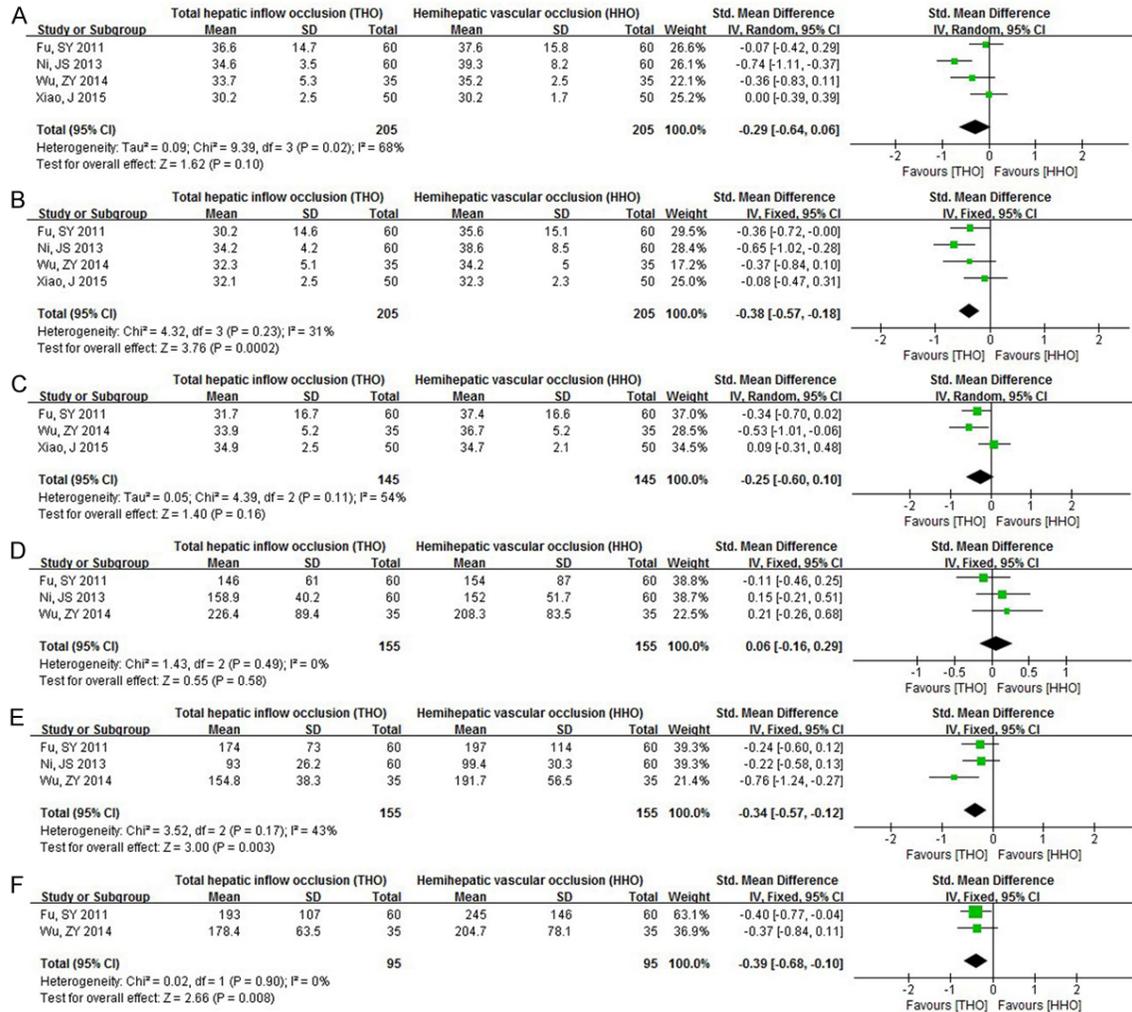


**Figure 5.** Forest plots of the Pringle maneuver (PM) versus hemihepatic blood flow occlusion (HHO) during hepatectomy. They are hospital stay (A), operative time (B), ischemic duration (C), operative blood loss (D), total bilirubin (TBIL) levels on the first (E), third (F) or seventh (G) day respectively.

ation. The fixed model showed that the PM group had a statistically significant, higher TBIL level (the third day, SMD = 0.33, 95% CI = [0.13, 0.52], P = 0.001; the seventh day, SMD = 0.31, 95% CI = [0.08, 0.54], P = 0.009) (Figure 5E-G).

In four studies [23, 26, 28, 29], including 410 patients ALB levels on the first and third days after operation were reported. Three trials [23, 28, 29] with 290 patients revealed ALB levels on the seventh day post-operation. The ALB

# Pringle maneuver versus hemihepatic blood flow occlusion



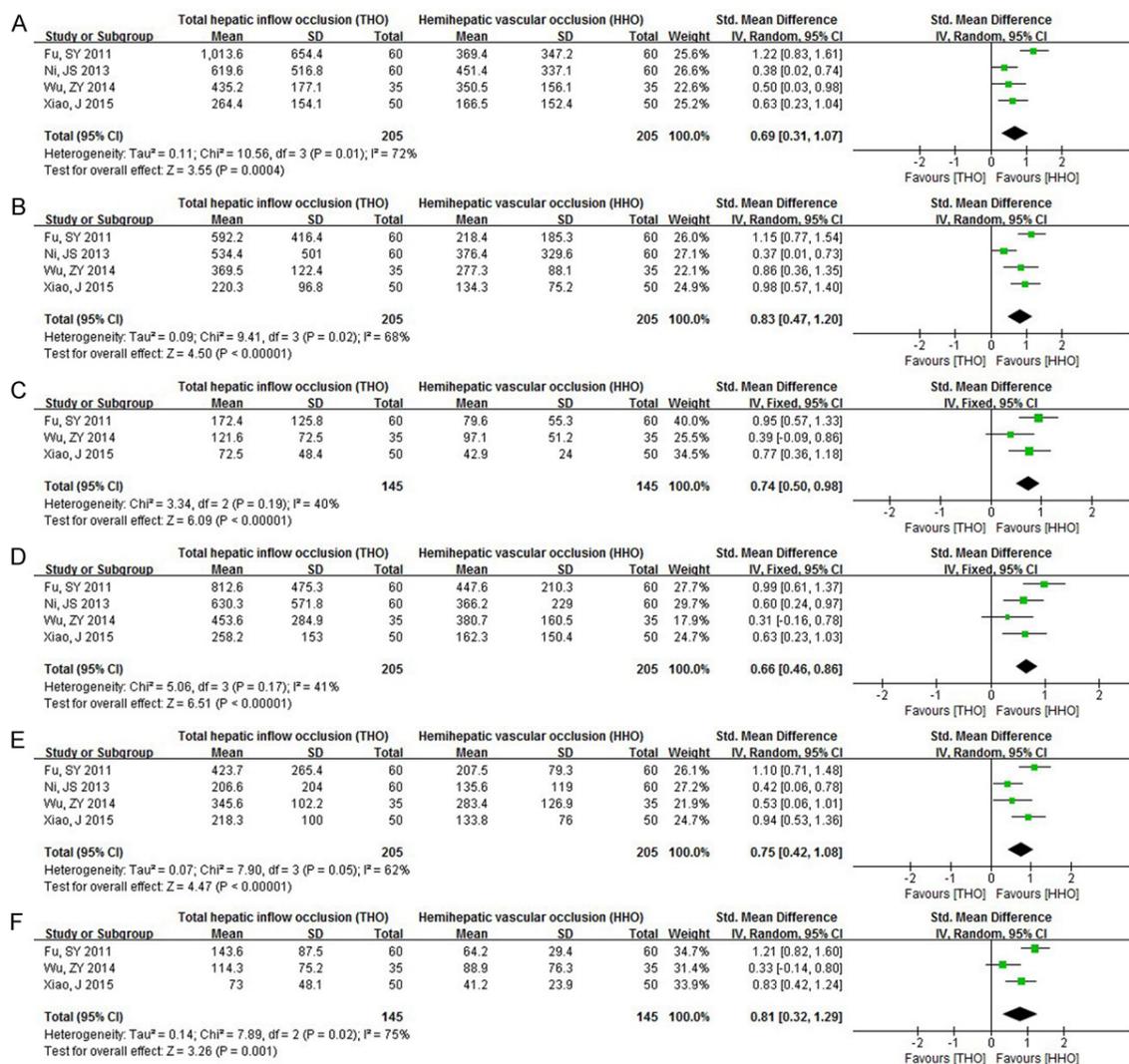
**Figure 6.** Forest plots of the Pringle maneuver (PM) versus hemihepatic blood flow occlusion (HHO) during hepatectomy. They are albumin (ALB) levels on the first (A), third (B) or seventh (C) day and prealbumin (PAB) levels on the first (D), third (E) or seventh (F) day respectively.

level of the first day showed significant heterogeneity ( $P = 0.02$ ,  $I^2 = 68\%$ ), and the random model showed no significant difference between the two groups (SMD = -0.29, 95% CI = [-0.64, 0.06],  $P = 0.10$ ). ALB data of the third day showed no significant heterogeneity ( $P = 0.23$ ,  $I^2 = 31\%$ ), and the fixed model showed a statistically significant difference between the two groups (SMD = -0.38, 95% CI = [-0.57, -0.18],  $P < 0.001$ ). However, the ALB level of the seventh day showed no statistical difference between the two groups (SMD = -0.25, 95% CI = [-0.60, 0.10],  $P = 0.16$ ) by the random model with heterogeneity ( $P = 0.11$ ,  $I^2 = 54\%$ ) (Figure 6A-C).

Three trials [23, 26, 28] including 310 patients reported the PAB on the first and third days

after operation, and two trials [23, 28] with 190 patients for the seventh day. The data showed no significant heterogeneity of PAB on the first day ( $P = 0.49$ ,  $I^2 = 0\%$ ), and the fixed model showed no significant difference between the two groups (SMD = 0.06, 95% CI = [-0.16, 0.29],  $P = 0.58$ ). The third day data showed heterogeneity ( $P = 0.17$ ,  $I^2 = 43\%$ ), and the fixed model showed a statistically significant, lower level of PAB in the PM group (SMD = -0.34, 95% CI = [-0.57, -0.12],  $P = 0.003$ ) compared to the HHO group. PAB level of the seventh day showed that the PM group had a statistically significant, lower pre-ALB level by fixed model (SMD = -0.39, 95% CI = [-0.68, -0.10],  $P = 0.008$ ) with no significant heterogeneity ( $P = 0.90$ ,  $I^2 = 0\%$ ) (Figure 6D-F).

## Pringle maneuver versus hemihepatic blood flow occlusion



**Figure 7.** Forest plots of the Pringle maneuver (PM) versus hemihepatic blood flow occlusion (HHO) during hepatectomy. They are alanine aminotransferase (ALT) levels on the first (A), third (B) or seventh (C) day and aspartate aminotransferase (AST) levels on the first (D), third (E) or seventh (F) day respectively.

### Biochemical markers of liver injury: ALT, AST

Four studies [23, 26, 28, 29] including 410 patients for ALT on the first and third days after operation, and three trials [23, 28, 29] with 290 patients for the seventh day post-operation. Significant heterogeneity was observed for the parameters of the first (P = 0.01, I<sup>2</sup> = 72%) and third (P = 0.02, I<sup>2</sup> = 68%) days after operation. The random model showed that the PM group had a statistically significant, higher ALT level (the first day, SMD = 0.69, 95% CI = [0.31, 1.07], P < 0.001; the third day, SMD = 0.83, 95% CI = [0.47, 1.20], P < 0.001) than the HHO group. ALT level of the seventh day showed no

significant heterogeneity (P = 0.19, I<sup>2</sup> = 40%), and the fixed model showed the same result as the first and third days after operation (SMD = 0.74, 95% CI = [0.50, 0.98], P < 0.001) (**Figure 7A-C**).

Four trials [23, 26, 28, 29] including 410 patients for AST on the first and third days after operation, and three trials [23, 28, 29] with 290 patients for the seventh day post-operation. The data showed no significant heterogeneity for AST levels on the first day post-operation (P = 0.17, I<sup>2</sup> = 41%). The fixed model showed a statistically significant higher AST level in the PM group compared to the HHO group on the

## Pringle maneuver versus hemihepatic blood flow occlusion

**Table 3.** Publication bias

Outcomes	SMD/OR Fluctuation	95% CI Fluctuation	Publication Bias (P value)
<b>Primary Outcomes</b>			
Mortality	0.34~3.05	0.01~76.39	N
Hepatic insufficiency	1.21~4.70	0.38~16.82	N
Peri-operative morbidity	1.62~1.96	1.11~2.87	0.453
Total infection	0.70~2.62	0.25~8.58	0.451
Wound infection	0.73~2.03	0.14~11.32	N
Bile leakage	1.02~1.41	0.48~3.17	0.799
Pleural effusion	1.30~1.63	0.58~3.91	0.832
Ascites	1.03~1.56	0.42~3.56	0.485
Postoperative hemorrhage	-0.16~0.04	-0.41~0.38	0.851
Total bleeding	2.07~3.14	0.49~20.23	N
Gastrointestinal bleeding	1.00~3.32	0.06~85.11	N
Quantitative transfusion (ml)	0.29~0.55	-0.09~0.99	0.245
Qualitative transfusion (person)	0.89~1.34	0.50~2.49	0.888
<b>Secondary Outcomes</b>			
Hospital stay	-0.30~0.32	-1.17~1.00	0.868
Operation time	-0.33~0.13	-0.66~0.25	0.067
Ischemic duration	0.03~0.15	-0.21~0.38	0.552
<b>TBIL</b>			
1st day	0.02~0.32	-0.31~0.69	0.241
3rd day	0.26~0.37	0.03~0.59	0.085
7th day	0.23~0.40	-0.07~0.69	0.828
<b>ALB</b>			
1st day	-0.39~0.11	-0.83~0.20	0.048
3rd day	-0.48~0.27	-0.70~0.04	0.265
7th day	-0.41~0.14	-0.82~0.40	0.275
<b>PAB</b>			
1st day	0.01~0.17	-0.28~0.46	0.911
3rd day	-0.43~0.23	-0.71~0.14	0.342
7th day	-0.41~0.40	-0.84~0.10	N
<b>ALT</b>			
1st day	0.50~0.75	0.17~1.25	0.205
3rd day	0.73~1.03	0.30~1.32	0.568
7th day	0.61~0.87	0.30~1.15	0.869
<b>AST</b>			
1st day	0.54~0.74	0.30~0.96	0.266
3rd day	0.63~0.89	0.26~1.24	0.099
7th day	0.60~1.03	-0.08~1.65	0.689

Note: P < 0.05: The existence of publication bias; N: Insufficient observations for analysis; SMD: Standardized mean difference.

first day after operation (SMD = 0.66, 95% CI = [0.46, 0.86], P < 0.001). Significant heterogeneity for the parameters of the third (P = 0.05, I<sup>2</sup> = 62%) and the seventh day (P = 0.02, I<sup>2</sup> = 75%) after operation was manifest. The random model showed that the PM group had a statistically significant, higher AST level than the HHO group (the third day, SMD = 0.75, 95%

CI = [0.42, 1.08], P < 0.001; the seventh day, SMD = 0.81, 95% CI = [0.32, 29], P = 0.001) (Figure 7D-F).

### Sensitivity analysis and publication bias

The sensitivity analysis [30] showed that, except for TBIL on the first and seventh days,

ALB on the seventh day, PAB on the third and seventh days, AST on the seventh day, and quantitative transfusion (ml), all results were consistently reported in all included studies, which means most of the study parameters are stable and reliable. To assess publication bias, we used the Egger's test [31, 32]. Only ALB on the first day had a low *P* value ( $< 0.05$ ) (**Table 3**), but both the fixed and random effects model results of ALB data were unchanged by the trim and fill method. Therefore, as shown, the results in our study are stable and valid.

### Discussion

This systematic review summarizes the best available evidence relating to the safety and effectiveness of the PM versus HHO during hepatectomy. After an extensive search of the literature, eight RCTs were identified and included in this review and analysis.

In our analysis, we mainly evaluated primary and secondary outcomes. The primary outcomes consisted of mortality, hepatic insufficiency, peri-operative morbidity, and transfusion requirements. The evidence regarding mortality, hepatic insufficiency, and the number of patients who needed transfusion suggests that there is no significant difference between PM and HHO, which is supported by the results of a retrospective study [33] and a meta-analysis [17]. However, Tanaka K et al. reported that a slightly lower proportion of patients needed transfusion in the PM group than in HHO group [13]. In addition, Yu W et al. found that more patients needed transfusion in the PM group than in HHO group because the average clamping frequency was  $1.6 \pm 0.7$  min and the average clamping period was  $17.1 \pm 4.7$  min in PM group, while one-time clamping was adopted and the mean clamping duration was  $20.9 \pm 5.3$  min in HHO group [34]. As for transfusion volume, our study suggests that there is a little difference between the two groups, similar to the findings of a retrospective study by Li MH et al. [33]. Regarding peri-operative morbidity, our results showed that there was no significant difference between groups in any type of complication. However, the overall peri-operative morbidity rate in the PM group was significantly higher than that in the HHO group, similar to that found by Zhang Y and his team [35]. Yi B et al. found that the incidence of complications in

the PM group (18.9%) was significantly higher than that of the HHO group [36]; however, they did not perform further research for any other type of complications.

The secondary outcomes included hospital stay, operating time, ischemic duration, operative blood loss, markers of liver function, and biochemical markers of liver injury. There was no difference between the PM and HHO group in hospital stay, which contradicts the findings of a retrospective study, that revealed the average hospitalization days for the PM and HHO groups were  $18.9 \pm 4.4$  and  $16.2 \pm 3.2$ , respectively, which represented a statistically significant difference between groups [34]. There was no significant difference between the PM and HHO groups in operating time, ischemic duration and operative blood loss, which contradicts the conclusions of previous retrospective studies [35, 36]. Zhang Y et al. showed that the mean amount of intraoperative blood loss in the PM group was significantly greater than that in the HHO group ( $568.2 \pm 325.1$  vs.  $420.7 \pm 307.2$  mL,  $P = 0.0444$ ) [35]. However, Li MH and his team found that the volume of blood loss was greater in the HHO group than in the PM group, but the difference was not significant ( $P > 0.05$ ) [33]. In addition, a meta-analysis by Wang HQ et al. suggested that blood loss in three trials showed no significant difference between the PM group and HHO group, further supporting our conclusion.

In our analysis, we used TBIL, ALB, and PAB to reflect post-operative liver function. Although TBIL showed no significant difference between the PM and HHO groups before the surgery and on day one, TBIL increased much more in the PM group than in the HHO group on days three and seven. ALB was lower in the PM group than in the HHO group on day three and PAB was lower in the PM group than in the HHO group on days three and seven. All of the post-operative liver function findings indicate that PM surgery can significantly induce ischemia reperfusion injury of the liver. The outcomes regarding biochemical markers of liver injury such as ALT and AST further support the above conclusion. Our analysis suggested that ALT and AST in the PM group were much higher than in the HHO group on days one, three, and seven. This conclusion is supported by many retrospective studies [33, 34, 36, 37]. For instance, Li MH et

al. found that ALT, AST, and TBIL increased much more in the PM group than in the HHO group [33]. However, Zhang Y et al. arrived at a different conclusion that no significant differences between the two groups were observed in ALT and AST levels on postoperative days one and three. Only on the postoperative day seven, the PM group showed significantly higher ALT and AST levels than the HHO group and the finding was against the authors' expectations mainly due to the dramatic variance in ALT and AST levels and the statistical variation of a small sample size [35].

Our results highlight the need for a high level, good quality research into the safety and effectiveness of the PM versus HHO maneuver during hepatectomy. Only RCTs were included in this systematic review and meta-analysis. We analyzed many trials, and the studies that met our inclusion criteria spanned a period from 1990 to 2013. Most of our parameters are stable as shown in our sensitivity analysis, and only one parameter showed publication bias, which means our result is reliable. This systematic review and meta-analysis has some limitations. First, incomplete reporting of important methodological issues, such as sample size calculations, randomization processes, and blinding assessment of trial quality, might raise doubts about the adequate power of these studies. Second, we did not analyze the indicator to reflect the hemodynamic change between the PM and HHO groups, which is an important part of evaluating the safety and effectiveness of PM versus HHO during hepatectomy, because no data is available. Lastly, although we searched for unpublished data, no unpublished data were available; therefore, our data analysis is based on published data only.

### Conclusions

In conclusion, the evidence shows a great advantage of the HHO over the PM, in terms of transfusion volume, peri-operative morbidity, markers of liver function, and biochemical markers of liver injury. However, no statistical difference was found in mortality, hepatic insufficiency, any type of complications, number of patients who need transfusion, hospital stay, operating time, ischemic duration, and operative blood loss between the PM and HHO groups. Our findings highlight the need for more

rigorous RCTs comparing PM versus HHO during hepatectomy and more robust, more convincing meta-analyses as well as uniformity in data selection and reporting.

### Acknowledgements

This work was supported by the National Natural Science Foundation of China (No. 81372631).

### Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Zhiming Wang, Department of General Surgery, Xiangya Hospital, Central South University, Xiangya Road 87, Changsha 410008, China. Tel: +8613808462382; E-mail: a846957007@163.com

### References

- [1] Bergoc RM and Caro RA. The competitive nature of reticuloendothelial "blockade". *Int J Nucl Med Biol* 1975; 2: 33-36.
- [2] Yi NJ, Suh KS, Kim T, Kim J, Shin WY and Lee KU. Current role of surgery in treatment of early stage hepatocellular carcinoma: resection versus liver transplantation. *Oncology* 2008; 75 Suppl 1: 124-128.
- [3] Jarnagin WR, Gonen M, Fong Y, DeMatteo RP, Ben-Porat L, Little S, Corvera C, Weber S and Blumgart LH. Improvement in perioperative outcome after hepatic resection: analysis of 1,803 consecutive cases over the past decade. *Ann Surg* 2002; 236: 397-406; discussion 406-397.
- [4] Li X, Jiang W, Feng T and Wang Z. Concurrent occurrence of primary hepatocellular and cholangiocellular carcinoma in the different part of the liver: a case report. *Int J Clin Exp Med* 2012; 5: 355-357.
- [5] Stephenson KR, Steinberg SM, Hughes KS, Vetto JT, Sugarbaker PH and Chang AE. Perioperative blood transfusions are associated with decreased time to recurrence and decreased survival after resection of colorectal liver metastases. *Ann Surg* 1988; 208: 679-687.
- [6] Wang ZM, Lu XS and Qiu F. Hepatectomy for spontaneous rupture of hepatocellular carcinoma without portal triad clamping. *Oncol Lett* 2017; 14: 3997-4004.
- [7] Bossola M, Pacelli F, Bellantone R and Doglietto GB. Influence of transfusions on perioperative and long-term outcome in patients following hepatic resection for colorectal metastases. *Ann Surg* 2005; 241: 381.

## Pringle maneuver versus hemihepatic blood flow occlusion

- [8] Wei AC, Tung-Ping Poon R, Fan ST and Wong J. Risk factors for perioperative morbidity and mortality after extended hepatectomy for hepatocellular carcinoma. *Br J Surg* 2003; 90: 33-41.
- [9] Pringle JH. V. Notes on the arrest of hepatic hemorrhage due to trauma. *Ann Surg* 1908; 48: 541-549.
- [10] Man K, Fan ST, Ng IO, Lo CM, Liu CL, Yu WC and Wong J. Tolerance of the liver to intermittent pringle maneuver in hepatectomy for liver tumors. *Arch Surg* 1999; 134: 533-539.
- [11] Wu CC, Hwang CR, Liu TJ and P'Eng FK. Effects and limitations of prolonged intermittent ischaemia for hepatic resection of the cirrhotic liver. *Br J Surg* 1996; 83: 121-124.
- [12] Makuuchi M, Mori T, Gunven P, Yamazaki S and Hasegawa H. Safety of hemihepatic vascular occlusion during resection of the liver. *Surg Gynecol Obstet* 1987; 164: 155-158.
- [13] Tanaka K, Shimada H, Togo S, Nagano Y, Endo I and Sekido H. Outcome using hemihepatic vascular occlusion versus the pringle maneuver in resections limited to one hepatic section or less. *J Gastrointest Surg* 2006; 10: 980-986.
- [14] Gotoh M, Monden M, Sakon M, Kanai T, Umeshita K, Nagano H and Mori T. Hilar lobar vascular occlusion for hepatic resection. *J Am Coll Surg* 1994; 178: 6-10.
- [15] Gurusamy KS, Sheth H, Kumar Y, Sharma D and Davidson BR. Methods of vascular occlusion for elective liver resections. *Cochrane Database Syst Rev* 2009; CD007632.
- [16] Lau WY, Lai EC and Lau SH. Methods of vascular control technique during liver resection: a comprehensive review. *Hepatobiliary Pancreat Dis Int* 2010; 9: 473-481.
- [17] Wang HQ, Yang JY and Yan LN. Hemihpatic versus total hepatic inflow occlusion during hepatectomy: a systematic review and meta-analysis. *World J Gastroenterol* 2011; 17: 3158-3164.
- [18] Pt HSJ. *Cochrane Handbook for Systematic Reviews of Interventions* 2009. 2009.
- [19] Higgins JP and Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002; 21: 1539-1558.
- [20] Demets DL. Methods for combining randomized clinical trials: strengths and limitations. *Stat Med* 1987; 6: 341-350.
- [21] DerSimonian R and Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; 7: 177-188.
- [22] Figueras J, Llado L, Ruiz D, Ramos E, Busquets J, Rafecas A, Torras J and Fabregat J. Complete versus selective portal triad clamping for minor liver resections: a prospective randomized trial. *Ann Surg* 2005; 241: 582-590.
- [23] Fu SY, Lau WY, Li GG, Tang QH, Li AJ, Pan ZY, Huang G, Yin L, Wu MC, Lai EC and Zhou WP. A prospective randomized controlled trial to compare Pringle maneuver, hemihepatic vascular inflow occlusion, and main portal vein inflow occlusion in partial hepatectomy. *Am J Surg* 2011; 201: 62-69.
- [24] Liang G, Wen T, Yan L, Li BO, Wu G, Yang J, Lu B, Chen Z, Liao Z, Ran S and Yu Z. A prospective randomized comparison of continuous hemihepatic with intermittent total hepatic inflow occlusion in hepatectomy for liver tumors. *Hepatogastroenterology* 2009; 56: 745-750.
- [25] Luo Y, Qin HJ and Luo W. A comparison of hemihepatic and total hepatic inflow occlusion in hepatectomy. *Chin J Postgrad Med* 2011; 34: 36-37.
- [26] Ni JS, Lau WY, Yang Y, Pan ZY, Wang ZG, Liu H, Wu MC and Zhou WP. A prospective randomized controlled trial to compare pringle manoeuvre with hemi-hepatic vascular inflow occlusion in liver resection for hepatocellular carcinoma with cirrhosis. *J Gastrointest Surg* 2013; 17: 1414-1421.
- [27] Wu CC, Yeh DC, Ho WM, Yu CL, Cheng SB, Liu TJ and P'Eng FK. Occlusion of hepatic blood inflow for complex central liver resections in cirrhotic patients: a randomized comparison of hemihepatic and total hepatic occlusion techniques. *Arch Surg* 2002; 137: 1369-1376.
- [28] Wu ZY, Feng JY, Wang JB, Li YH, Hu YH and Wang JF. Study of Glisson clinic cross-sectional hepatectomy in liver cancer. *Journal of Hepatopancreatobiliary Surgery* 2014; 26: 342-4.
- [29] Xiao J, Zhong TM, Liu QQ, Deng XM, Wu YX and Lu BZ. Value of high selective inflow occlusion in hemihepatectomy. *Chinese Journal of Clinical Rational Drug Use* 2015; 94-95.
- [30] Sweeting MJ, Sutton AJ and Lambert PC. What to add to nothing? Use and avoidance of continuity corrections in meta-analysis of sparse data. *Stat Med* 2004; 23: 1351-1375.
- [31] Duval S and Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 2000; 56: 455-463.
- [32] Egger M, Davey Smith G, Schneider M and Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; 315: 629-634.
- [33] Li M, Zhang C, Zhang T, Wang L, Ding Y, Niu Z, He S and Yang Z. Outcome using selective hemihepatic vascular occlusion and Pringle maneuver for hepatic resection of liver cavernous hemangioma. *World J Surg Oncol* 2015; 13: 267.
- [34] Wen Y, Miao X, Xiong L, Xiong G, Hu J, Zhong D, Li Q and Liu W. Application of hemihepatic vas-

## Pringle maneuver versus hemihepatic blood flow occlusion

- cular occlusion with hanging maneuver in hepatectomy. *Hepatogastroenterology* 2009; 56: 442-446.
- [35] Zhang Y, Yang H, Deng X, Chen Y, Zhu S and Kai C. Intermittent Pringle maneuver versus continuous hemihepatic vascular inflow occlusion using extra-glissonian approach in laparoscopic liver resection. *Surg Endosc* 2016; 30: 961-970.
- [36] Yi B, Qiu YH, Liu C, Luo XJ, Jiang XQ, Tan WF and Wu MC. Hepatic blood inflow occlusion with/without hemihepatic artery control versus the Pringle maneuver in resection of hepatocellular carcinoma: a retrospective comparative analysis. *Chin Med J (Engl)* 2010; 123: 1413-1416.
- [37] Chau GY, Lui WY, King KL and Wu CW. Evaluation of effect of hemihepatic vascular occlusion and the Pringle maneuver during hepatic resection for patients with hepatocellular carcinoma and impaired liver function. *World J Surg* 2005; 29: 1374-1383.

# Pringle maneuver versus hemihepatic blood flow occlusion

**Supplementary Table 1.** Search strategies

Database	Amount	Search strategy used
Pubmed	2340	(((Hemihepatic[Title/Abstract] OR half-hepatic[Title/Abstract] OR selective[Title/Abstract] OR portal[Title/Abstract] OR alternative[Title/Abstract] OR selectional[Title/Abstract] OR elective[Title/Abstract] OR preferential[Title/Abstract] OR optional[Title/Abstract]) AND (occlusion[Title/Abstract] OR control[Title/Abstract] OR clamping[Title/Abstract] OR interdict[Title/Abstract] OR cut off[Title/Abstract] OR Blocking[Title/Abstract] OR Infubulation[Title/Abstract] OR (half[Title/Abstract] AND Pringle[Title/Abstract])) AND (Pringle[Title/Abstract] OR ((Hepatic[Title/Abstract] OR Liver[Title/Abstract]) AND (occlusion[Title/Abstract] OR control[Title/Abstract] OR clamping[Title/Abstract] OR interdict[Title/Abstract] OR cut off[Title/Abstract] OR Blocking[Title/Abstract] OR Infubulation[Title/Abstract] OR artery[Title/Abstract] OR portal[Title/Abstract] OR venous[Title/Abstract] OR vesse[Title/Abstract] OR flow[Title/Abstract] OR inflow[Title/Abstract])) AND (((Liver[MeSH Terms] OR Liver Neoplasms[MeSH Terms] OR Liver Diseases[MeSH Terms] OR liver[Title/Abstract] OR hepatic[Title/Abstract]) AND (Operation[Title/Abstract] OR Surgery[Title/Abstract] OR Segmentectomy[Title/Abstract] OR resection[Title/Abstract] OR excision[Title/Abstract] OR transplant*[Title/Abstract] OR graft*[Title/Abstract])) OR (Hepatectomy[MeSH Terms] OR Liver Transplantation[MeSH Terms])) AND (Clinical Trial[Publication Type] OR Multicenter Study [Publication Type] OR Clinical Trials as Topic[MeSH Terms] OR Perspect*[Title/Abstract] OR Multicent*[Title/Abstract] OR follow-up[Title/Abstract] OR Follow[Title/Abstract] OR Following[Title/Abstract] OR Meta-Analysis[Title/Abstract] OR (Meta[Title/Abstract] AND Analysis[Title/Abstract]) OR Random*[Title/Abstract] OR Stochastic[Title/Abstract] OR Placebo*[Title/Abstract] OR Blind[Title/Abstract] OR Blinding[Title/Abstract] OR Control*[Title/Abstract] OR Compar*[Title/Abstract] OR Contrast[Title/Abstract] OR EDCC[Title/Abstract] OR group[Title/Abstract] OR groups[Title/Abstract]))
Embase	3967	(((Hemihepatic:ti,ab OR half-hepatic:ti,ab OR selective:ti,ab OR portal:ti,ab OR alternative:ti,ab OR selectional:ti,ab OR elective:ti,ab OR preferential:ti,ab OR optional:ti,ab) AND (occlusion:ti,ab OR control:ti,ab OR clamping:ti,ab OR interdict:ti,ab OR (cut:ti,ab AND off:ti,ab) OR Blocking:ti,ab OR Infubulation:ti,ab) OR (half:ti,ab AND Pringle:ti,ab)) AND (Pringle:ti,ab OR ((Hepatic:ti,ab OR Liver:ti,ab) AND (occlusion:ti,ab OR control:ti,ab OR clamping:ti,ab OR interdict:ti,ab OR (cut:ti,ab AND off:ti,ab) OR Blocking:ti,ab OR Infubulation:ti,ab))) AND (Vascular:ti,ab OR Vein:ti,ab OR artery:ti,ab OR portal:ti,ab OR venous:ti,ab OR vessel:ti,ab OR flow:ti,ab OR inflow:ti,ab) AND (((‘Liver’/exp OR ‘liver tumor’/exp OR ‘liver disease’/exp OR liver:ti,ab OR hepatic:ti,ab) AND (Operation:ti,ab OR Surgery:ti,ab OR Segmentectomy:ti,ab OR resection:ti,ab OR excision:ti,ab OR transplant*:ti,ab OR graft*:ti,ab)) OR (‘liver resection’/exp OR ‘Liver Transplantation’/exp)) AND (‘comparative study’/exp OR ‘controlled study’/exp OR ‘first in human study’/exp OR ‘human’/exp OR ‘human versus animal comparison’/exp OR ‘field study’/exp OR ‘clinical study’/exp OR ‘human experiment’/exp OR ‘in vivo culture’/exp OR ‘methodology’/exp OR ‘prevention study’/exp OR ‘validation study’/exp OR ‘replication study’/exp OR Perspect*:ti,ab OR Multicent*:ti,ab OR follow-up:ti,ab OR Follow:ti,ab OR Following:ti,ab OR Meta-Analysis:ti,ab OR (Meta:ti,ab AND Analysis:ti,ab) OR Random*:ti,ab OR Stochastic:ti,ab OR Placebo*:ti,ab OR Blind:ti,ab OR Blinding:ti,ab OR Control*:ti,ab OR Compar*:ti,ab OR Contrast:ti,ab OR EDCC:ti,ab OR group:ti,ab OR groups:ti,ab) AND [embase]/lim
Cochrane Library	197	(((Hemihepatic:ti,ab OR half-hepatic:ti,ab OR selective:ti,ab OR portal:ti,ab OR alternative:ti,ab OR selectional:ti,ab OR elective:ti,ab OR preferential:ti,ab OR optional:ti,ab) AND (occlusion:ti,ab OR control:ti,ab OR clamping:ti,ab OR interdict:ti,ab OR (cut:ti,ab AND off:ti,ab) OR Blocking:ti,ab OR Infubulation:ti,ab) OR (half:ti,ab AND Pringle:ti,ab)) AND (Pringle:ti,ab OR ((Hepatic:ti,ab OR Liver:ti,ab) AND (occlusion:ti,ab OR control:ti,ab OR clamping:ti,ab OR interdict:ti,ab OR (cut:ti,ab AND off:ti,ab) OR Blocking:ti,ab OR Infubulation:ti,ab))) AND (Vascular:ti,ab OR Vein:ti,ab OR artery:ti,ab OR portal:ti,ab OR venous:ti,ab OR vessel:ti,ab OR flow:ti,ab OR inflow:ti,ab) AND ((([mh Liver] OR [mh ‘Liver Neoplasms’] OR [mh ‘Liver Diseases’] OR liver:ti,ab OR hepatic:ti,ab) AND (Operation:ti,ab OR Surgery:ti,ab OR Segmentectomy:ti,ab OR resection:ti,ab OR excision:ti,ab OR transplant*:ti,ab OR graft*:ti,ab)) OR ([mh Hepatectomy] OR [mh ‘Liver Transplantation’]))
Ovid	2739	(((Hemihepatic:ti,ab OR half-hepatic:ti,ab OR selective:ti,ab OR portal:ti,ab OR alternative:ti,ab OR selectional:ti,ab OR elective:ti,ab OR preferential:ti,ab OR optional:ti,ab) AND (occlusion:ti,ab OR control:ti,ab OR clamping:ti,ab OR interdict:ti,ab OR (cut:ti,ab AND off:ti,ab) OR Blocking:ti,ab OR Infubulation:ti,ab) OR (half:ti,ab AND Pringle:ti,ab)) AND (Pringle:ti,ab OR ((Hepatic:ti,ab OR Liver:ti,ab) AND (occlusion:ti,ab OR control:ti,ab OR clamping:ti,ab OR interdict:ti,ab OR (cut:ti,ab AND off:ti,ab) OR Blocking:ti,ab OR Infubulation:ti,ab))) AND (Vascular:ti,ab OR Vein:ti,ab OR artery:ti,ab OR portal:ti,ab OR venous:ti,ab OR vessel:ti,ab OR flow:ti,ab OR inflow:ti,ab) AND (((exp Liver/OR exp Liver Neoplasms/OR exp Liver Diseases/OR liver:ti,ab OR hepatic:ti,ab) AND (Operation:ti,ab OR Surgery:ti,ab OR Segmentectomy:ti,ab OR resection:ti,ab OR excision:ti,ab OR transplant*:ti,ab OR graft*:ti,ab)) OR (exp Hepatectomy/OR exp Liver Transplantation/)) AND (Exp Clinical Trial/OR exp Multicenter Study/OR exp Clinical Trials as Topic/OR Perspect*:ti,ab OR Multicent*:ti,ab OR follow-up:ti,ab OR Follow:ti,ab OR Following:ti,ab OR Meta-Analysis:ti,ab OR (Meta:ti,ab AND Analysis:ti,ab) OR Random*:ti,ab OR Stochastic:ti,ab OR Placebo*:ti,ab OR Blind:ti,ab OR Blinding:ti,ab OR Control*:ti,ab OR Compar*:ti,ab OR Contrast:ti,ab OR EDCC:ti,ab OR group:ti,ab OR groups:ti,ab)
WOS	2918	(((TS=Hemihepatic OR TS=half-hepatic OR TS=selective OR TS=portal OR TS=alternative OR TS=selectional OR TS=elective OR TS=preferential OR TS=optional) AND (TS=occlusion OR TS=control OR TS=clamping OR TS=interdict OR TS=(cut AND off) OR TS=Blocking OR TS=Infubulation) OR TS=(half AND Pringle) AND (TS=Pringle OR ((TS=Hepatic OR TS=Liver) AND (TS=occlusion OR TS=control OR TS=clamping OR TS=interdict OR TS=(cut AND off) OR TS=Blocking OR TS=Infubulation))) AND (TS=Vascular OR TS=Vein OR TS=artery OR TS=portal OR TS=venous OR TS=vessel OR TS=flow OR TS=inflow) AND (((TS=Liver OR TS=(Liver AND Neoplasms) OR TS=(Liver AND Diseases) OR TS=hepatic) AND (TS=Operation OR TS=Surgery OR TS=Segmentectomy OR TS=resection OR TS=excision OR TS=transplant* OR TS=graft*)) OR (TS=Hepatectomy OR TS=(Liver AND Transplantation))) AND (TS=(Perspect* OR Multicent* OR follow-up OR Follow OR Following OR Meta-Analysis OR (Meta AND Analysis) OR Random* OR Stochastic OR Placebo* OR Blind OR Blinding OR Control* OR Compar* OR Contrast OR EDCC OR group OR groups))

## Pringle maneuver versus hemihepatic blood flow occlusion

Scopus	3106	((((TITLE-ABS(Hemih hepatic) OR TITLE-ABS(half-hepatic) OR TITLE-ABS(selective) OR TITLE-ABS(portal) OR TITLE-ABS(alternative) OR TITLE-ABS(selectional) OR TITLE-ABS(elective) OR TITLE-ABS(preferential) OR TITLE-ABS(optional)) AND (TITLE-ABS(occlusion) OR TITLE-ABS(control) OR TITLE-ABS(clamping) OR TITLE-ABS(interdict) OR TITLE-ABS(cut AND off) OR TITLE-ABS(Blocking) OR TITLE-ABS(Infibulation)) OR TITLE-ABS(half AND Pringle)) AND (TITLE-ABS(Pringle) OR ((TITLE-ABS(Hepatic) OR TITLE-ABS(Liver)) AND (TITLE-ABS(occlusion) OR TITLE-ABS(control) OR TITLE-ABS(clamping) OR TITLE-ABS(interdict) OR TITLE-ABS(cut AND off) OR TITLE-ABS(Blocking) OR TITLE-ABS(Infibulation)))))) AND (TITLE-ABS(Vascular) OR TITLE-ABS(Vein) OR TITLE-ABS(artery) OR TITLE-ABS(portal) OR TITLE-ABS(venous) OR TITLE-ABS(vessel) OR TITLE-ABS(flow) OR TITLE-ABS(inflow))) AND (((TITLE-ABS(Liver) OR TITLE-ABS(Liver AND Neoplasms) OR TITLE-ABS(Liver AND Diseases) OR TITLE-ABS(hepatic)) AND (TITLE-ABS(Operation) OR TITLE-ABS(Surgery) OR TITLE-ABS(Segmentectomy) OR TITLE-ABS(resection) OR TITLE-ABS(excision) OR TITLE-ABS(transplant*) OR TITLE-ABS(graft*))) OR (TITLE-ABS(Hepatectomy) OR TITLE-ABS(Liver AND Transplantation))) AND (TITLE-ABS(Perspect* OR Multicent* OR follow-up OR Follow OR Following OR Meta-Analysis OR Random* OR Stochastic OR Placebo* OR Blind OR Blinding OR Control* OR Compar* OR Contrast OR EDCC OR group OR groups) OR TITLE-ABS(Meta AND Analysis))
WANFANG	317	Adjust according search strategy of Pubmed (search in Chinese)
CNKI	126	Adjust according search strategy of Pubmed (search in Chinese)
CBM	88	Adjust according search strategy of Pubmed (search in Chinese)
Total	15798	