Systematic Review/Meta-analysis

ANNALS OF MEDICINE & SURGERY

OPEN

Comparison of the benefits and risks of hemihepatic inflow occlusion: a systematic review and meta-analysis

Lianming Guo, MD, Weiqiang Gong, MD*

Background: Application of hemihepatic inflow occlusion (HIO) and total hepatic inflow occlusion (TIO) are two common approaches for hepatectomy. However, their efficacy and safety remain controversial.

Methods: Randomized control trials (RCTs) published before 15t January 2023 were included by a systematic literature search, which compared the clinical outcomes between HIO and TIO. The primary outcome was the estimated blood loss (EBL). Three independent authors screened and extracted the data and resolved disagreements by consensus. The ROB2.0 tool was used for evaluating the risk of bias.

Results: A total of 1026 patients (511 TIO and 515 HIO) from 9 studies were analyzed in the meta-analyses. The EBL between TIO and HIO group was similar, while HIO was associated with a lower proportion of patients required transfusion ($P = 0.002$), less units of blood transferred ($P < 0.001$) and a lower overall complication rate ($P = 0.008$). There were no significant differences between TIO and HIO in mortality ($P = 0.37$), length of stay ($P = 0.97$), bile leak rate ($P = 0.58$), liver failure rate ($P = 0.96$), reoperation rate ($P = 0.48$), postoperative haemorrhage rate ($P = 0.93$) and incidence of postoperative ascites ($P = 0.96$). The operative time of HIO was usually no more than 15 min longer than that of TIO ($P < 0.001$).

Conclusions: Comparing with the TIO, HIO increased the operative time and failed to further reduce the EBL in patients with liver surgery. However, despite the complexity of the operation, HIO was recommended due to the similar effect on the consumption of blood products and the postoperative complications.

Keywords: hepatic inflow occlusion, postoperative complication, meta-analysis

Introduction

Hepatectomy is recommended as a well-established therapeutic option for benign and malignant liver disease[1]. One of the major issues in liver resection is the intraoperative control of bleeding due to the abundant blood supply, and a systematic association has been found between increased blood loss and transfusion during hepatectomy and increased morbidity[2,3]. When hepatectomy is scheduled, an ischaemic period is often required to prevent bleeding or blood transfusions by Pringle manoeuvre, while the liver function is often compromised by an excessively long ischaemia time and ischaemia/reperfusion (I/R) injury[4]. Therefore, alternative modes of therapy are required in order to avoid these complications.

Hemihepatic occlusion (HIO) was first reported in 1987[5]. HIO entails occlusion of hepatic vascular inflow and outflow of the half liver by Pringle manoeuvre and extrahepatic clamping of major hepatic veins rather than the whole liver. Although HIO may reduce the complications caused by hepatic ischaemia and I/R injury, it is controversial because of the potentially increased risk of bleeding during hepatectomy[6].

The debates about HIO fail to reach a consensus through the current randomized control trials (RCTs) and meta-analyses. The safety and effectiveness of published RCT studies were reviewed and compared between HIO and total hepatic inflow occlusion (TIO) by systematic review and meta-analysis to resolve the above controversy.

HIGHLIGHTS

- Hemihepatic inflow occlusion (HIO) and total inflow occlusion (TIO) are optional.
- The validity of HIO in hepatectomy showed similar effects as TIO.
- HIO showed a lower incidence of postoperative complications than TIO.

Department of Hepatobiliary & Pancreatic Surgery, Weifang People's Hospital, Weifang, Shandong Province, China

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

**Corresponding author. Address: Guangwen street 15, Kuiwen District, Department of Hepatobiliary & Pancreatic Surgery, Weifang People's Hospital, Weifang, Shandong Province, China. Tel.: +861 385 445 3020. E-mail: (weifanggwq@163.com) (W. Gong).*

Annals of Medicine & Surgery (2024) 86:4083–4091

Received 8 January 2024; Accepted 29 April 2024

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.lww.com/annals-of-medicine-and-surgery.

Published online 22 May 2024

http://dx.doi.org/10.1097/MS9.0000000000002165

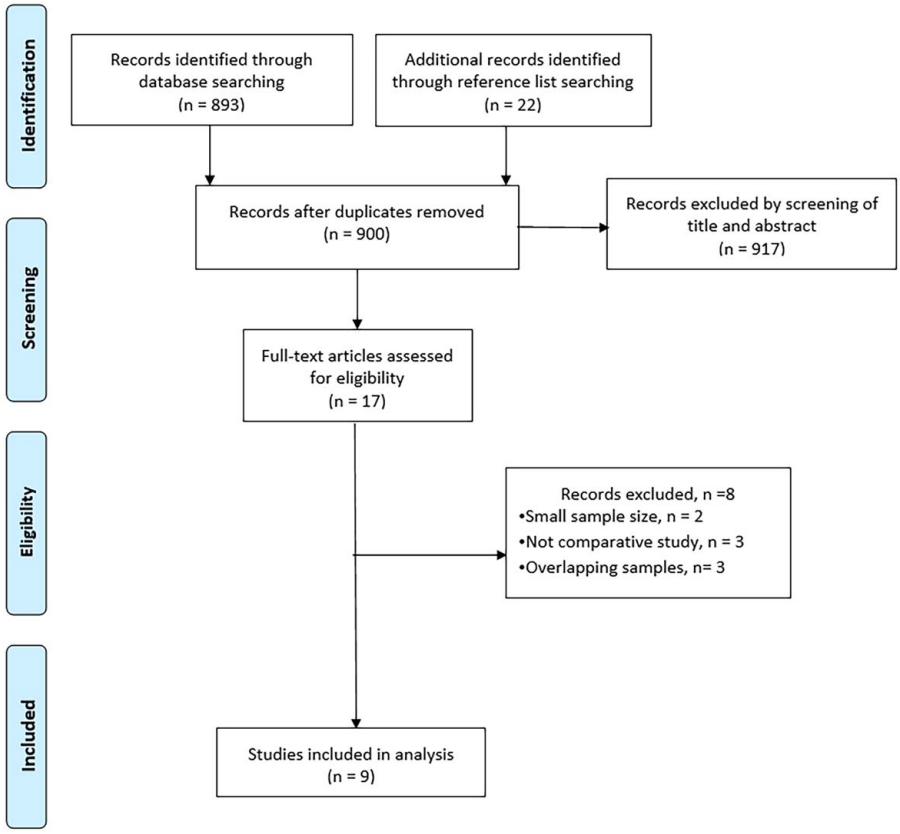

Figure 1. PRISMA flowchart. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Methods

Literature search

The search strategies to be used in this systematic review and meta-analysis for PubMed database will follow the recommendations of the *Cochrane Handbook for Systematic Reviews of Interventions*, and this research was complied with the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA, Supplemental Digital Content 1, http://links.lww.com/MS9/A489) statement and Assessing the Methodological Quality of Systematic Reviews (AMSTAR, Supplemental Digital Content 2, http://links.lww.com/MS9/A490)[7–9]. Randomized control trials (RCT) published before 15 January 2023 were included, and the search strategy was developed in collaboration with an expert in the field of evidence-based medicine. The search strategy was as follows: (liver resection) AND (selective portal triad clamping OR pringle OR hemihepatic inflow occlusion OR total hepatic inflow occlusion). Moreover, the reference lists of all identified research were screened for additional relevant literature. Titles, abstracts, and full texts were screened independently by two authors following the inclusion and exclusion criteria, and disagreements were resolved with advice of the third author.

Study selection and data extraction

Eligible studies were RCT studies which compared the clinical outcomes between HIO and TIO. The studies were excluded if the estimated blood loss (EBL) was not reported. If the studies were overlapping in population, the most recent studies were remained. Studies with a population fewer than 10 patients in any group were excluded to avoid the unreliable estimates. A data extraction sheet was designed to extract the data by the two designated researchers independently. The discrepancies and missing data were resolved by reaching a consensus in discussions. Mean and standard deviation were estimated using the median and interquartile (IQR) or median and range[10,11].

Outcomes

The primary outcome was EBL. The secondary outcomes were patients required transfusion, units of blood transferred, mortality, overall complications, length of stay, operative time, bile leak, liver failure, reoperation, postoperative haemorrhage, and postoperative ascites.

Risk of bias

All studies were critically appraised according to the revised tool for risk of bias with ROB2.0, which addresses bias arising from randomization, exposure measurement, blinding, completeness of outcome data and selectivity of reporting[12]. The risk of bias was assessed by two authors independently and adjudicated by the third when required.

Table 1

The basic characteristics of the included studies

Study	Country	No. participants		Age		Outcome measures	ROB 2.0 bias
		TIO	HIO	TIO	HIO		
Peng *et al.*, 2022[13]	China	129	129	52.4	52.7	1, 2, 4–9, 11, 12	Low
Tongsiri, 2020[14]	Thailand	20	20	57.4	61.1	1, 3, 4, 7–9	Low
Si-yuan *et al.*, 2014[15]	China	80	80	48.3	49.2	1–11	Some concerns
Ni *et al.*, 2013[16]	China	60	60	55.2	56.1	1–5, 7–9, 11, 12	Some concerns
Yuan, 2010	China	60	60	49.6	49.3	1–11	High
Liang *et al.*, 2009[18]	China	40	40	49.55	49.40	1–12	High
Figueras *et al.*, 2005[19]	Spain	39	41	61.8	62	1–10, 12	Some concerns
Smyrniotis *et al.*, 2003[20]	Greece	55	55	62	61	1–12	High
Wu *et al.*, 2002[21]	China	28	30	57.5	53.2	1, 2, 4–10, 12	High

1 Estimated blood loss; 2 Patients required transfusion; 3 Units of blood transferred; 4 Mortality; 5 Overall complications; 6 Length of stay; 7 Operative time; 8 Bile leak; 9 Liver failure; 10 Reoperation; 11 Postoperative haemorrhages; 12 Ascites;
HIO, hemihepatic inflow occlusion; ROB 2.0, risk of bias Cochrane tool version 2; TIO, total hepatic inflow occlusion.

Table 2

Summary of the pooled effects

Outcomes	No. studies	No. patients		Findings (95% CI)	*P*	*2*, %
		TIO	HIO			
Estimated blood loss	9	511	515	MD, 13.63 (– 1.21, 28.48)	0.07	94
Patients required transfusion	8	491	525	OR, 1.76 (1.22, 2.53)	< 0.01	52
Units of blood transferred	7	447	416	MD, 0.21 (0.11, 0.32)	< 0.01	48
Operative time	9	604	575	MD, – 13.86 (– 17.80, – 9.93)	< 0.01	88
Overall complications	8	584	555	OR, 1.44 (1.10, 1.89)	< 0.01	0
Mortality	9	604	575	OR, 1.90 (0.47, 7.78)	0.37	0
Length of stay	7	524	495	MD, 0.01 (– 0.42, 0.44)	0.97	88
Bile leak	9	604	575	OR, 0.86 (0.50, 1.48)	0.58	0
Liver failure	9	604	576	OR, 1.02 (0.50, 2.07)	0.96	34
Reoperation	6	395	366	OR, 0.63 (0.18, 2.26)	0.48	0
Postoperative haemorrhage	6	517	484	OR, 0.96 (0.37, 2.50)	0.93	0
Ascites	6	351	355	OR, 1.02 (0.53, 1.96)	0.96	0

HIO, hemihepatic inflow occlusion; MD, mean difference; OR, odds ratio; TIO, total hepatic inflow occlusion.

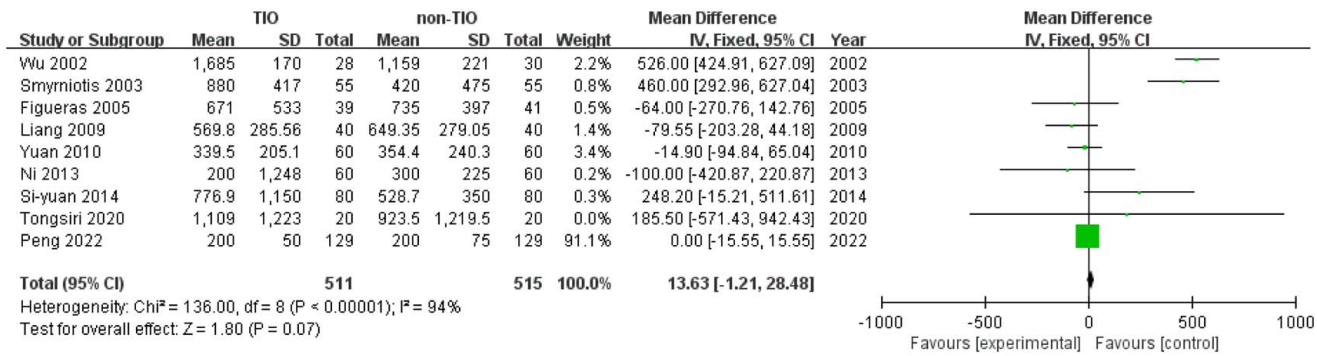

Figure 2. Meta-analysis of estimated blood loss in randomized controlled trials comparing total hepatic inflow occlusion with non-total hepatic inflow occlusion. TIO, total hepatic inflow occlusion.

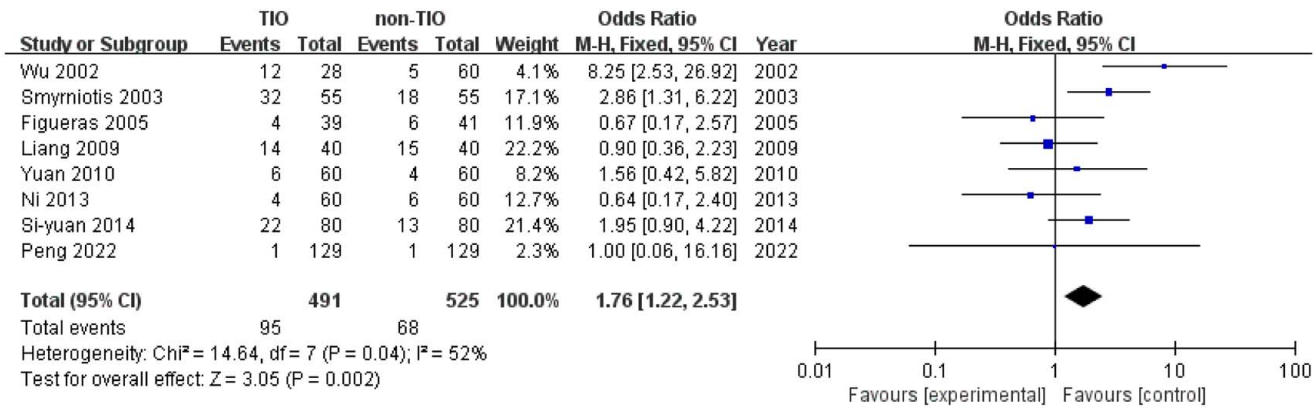

Figure 3. Meta-analysis of patients required transfusion in randomized controlled trials comparing total hepatic inflow occlusion with non-total hepatic inflow occlusion. TIO, total hepatic inflow occlusion.

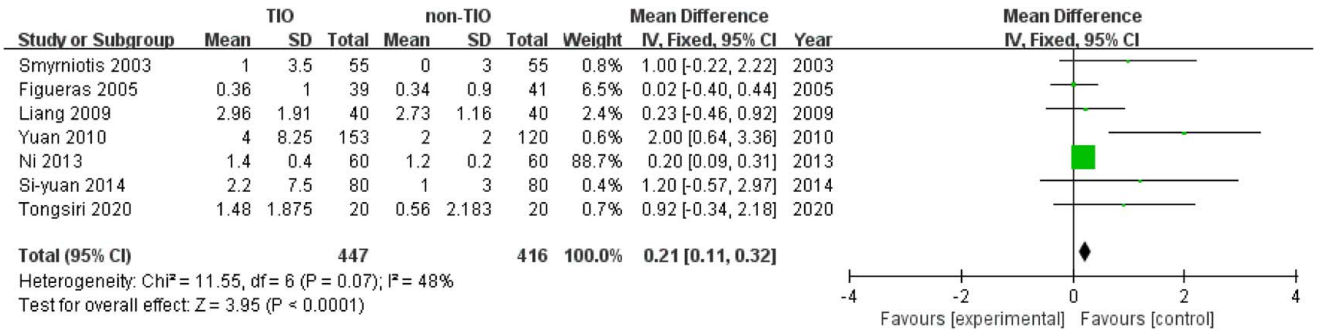

Figure 4. Meta-analysis of units of blood transferred in randomized controlled trials comparing total hepatic inflow occlusion with non-total hepatic inflow occlusion. TIO, total hepatic inflow occlusion.

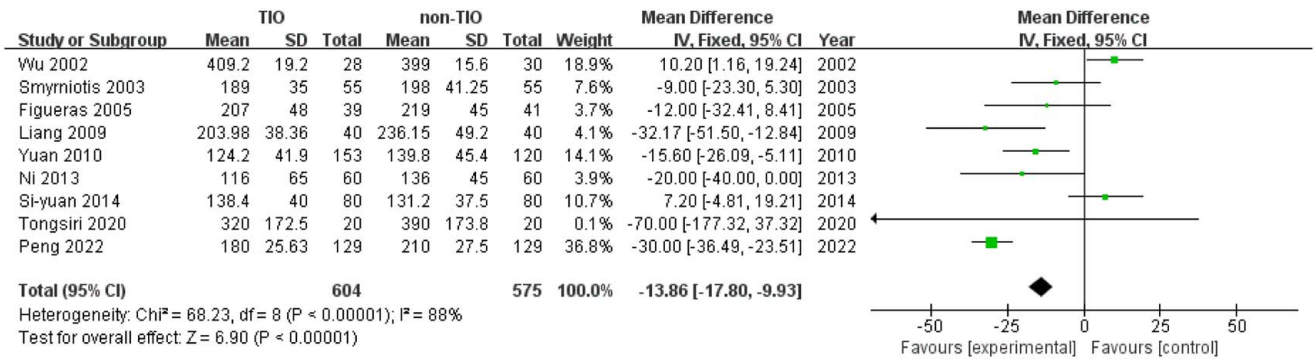

Figure 5. Meta-analysis of mortality in randomized controlled trials comparing total hepatic inflow occlusion with non-total hepatic inflow occlusion. TIO, total hepatic inflow occlusion.

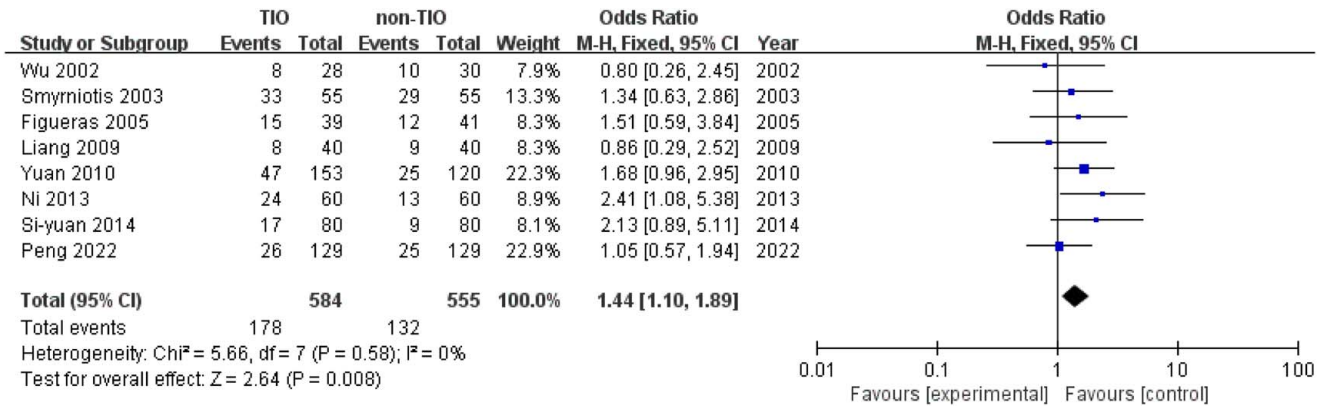

Figure 6. Meta-analysis of overall complications in randomized controlled trials comparing total hepatic inflow occlusion with non-total hepatic inflow occlusion. TIO, total hepatic inflow occlusion.

Figure 7. Meta-analysis of length of stay in randomized controlled trials comparing total hepatic inflow occlusion with non-total hepatic inflow occlusion. TIO, total hepatic inflow occlusion.

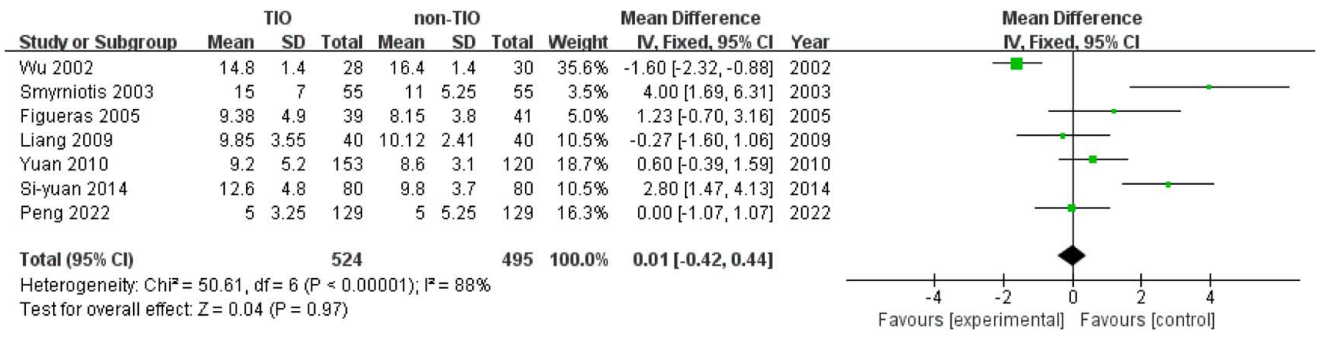

Figure 8. Meta-analysis of operative time in randomized controlled trials comparing total hepatic inflow occlusion with non-total hepatic inflow occlusion. TIO, total hepatic inflow occlusion.

Figure 9. Meta-analysis of bile leak in randomized controlled trials comparing total hepatic inflow occlusion with non-total hepatic inflow occlusion. TIO, total hepatic inflow occlusion.

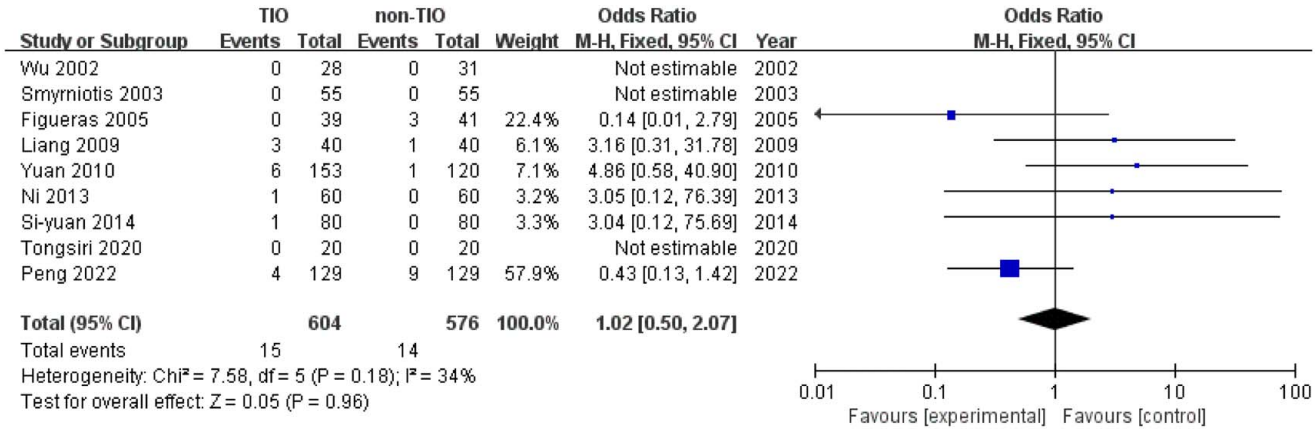

Figure 10. Meta-analysis of liver failure in randomized controlled trials comparing total hepatic inflow occlusion with non-total hepatic inflow occlusion. TIO, total hepatic inflow occlusion.

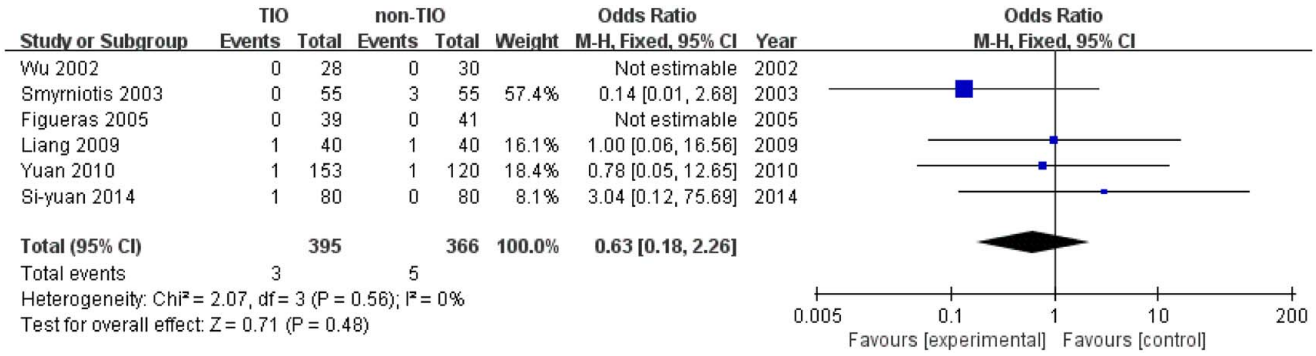

Figure 11. Meta-analysis of reoperation in randomized controlled trials comparing total hepatic inflow occlusion with non-total hepatic inflow occlusion. TIO, total hepatic inflow occlusion.

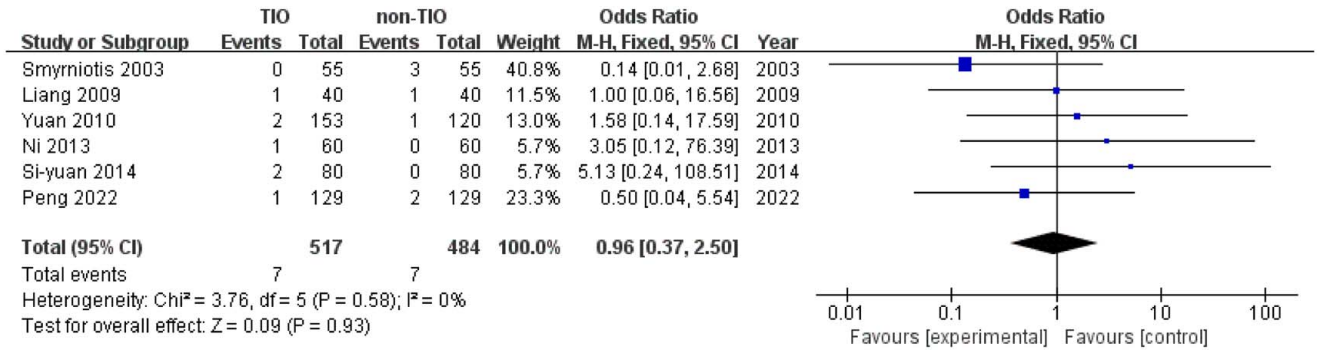

Figure 12. Meta-analysis of postoperative haemorrhage in randomized controlled trials comparing total hepatic inflow occlusion with non-total hepatic inflow occlusion. TIO, total hepatic inflow occlusion.

Data analysis

This meta-analysis will be conducted with the guidance of the Cochrane guidelines for systematic reviews[7]. For categorical data, the odds ratio (OR) and its 95% CI will be calculated with the Mantel–Haenszel model. Continuous data will be expressed as mean differences (MD) with their 95% CI and will be analyzed using the inverse variance model. The I^2 test was used to assess heterogeneity. When I^2less than 25%, the fixed-effects model will be used. Otherwise, the random-effects model will be applied. Statistical analyses were performed using REVMAN 5. Statistical significance of the estimates was set at a bilateral P value less than 0.05.

Results

The literature search yielded 893 studies. After duplicates removed and the titles and abstracts screened, 900 studies were retrieved, including 17 full-text articles assessed (Fig. 1). In total, 9 articles (1026 patients, 511 TIO and 515 HIO) were identified and included in the analysis[13–21].

Table 1 summarizes the characteristics of the 9 studies. EBL was reported in all studies. Two studies were low risk of bias, three studies indicated some concerns for risk of bias, and four studies were high risk of bias (Supplemental figure, Supplemental Digital Content 3, http://links.lww.com/MS9/A491).

The summary of the pooled effects of the primary and secondary outcomes were shown in Table 2. EBL, proportion of patients required transfusion, and units of blood transferred were used to compare the effects of TIO and HIO in reducing blood loss during the liver surgery. The EBL between TIO and HIO group was similar [TIO vs. HIO, MD 13.63, 95% CI (– 1.21, 28.48), $P = 0.07$, $I^2 = 94\%$, Fig. 2], while HIO was associated with lower proportion of patients required transfusion [TIO vs. HIO, OR 1.76, 95% CI (1.22, 2.53), $P = 0.002$, $I^2 = 52\%$, Fig. 3], and less units of blood transferred [TIO vs. HIO, MD 0.21, 95% CI (0.11, 0.32), $P < 0.001$, $I^2 = 48\%$, Fig. 4]. The operative time of HIO was usually longer than that of TIO [TIO vs. HIO, MD – 13.86, 95% CI (– 17.80, – 9.93), $P < 0.001$, $I^2 = 88\%$, Fig. 5].

HIO was associated with lower overall complication rate (TIO vs. HIO, OR 1.44, 95% CI 1.10–1.89, $P = 0.008$, $I^2 = 0\%$, Fig. 6). There were no significant differences between TIO and HIO in mortality [TIO vs. HIO, OR 1.90, 95% CI (0.47, 7.78), $P = 0.37$, $I^2 = 0\%$, Fig. 7], length of stay [TIO vs. HIO, MD 0.01, 95% CI (– 0.42, 0.44), $P = 0.97$, $I^2 = 88\%$, Fig. 8], bile leak rate [TIO vs. HIO, OR 0.86, 95% CI (0.50, 1.48), $P = 0.58$, $I^2 = 0\%$, Fig. 9], liver failure rate [TIO vs. HIO, OR 1.02, 95% CI (0.50, 2.07), $P = 0.96$, $I^2 = 34\%$, Fig. 10], reoperation rate [TIO vs. HIO, OR 0.63, 95% CI (0.18, 2.26), $P = 0.48$, $I^2 = 0\%$, Fig. 11], postoperative haemorrhage rate [TIO vs. HIO, OR 0.96, 95% CI (0.37, 2.50), $P = 0.93$, $I^2 = 0\%$, Fig. 12] and incidence of postoperative ascites [TIO vs. HIO, OR 1.02, 95% CI (0.53, 1.96), $P = 0.96$, $I^2 = 0\%$, Fig. 13].

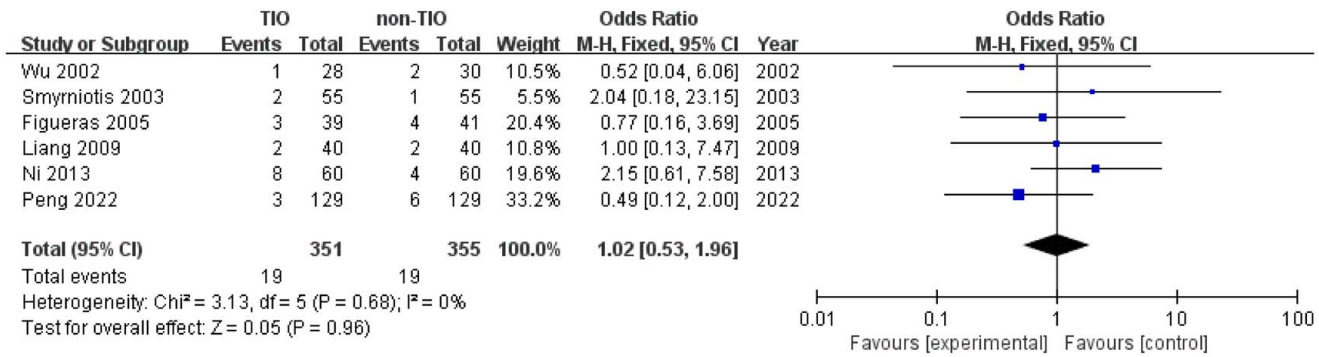

Figure 13. Meta-analysis of ascites in randomized controlled trials comparing total hepatic inflow occlusion with non-total hepatic inflow occlusion. TIO, total hepatic inflow occlusion.

Discussion

The evidences of the meta-analyses are current to January 2023, a significant superiority of HIO was indicated in a lower proportion of patients required transfusion, units of blood transferred and lower overall complication rate. Meanwhile, HIO and TIO were comparable in EBL, mortality, length of stay, bile leak rate, liver failure rate, reoperation rate, postoperative haemorrhage rate and incidence of postoperative ascites. It was notable that longer operative time was required in HIO.

The results of our study are consistent with most studies, that is, HIO does not significantly reduce EBL and the proportion of patients required transfusion compared with TIO. Our studies have found that HIO can reduce blood transfusion, although this advantage was statistically significant in few studies[16,17]. HIO requires more complex anatomical procedures, so HIO takes longer than TIO in most studies, which is consistent with the results of our study[13,18]. HIO was indicated to reduce postoperative complications, but this advantage of HIO was only reported in early research[16]. Paradoxically, there was no significant difference in length of stay, biliary fistula, liver failure, reoperation rate, mortality, postoperative haemorrhage, and postoperative ascites in our study, which was inconsistent with the reduction of postoperative complications.

The possible reasons for the inconsistent results are as follows. Firstly, some of the original studies are poorly designed and have a high risk of bias. Secondly, the difference in blood loss between HIO and TIO is so small that the difference is of no clinical significance. Further, the significant haemorrhage rate ($\geq$ 400 ml) and blood transfusion rate may be better outcomes. Thirdly, the main manifestation of hepatic I/R injury is the abnormality of liver biochemical indexes after surgery, and liver failure is a serious but rare complication[22]. However, some studies have compared the speed at which alanine aminotransferase/aspartate aminotransferase returns to normal after surgery, and the results show that there is no significant difference between HIO and TIO, suggesting that the liver damage caused by TIO is mild in a limited time[23]. Fourthly, the explanation for the reduction of complications in HIO was limited by the lack of original research and the limitations of clinical outcomes. At last, although the length of stay will be affected by the speed of liver function recovery, it is also affected by many other factors, such as culture, health insurance policy[24].

Our study reviewed the safety and effectiveness between HIO and TIO through systematic review and meta-analysis for the first time. However, there are still some limitations in our research. The original RCT studies comparing HIO and TIO are too few to evaluate the source of heterogeneity. In addition, most of the included studies had concerning or high risks of bias, strictly designed multicenter RCT studies were needed to further verify the conclusions of this study.

Conclusions

In summary, based on the effectiveness and safety of bleeding control, HIO showed similar effectiveness as TIO. However, HIO may reduce the demand for blood products caused by haemorrhage. Although HIO surgery usually takes longer time, the overall incidence of postoperative complications can be reduced. Therefore, HIO is recommended as an alternative to TIO. Strictly designed multicenter RCT studies are needed to further verify the conclusions of this study.

Ethical approval

Ethics approval was not required for this systematic review.

Consent

Informed consent was not required for this systematic review.

Source of funding

The authors declare they received no fund for this study.

Author contribution

W.G. designed and concepted the manuscript. W.G. and L.G. performed the literature search and statistical analysis. L.G. interpreted the data and drafted the manuscript. All authors read and approved the final manuscript.

Conflicts of interest disclosure

The authors have no conflicts of interest or financial ties to disclose.

Research registration unique identifying number (UIN)

1. Name of the registry: PROSPERO.
2. Unique Identifying number or registration ID: CRD42023486110.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked).

Guarantor

Weiqiang Gong.

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

References

[1] European Association For The Study Of The Liver; European Organisation For Research And Treatment Of Cancer. EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. J Hepatol 2012;56:908–43.
[2] Smyrniotis V, Farantos C, Kostopanagiotou G, *et al*. Vascular control during hepatectomy: review of methods and results. World J Surg 2005; 29:1384–96.
[3] Abu Hilal M, Aldrighetti L, Dagher I, *et al*. The Southampton Consensus Guidelines for Laparoscopic Liver Surgery: From Indication to Implementation. Ann Surg 2018;268:11–8.

[4] Weigand K, Brost S, Steinebrunner N, *et al*. Ischemia/reperfusion injury in liver surgery and transplantation: pathophysiology. HPB Surg 2012; 2012:176723.
[5] Makuuchi M, Mori T, Gunvén P, *et al*. Safety of hemihepatic vascular occlusion during resection of the liver. Surg Gynecol Obstet 1987;164: 155–8.
[6] Li AJ, Pan ZY, Zhou WP, *et al*. Comparison of two methods of selective hepatic vascular exclusion for liver resection involving the roots of the hepatic veins. J Gastrointest Surg 2008;12:1383–90.
[7] C J, Higgins JPT, T J, Cumpston M, *et al*, Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019). Cochrane (2019).
[8] Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Int J Surg 2021;88: 105906.
[9] Shea BJ, Reeves BC, Wells G, *et al*. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ 2017;358: j4008.
[10] Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol 2005;5:13.
[11] D. J, Higgins JPT, L T, Chapter 6: Choosing effect measures and computing estimates of effect. Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019), Cochrane (2019).
[12] Sterne JAC, Savović J, Page MJ, *et al*. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019;366:l4898.
[13] Peng Y, Yang Y, Chen K, *et al*. Hemihepatic versus total hepatic inflow occlusion for laparoscopic hepatectomy: a randomized controlled trial. Int J Surg 2022;107:106961.
[14] Tongsiri SS, Impool T N. Comparison of early clinical outcomes between intermittent vascular inflow occlusion versus intermittent selective hepatic vascular exclusion in hepatic resections for cholangiocarcinoma patients: a prospective randomized controlled trial study. J Med Assoc Thai 2020;103:521–8.
[15] Si-Yuan F, Yee LW, Yuan Y, *et al*. Pringle manoeuvre versus selective hepatic vascular exclusion in partial hepatectomy for tumours adjacent to the hepatocaval junction: a randomized comparative study. Int J Surg 2014;12:768–73.
[16] Ni JS, Lau WY, Yang Y, *et al*. 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;17:1414–21.
[17] Yang Y, Zhao LH, Fu SY, *et al*. Selective hepatic vascular exclusion versus pringle maneuver in partial hepatectomy for liver hemangioma compressing or involving the major hepatic veins. Am Surg 2014;80: 236–40.
[18] Liang G, Wen T, Yan L, *et al*. A prospective randomized comparison of continuous hemihepatic with intermittent total hepatic inflow occlusion in hepatectomy for liver tumors. Hepatogastroenterology 2009;56:745–50.
[19] Figueras J, Llado L, Ruiz D, *et al*. Complete versus selective portal triad clamping for minor liver resections: a prospective randomized trial. Ann Surg 2005;241:582–90.
[20] Smyrniotis VE, Kostopanagiotou GG, Contis JC, *et al*. Selective hepatic vascular exclusion versus Pringle maneuver in major liver resections: prospective study. World J Surg 2003;27:765–9.
[21] Wu CC, Yeh DC, Ho WM, *et al*. 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;137:1369–76.
[22] Wang HQ, Yang JY, Yan LN. Hemihepatic versus total hepatic inflow occlusion during hepatectomy: a systematic review and meta-analysis. World J Gastroenterol 2011;17:3158–64.
[23] Lan X, Li H, Liu F, *et al*. Does liver cirrhosis have an impact on the results of different hepatic inflow occlusion methods in laparoscopic liver resection? a propensity score analysis. HPB (Oxford) 2019;21:531–8.
[24] Wang M, Li D, Chen R, *et al*. Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours: a multicentre, open-label, randomised controlled trial. Lancet Gastroenterol Hepatol 2021;6: 438–47.