Original Article

The efficacy and safety of ^{125}I seeds combined with biliary stent placement versus stent placement alone for malignant biliary obstruction: a systematic review and meta-analysis

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Background: Currently, it is unknown whether iodine-125 (^{125}I) stent implantation has the same therapeutic effect on patients with malignant biliary obstruction (MBO) caused by different cancers. This meta-analysis aimed to investigate whether ^{125}I implantation in patients with MBO is superior to biliary stent placement in efficacy and safety, and to further explore the difference in efficacy and safety of seed implantation in different patients through subgroup analysis.

Methods: A systematic search of the PubMed, Wiley Online Library, Cochrane library, Google Scholar, the Web of Science, China National Knowledge Infrastructure (CNKI), VIP, and Wanfang databases was conducted to screen all relevant studies up to October 30, 2022. Articles were not subjected to language or geographical limitations, but were required to meet the inclusion and exclusion criteria for this study. The Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of articles. The primary endpoint was survival, which was defined as the interval between initial treatment and death or the end of study. Meta analysis was performed using Stata/SE15.0.

Results: A total of 12 eligible studies were enrolled including 679 patients. All the included studies were single-center studies carried out in China. The results showed that the death risk and stent occlusion risk in the ^{125}I group was 0.441 times [95% confidence interval (CI): 0.315 to 0.619, P<0.001; I^2=0%, fixed, IV] and 0.534 times (95% CI: 0.433 to 0.658, P=0.003; I^2=45.4%, fixed, IV) lower than the control group, respectively. There was no significant statistical difference in the risk of complications between the 2 groups [risk ratio (RR) =1.024, 95% CI: 0.963 to 1.090, P=0.450; P_Q=0.640; I^2=0%]. The reduction level of total bilirubin [TBIL; weighted mean differences (WMDs) =−14.969, 95% CI: −28.670 to −1.267, P=0.032; P_Q=0.409, I^2=2.1%) and aspartate transaminase (AST; WMD =−14.653, 95% CI: −23.246 to −6.060, P=0.001; P_Q=0.900, I^2=0%) in the ^{125}I group was higher than that in the control group 1 week after surgery. The efficacy and safety of ^{125}I for MBO patients were found to be independent of the type of tumor causing MBO (P for meta regression >0.05).

Conclusions: For patients with MBO caused by hilar tumor or other tumors, ^{125}I seed implantation can reduce the death risk and stent occlusion risk, prolong the time of survival and stent patency, and does not increase the complication risk. Due to the limitations of the study population, these findings should be further validated in other populations and regions.

Keywords: Malignant biliary obstruction (MBO); ^{125}I implantation; survival; stent occlusion; complication

Submitted Aug 04, 2022. Accepted for publication May 04, 2023. Published online May 10, 2023.
doi: 10.21037/qims-22-824
View this article at: https://dx.doi.org/10.21037/qims-22-824

Introduction

Malignant biliary obstruction (MBO), characterized by stenosis and blockage of extrahepatic or intrahepatic bile ducts, is a common clinical disease primarily caused by various cancers including cholangiocarcinoma, pancreatic cancer, gallbladder cancer, and cancer metastasis (1-3). Due to the silent and occult clinical manifestations, MBO patients are always diagnosed at the advanced stage when painless obstructive jaundice develops (4,5). By this time, most patients have bypassed the optimal treatment period and cannot benefit from radical resection due to extensive tumor growth (5). About 70% of MBO cases are unresectable, resulting in poor quality of life and low survival for most MBO patients (3). During the recent 3 decades, surgeons and interventional therapists have endeavored to alleviate patients' clinical symptoms and correct complications by means of conventional or minimally invasive approaches (6,7). Palliative treatment of stent implantation is one of the common therapeutic methods for MBO, which has been widely accepted and used for decades (8).

A high recurrence rate has been found in patients implanted with non-therapeutic stents (9-12). On the one hand, because the stent itself has no therapeutic effect on the tumor, stent occlusion can be caused by the growth of tumor tissue into the lumen through the stent mesh. On the other hand, stent occlusion can be caused by epithelial hyperplasia, biofilm deposition, biliary sludge, and granulation tissue formation over the duration of stent placement (13). Compared to the stent placement alone, Iodine-125 (^{125}I) seeds combined with biliary stent placement can effectively reduce the stent occlusion rate because the ^{125}I seeds can inhibit the tumor growth (14). The suggestion that permanently radioactive seed implantation can be used to treat MBO was made by several scholars in the early 1900s. ^{125}I, a persistent radiation material, is a preferred material for particle scaffolds due to its function of directly injuring the DNA double helix to inhibit the replication of tumor cells and inducing apoptosis (15). Efforts have been made to introduce irradiation stents loaded with ^{125}I seeds in China and various types of biliary stents with special structure and materials have been designed for MBO treatment by percutaneous transhepatic cholangiography (PTC) or endoscopic retrograde cholangiopancreatography (ERCP) (8).

Recently, animal experiments, cohort studies, and randomized controlled trials (RCTs) on the treatment of MBO patients with particle stents have been published successively, and the finding that ^{125}I seed implantation can improve the prognosis of patients has been confirmed by meta-analysis (16,17). However, the participants included in these population studies were mostly mixed populations, including patients with MBO caused by various cancers such as cholangiocarcinoma, gallbladder cancer, pancreatic cancer, gastric cancer, colorectal cancer, and primary liver cancer. Currently, it is unknown whether ^{125}I stent implantation has the same therapeutic effect on patients with MBO caused by different cancers, and 2 published meta-analyses have failed to clarify the issue. Therefore, we performed this meta-analysis, aiming to verify the efficacy and safety of ^{125}I implantation for MBO patients, and to further explore the differences in the efficacy and safety of seed implantation among different patients through subgroup analysis. We present this article in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-22-824/rc).

Methods

Eligibility criteria

Databases such as PubMed, Wiley Online Library, Cochrane library, Google Scholar, the Web of Science, China National Knowledge Infrastructure (CNKI), VIP, and Wanfang were screened for related articles published from inception to October 30, 2022. The following keywords were used: ^{125}I seeds stent *OR* iodine seeds stent *OR* iodine-125 seeds *OR* biliary stenting combined with iodine-125 seed *AND* malignant biliary obstruction *OR* malignant biliary stricture *OR* malignant bile duct obstruction *OR* malignant obstructive jaundice *OR* malignant extrahepatic biliary obstruction. The articles were selected by 2 independent reviewers by reviewing the

title and abstract of each study. In addition, references cited in systematic review reports on the same or a similar topic were also screened for relating articles. Articles were not subjected to language or geographical limitations, but were required to meet the following inclusion criteria: (I) RCT or cohort study on MBO caused by unresectable tumor (distal or proximal); (II) Patients in the treatment group received stent combined with ^{125}I particle treatment, whereas patients in the control group received stent monotherapy (only metal stent implantation); (III) single and multi-center studies; (IV) both endoscopic and percutaneous approaches for stent implantation. The exclusion criteria were as follows: (I) no information on patient survival time or survival rate was provided; (II) patients received other radiotherapy; (III) single-arm study; (IV) no baseline patient information such as age and gender were provided, or the baseline information between the 2 groups was not balanced; (V) animal experiments, narrative reviews, and conference abstracts. Any disagreements between the 2 reviewers in the above process were resolved by a third reviewer. The study was not registered on a specific platform.

Data collection

Two authors independently extracted the following information to a database established by Microsoft Excel 2016 software (Microsoft Corp., Redmond, WA, USA): (I) basic information of each article, such as author's name, year and type of publication, and country; (II) patient characteristics and treatment information; and (III) information on efficacy and adverse reactions. We extracted the number of events and the total number for dichotomous variables and the means and standard deviations for continuous variables.

Quality appraisal

The Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of articles (18,19). NOS, which is one of the commonly used quality evaluation methods in prospective studies, evaluates the quality of the study from 9 aspects including the selection of the study population, the comparability between groups, and the measurement of results. The total score is 9 points, and articles scoring 7–9 points were considered high-quality articles. For randomized trials, the Cochrane risk of bias tool (Cochrane Collaboration, Copenhagen, Denmark) was also used to assess potential bias risk. Any disagreement was discussed with a third author to reach a consensus.

Definition of outcome

The primary endpoint was survival, which was defined as the interval between initial treatment and death or the end of the study. Secondary outcomes included complication, stent occlusion, and biochemical response within 1 week. Complication-related indicators included pancreatitis, cholecystitis, cholangitis, and hemobilia. Stent patency referred to the recurrence of biliary obstruction after stent placement. Stent patency time was defined as the time from stent placement to recurrence of biliary obstruction or the end of study. Biochemical indicators within 1 week included alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), and direct bilirubin (DBIL).

Statistical analysis

Risk ratios (RRs) with 95% confidence intervals (CIs) were chosen to measure the effects of ^{125}I seed implantation for stent patency, patient survival, and complications, and weighted mean differences (WMDs) to measure the stent patency time, patient survival time, and laboratory values. All comparisons were performed by Stata software version 15.0 (StataCorp. LLC, College Station, TX, USA). The I^2 test and Q test were used to estimate the heterogeneity among the studies. A P value for Cochrane's $\chi^2<0.05$ or $I^2>50\%$ indicated that there was a high heterogeneity between the studies, and a random effects model was selected for the meta-analysis; otherwise, a fixed effects model was used. Sensitivity analysis was performed using the leave-one-out method to evaluate the robustness of the final result. Egger's test was used to assess publication bias. Subgroup analysis and meta-regression were used to explore the differences in the results of different study populations and different study designs.

Results

Search results

A total of 4,059 articles were identified by the database research (Table S1), and 35 articles were identified by the previous systemic reviews. After removing 720 duplicates, 3,374 articles were assessed. A further 3,335 articles were excluded because the titles and abstracts were not relevant to the research purpose. Among the remaining 39 articles,

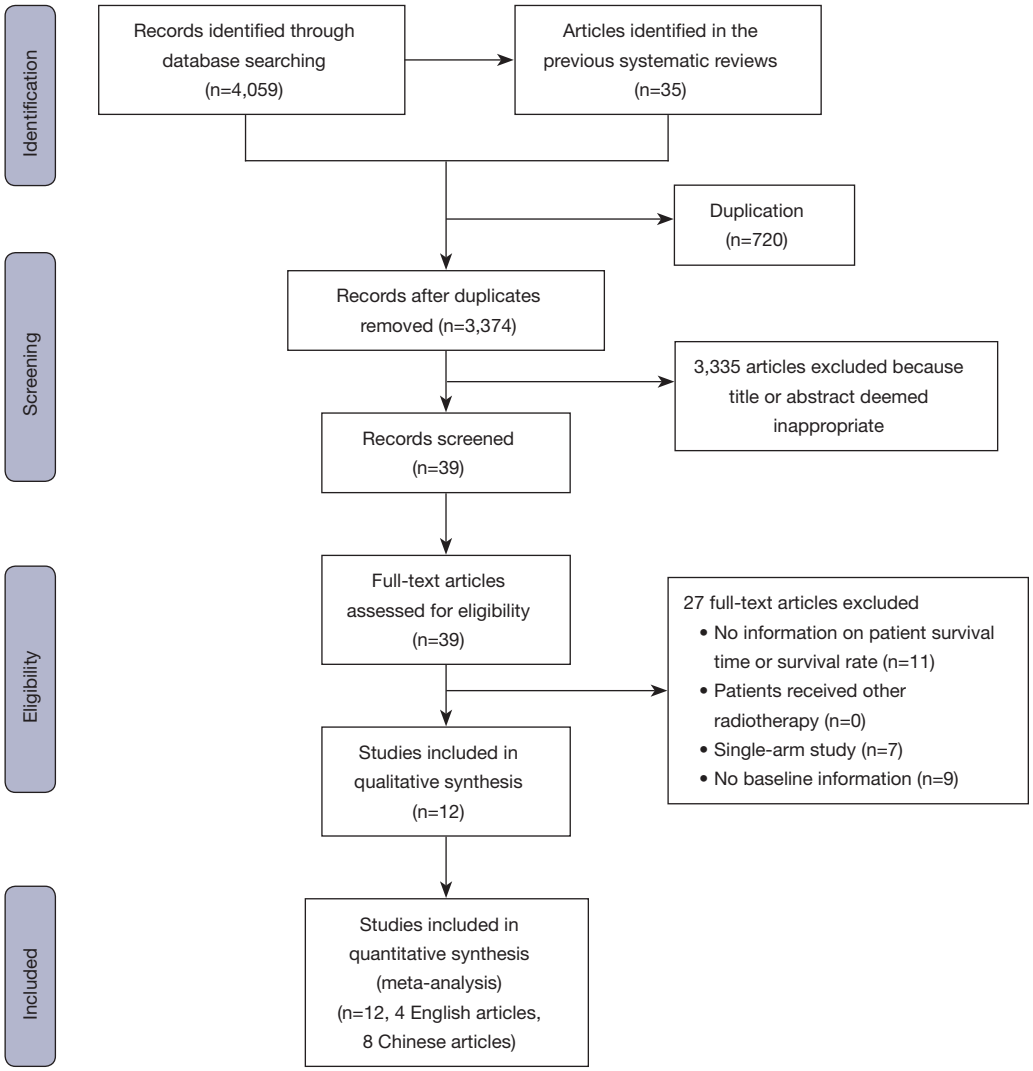

Figure 1 Flow chart of study inclusion.

27 studies were excluded due to violations of the inclusion and exclusion criteria. Finally, 12 studies were included for meta-analysis. The specific screening process was shown in *Figure 1*. The 12 eligible studies included 4 English (14,20-22) articles and 8 Chinese articles (23-30), and the detailed information is shown in *Table 1* and Table S2. All articles were single center studies conducted within China, with a quality score of 7–9 (Tables S3,S4). Of the 12 studies (Table S5), 2 included patients with MBO caused by hilar cholangiocarcinoma (cholangiocarcinoma group) (23,28), 5 included patients with MBO caused by unresectable hilar cancers (MHBO group; including cholangiocarcinoma, gallbladder cancer, liver cancer, etc.) (20,24,25,27,29), and the remaining 5 included patients with MBO of unlimited etiology (MMBO group) (14,21,22,26,30). Except for 3 RCTs (14,21,22), the remaining 9 articles were prospective cohort studies.

A total of 679 patients were enrolled, among whom 329 received ^{125}I stent implantation (^{125}I group) and 350 received only stent implantation (control group). There were 204 males and 146 females in the ^{125}I group, and 180 males and 149 females in the control group. The baseline information, such as age and gender, was balanced and comparable between the 2 groups.

Death risk

A total of 310 patients died in the control group and 253

Table 1 The information of included studies

Study	Sample size	Study time	Design	Age (years)*		Gender (male/female)		Follow-up
				Control group	^{125}I group	Control group	^{125}I group	
Asihaer Hasimu [2017] (20)	55	July 2011 to June 2014	RCT	70.93±8.58	70.93±8.58	14/13	11/17	7–362 days
Hai-Dong Zhu [2012] (14)	23	November 2008 to October 2010	RCT	71.00±22.00	62.50±21.00	9/2	7/5	4.5 months (range, 0.2–12.5 months)
Hui-Wen Wang [2021] (21)	67	January 2016 to June 2018	RCT	63.46±10.43	63.25±9.92	15/20	16/16	Every 2 months
Chuanguo Zhou [2019] (22)	76	January 2017 to July 2018	Cohort study	68.1±12.2	70.2±13.8	21/15	21/19	Every 3 months
Hao Jiang [2015] (23)	54	January 2007 to February 2015	Cohort study	52±10	52±10	19/5	30/18	3–18 months
Chuanguo Zhou [2018] (24)	38	January 2016 to May 2018	Cohort study	67.5±13.5	4.7±10.6	12/8	9/9	1 month after surgery, and every 3 months
Chenglong Han [2015] (25)	40	June 2011 to March 2014	Cohort study	–	–	12/6	16/6	3 days, 7 days, 14 days, 1 month, 3 months, 5 months, 7 months, 9 months, 12 months
Xuejun Wang [2019] (26)	65	January 2016 to April 2018	Cohort study	49.9±7.3	47.6±6.8	12/18	19/16	1 day, 1 week, 1 month, 3 months
Chao Zhu [2020] (27)	42	January 2013 to January 2019	Cohort study	64.8±11.8	69.0±7.0	11/9	10/12	
Shengxian Fei [2015] (28)	52	October 2012 to October 2014	Cohort study	73±11	70±12	26/11	10/16	3–24 months
Xiaoxi Fan [2017] (29)	25	June 2013 to August 2015	Cohort study	71±9	70±10	7/6	8/7	3 days, 7 days, 14 days, 1 month, 3 months, 6 months, 9 months, 12 months
Hongdou Xu [2020] (30)	147	November 2015 to February 2018	Cohort study	62.7 (33~87)	64.5 (35~92)	61/31	35/15	^{125}I=5.2 (2–12.5) months; control =7.8 (2–12.5) months

The baseline data of the 2 groups are balanced and comparable. *, data are presented as mean ± standard deviation, median (interquartile range). RCT, randomized controlled trial; ^{125}I, ^{125}iodine.

died in the ^{125}I group. The death risk in the ^{125}I group was 0.441 times (95% CI: 0.315 to 0.619, P<0.001) lower than in the control group, indicating that ^{125}I seed implantation reduced the mortality rate of MBO patients (*Figure 2A* and *Table 2*). Fixed effects models were adopted for meta-analyses since no significant heterogeneity was observed (χ^2_Q=1.67, P_Q=0.998; I^2=0%). The sensitivity analysis (*Table 2*) showed that the final result was robust. Subgroup analysis (*Figure 2B*) suggested that ^{125}I seed implantations reduced the death risk by 0.322 times (95% CI: 0.129 to 0.805, P=0.015; P_Q=0.856, I^2=0%) in cholangiocarcinoma patients, 0.443 times (95% CI: 0.207 to 0.948, P=0.036; P_Q=0.938, I^2=0%) in MHBO patients, and 0.482 times (95% CI: 0.320 to 0.726, P<0.001; P_Q=0.980, I^2=0%) in MMBO patients. Meta-regression verified that the impact of seed implantation on death risk in MHBO patients (β=–13.00, 95% CI: –72.86 to 46.86, P=0.630) and MMBO patients (β=24.00, 95% CI: –37.96 to 85.96, P=0.398) was not different from than that in cholangiocarcinoma patients. Subgroup analysis and meta-regression also demonstrated that the death risk (Figure S1) calculated by RCTs (RR =0.349, 95% CI: 0.105 to 1.157, P=0.085; P=0.998, I^2=0%)

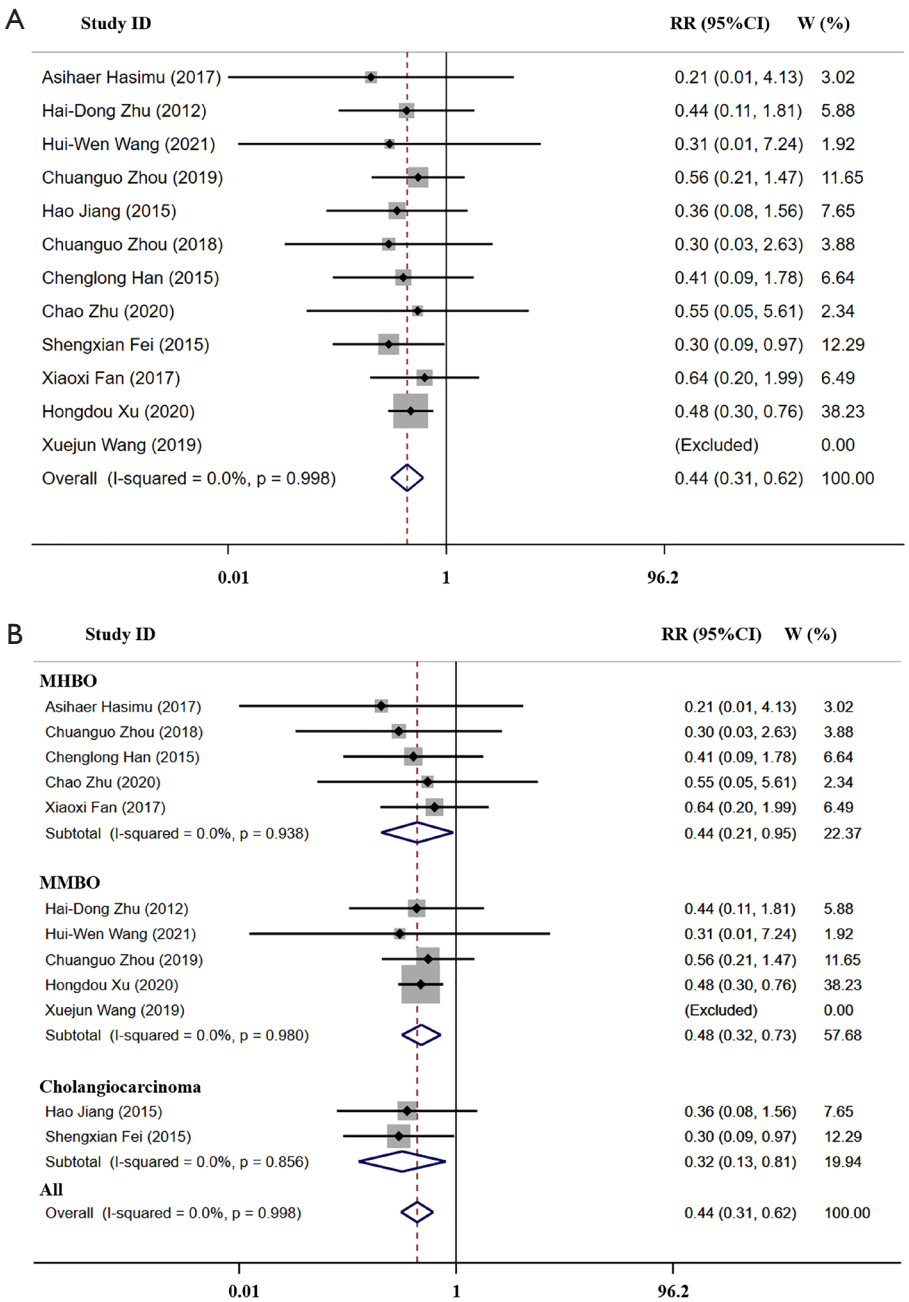

Figure 2 Comparison of death risk between 125I groups and control groups. (A) Meta-analysis; (B) subgroup analysis by study population. RR, risk ratio; CI, confidence interval; W, weight; MBO, malignant biliary obstruction; MMBO, mixed MBO patients caused by various tumors; MHBO, patients with malignant hilar biliary obstruction.

and calculated by prospective studies (RR =0.453, 95% CI: 0.318 to 0.644, P<0.001; P=0.897, I^2=0%) was also not statistically different (β=−10.29, 95% CI: −62.68 to 42.10, P=0.667). Egger's test (β=15.69, P=0.826) and the funnel plot (Figure S2) indicated that no potential publication biases were present.

Totals of 9 and 7 articles reported the mean survival time and median survival time, respectively. The pooled WMD of mean survival time between 2 groups was 3.310 months (95% CI: 2.848 to 3.771, P<0.001) and the

Table 2 The pooled death risk of malignant biliary obstruction patients

Study	Control group		^{125}I group		RR (95% CI)	Sensitivity analysis
	Alive	Dead	Alive	Dead		
Asihaer Hasimu [2017] (20)	0	27	2	26	0.207 (0.010–4.126)	0.449 (0.319–0.631)
Hai-Dong Zhu [2012] (14)	2	9	5	7	0.436 (0.105–1.807)	0.442 (0.312–0.626)
Hui-Wen Wang [2021] (21)	0	35	1	31	0.306 (0.013–7.242)	0.444 (0.316–0.624)
Chuanguo Zhou [2019] (22)	5	31	10	30	0.556 (0.210–1.472)	0.426 (0.297–0.612)
Hao Jiang [2015] (23)	2	22	7	23	0.357 (0.082–1.564)	0.448 (0.317–0.634)
Chuanguo Zhou [2018] (24)	1	19	3	15	0.300 (0.034–2.632)	0.447 (0.317–0.630)
Chenglong Han [2015] (25)	2	16	6	16	0.407 (0.093–1.779)	0.444 (0.314–0.628)
Xuejun Wang [2019] (26)	0	30	0	35	–	0.441 (0.315–0.619)
Chao Zhu [2020] (27)	1	19	2	20	0.550 (0.054–5.612)	0.439 (0.312–0.618)
Shengxian Fei [2015] (28)	3	23	10	16	0.300 (0.093–0.967)	0.461 (0.324–0.657)
Xiaoxi Fan [2017] (29)	3	8	6	8	0.636 (0.204–1.988)	0.428 (0.300–0.610)
Hongdou Xu [2020] (30)	21	71	24	26	0.476 (0.296–0.764)	0.420 (0.264–0.670)
Pooled results	40	310	76	253	0.441 (0.315–0.619)	0.441 (0.315–0.619)

^{125}I, ^{125}iodine; RR, risk ratio; CI, confidence interval; SD, standard deviation; MBO, malignant biliary obstruction.

median survival time was 3.458 months (95% CI: 2.658 to 4.259, P<0.001), suggesting that ^{125}I seed implantations increased the survival time compared with control groups (Figure S3 and Table S6). Random effects models were used due to high heterogeneity (mean survival: I^2=87.4%, P_Q<0.001; median survival: I^2=95.9%, P_Q<0.001). However, the results of sensitivity analysis (Table S6) showed that the final result was robust. Egger's test (mean survival: β=6.036, P=0.067; median survival: β=3.286, P=0.544) indicated that no potential publication biases were present.

Complication risk

A total of 11 articles documented the occurrence of postoperative complications, including 333 patients in the control group and 326 patients in the ^{125}I group. Complications occurred in 45 patients in the control group and 50 patients in the ^{125}I group. Meta-analysis showed that seed implantations did not increase the risk of postoperative complications (RR =1.024, 95% CI: 0.963 to 1.090, P=0.450; *Figure 3*). Fixed effects models were used to conduct analyses since no significant heterogeneity was detected (P_Q=0.640; I^2=0%). Sensitivity analysis (*Table 3*) showed that the final result was robust. Subgroup analysis (Figure S4) and meta regression also indicated that the pooled complication risk was not significantly different in different study populations (cholangiocarcinoma *vs.* MHBO: β=0.06, 95% CI: −0.11 to 0.24, P=0.425; cholangiocarcinoma *vs.* MMBO: β=0.03, 95% CI: −0.08 to 0.14, P=0.555) and different study types (β=−0.01, 95% CI: −0.11 to 0.10, P=0.886). Egger's test (β=0.339, P=0.472) and funnel plot (Figure S5) analysis indicated that no potential publication biases were present.

Stent occlusion risk

The postoperative biliary stent patency rate was reported on 10 articles. Among the total of 222 patients included in the control group, 157 developed stent occlusion, and among the 289 patients included in the ^{125}I group, 101 developed stent occlusion. The stent occlusion risk in ^{125}I group was 0.534 times (95% CI: 0.433 to 0.658, P<0.001; *Figure 4*) lower than the control group. Fixed effects models were used due to acceptable heterogeneity (P_Q=0.057, I^2=45.4%). The sensitivity analysis (*Table 4*) showed that the pooled stent occlusion risk was robust. Subgroup analysis (Figure S6) and meta regression manifested that the pooled stent occlusion risk was not significantly different in different study populations (cholangiocarcinoma *vs.* MHBO: β=0.05, 95% CI: −0.58 to 0.68, P=0.862;

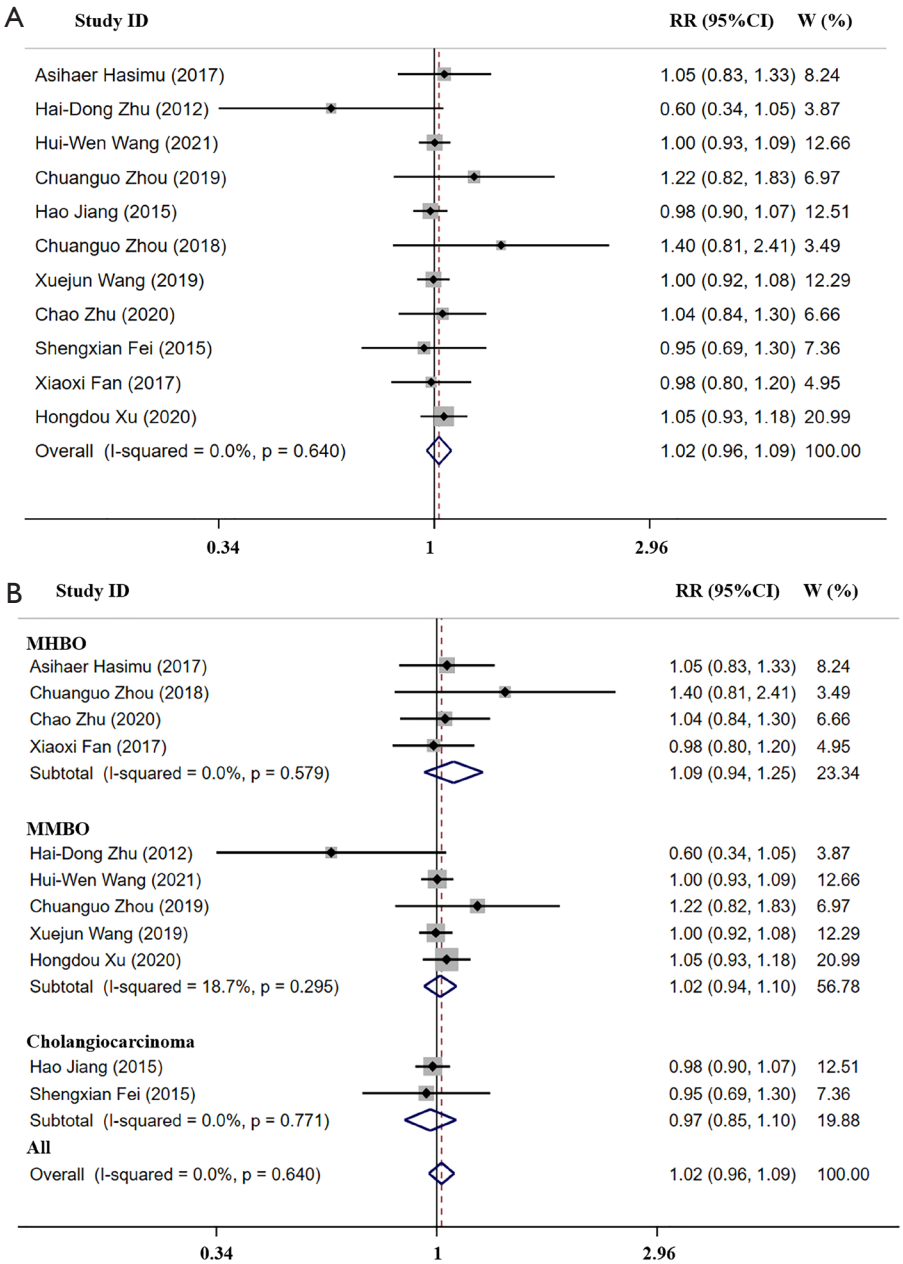

Figure 3 Comparison of complication risk between 125I groups and control groups. (A) Meta-analysis. (B) Subgroup analysis by population. RR, risk ratio; CI, confidence interval; W, weight; MBO, malignant biliary obstruction; MMBO, mixed MBO patients caused by various tumors; MHBO, patients with malignant hilar biliary obstruction.

cholangiocarcinoma *vs.* MMBO: β=0.23, 95% CI: −0.54 to 0.99, P=0.504) and different study types (β=0.11, 95% CI: −0.42 to 0.65, P=0.641). Egger's test (β=−0.656, P=0.195) and funnel plot (Figure S7) analysis indicated that no potential publication biases were present.

Information of mean stent patency time was provided in 6 articles, 2 of which also reported median stent patency time. The WMD of mean survival time between 2 groups was 3.394 months (95% CI: 2.639 to 4.148, P<0.001) and median survival time was 3.174 months (95% CI: 2.785 to 3.562, P<0.001), suggesting that ^{125}I seeds implantations increased the stent patency time of MBO patients compared

Table 3 The pooled complication risk of malignant biliary obstruction patients

Study	Control group		^{125}I group		RR (95% CI)	Sensitivity analysis
	Yes	No	Yes	No		
Asihaer Hasimu [2017] (20)	5	22	4	24	1.052 (0.832–1.331)	1.022 (0.958–1.090)
Hai-Dong Zhu [2012] (14)	5	6	1	11	0.595 (0.338–1.048)	1.041 (0.979–1.108)
Hui-Wen Wang [2021] (21)	0	35	0	32	1.002 (0.926–1.085)	1.027 (0.958–1.102)
Chuanguo Zhou [2019] (22)	14	22	20	20	1.222 (0.815–1.832)	1.009 (0.952–1.070)
Hao Jiang [2015] (23)	0	24	0	50	0.980 (0.900–1.068)	1.030 (0.961–1.105)
Chuanguo Zhou [2018] (24)	6	14	9	9	1.400 (0.813–2.412)	1.011 (0.951–1.074)
Xuejun Wang [2019] (25)	0	30	0	35	0.996 (0.917–1.081)	1.028 (0.959–1.102)
Chao Zhu [2020] (27)	2	18	3	19	1.042 (0.835–1.300)	1.023 (0.959–1.091)
Shengxian Fei [2015] (28)	7	19	6	20	0.950 (0.694–1.301)	1.030 (0.968–1.096)
Xiaoxi Fan [2017] (29)	0	11	0	14	0.985 (0.805–1.205)	1.026 (0.962–1.095)
Hongdou Xu [2020] (30)	7	85	6	44	1.050 (0.933–1.181)	1.017 (0.947–1.093)
Pooled RR	45	288	50	276	1.024 (0.963–1.090)	1.024 (0.963–1.090)

^{125}I, ^{125}iodine; RR, risk ratio; CI, confidence interval; MBO, malignant biliary obstruction.

with control groups (Figure S4). The random effects model and fixed effects model were performed for meta-analysis of the mean patency time (I^2=96.7%, P_Q<0.001) and median patency time (I^2=7.1%, P_Q=0.299), respectively. However, sensitivity analysis (Table S7) showed that the pooled result of mean patency time was robust. According to the results of Egger's test, no potential publication bias was present (β=1.949, P=0.824).

Biochemical response within 1 weeks

A total of 4 studies recorded ALT levels before and 1 week after surgery; 3 studies recorded AST levels; 7 studies recorded TBIL levels; and 5 studies recorded DBIL levels. All indicators were balanced and comparable before surgery (Figure S8A-S8D). Meta-analysis showed that the improvement of TBIL (WMD =−14.969, 95% CI: −28.670 to −1.267, P=0.032; P_Q=0.409, I^2=2.1%; Figure S9A) and AST (WMD =−14.653, 95% CI: −23.246 to −6.060, P=0.001; P_Q=0.900, I^2=0%; Figure S9D) levels in the ^{125}I group 1 week after operation was significantly better than that of the control group, but no differences were observed in DBIL (WMD =−7.064, 95% CI: −17.910 to 3.782. P=0.202; P_Q=0.834, I^2=0%; Figure S10A) and ALT (WMD =−7.974, 95% CI: −22.920 to 6.972, P=0.296; P_Q=0.086, I^2=54.5%; Figure S10C). Both the control group (Figure S11A-S11D and Table S7) and the ^{125}I group (Figure S12A-S12D and Table S8) showed improvement in all indicators 1 week after surgery. Sensitivity analysis showed that the final result of all indicators was robust and Egger's test indicated that no potential publication biases were present (all P>0.05).

Discussion

MBO greatly reduces the quality of life of patients, increases patient mortality, and also incurs a heavy social economic burden (31,32). At present, local chemoradiotherapy in combination with stent drainage, which has the advantages of effectiveness and minimal invasiveness, is the first choice for treatment of MBO patients with unresectable tumors (33,34). Previous studies have demonstrated that this therapy could prolong patient survival and reduces the risk of recurrent stent occlusion compared with conventional therapy. On the basis of previous studies, through meta-analysis, the current study further confirmed that ^{125}I stent implantation can reduce the MBO patients' death risk and extend the patency time on the condition without increasing the risk of complications.

Our findings further confirmed the results of 2 meta-analyses published in recent years. Abuduwaili *et al.* found that patients treated with irradiated stents had longer

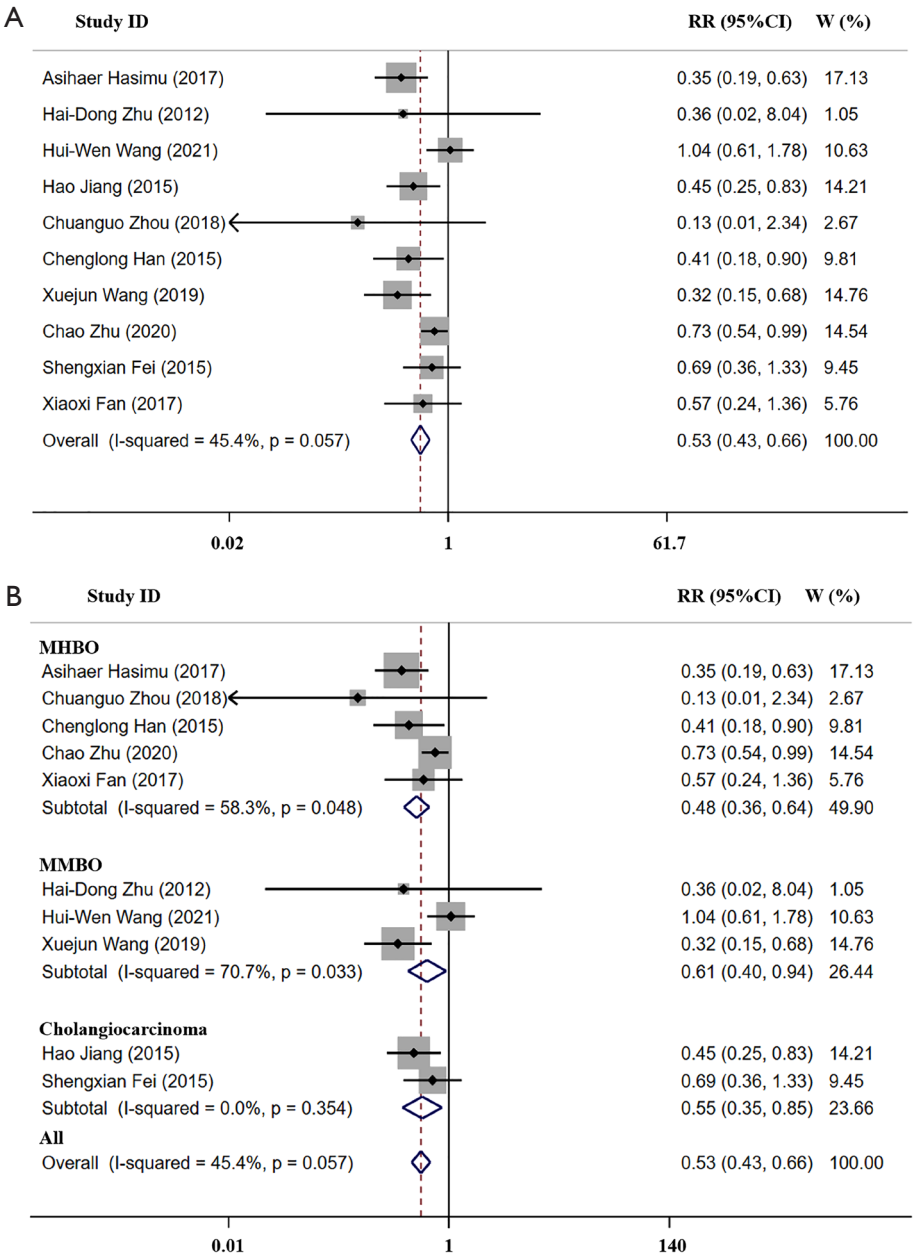

Figure 4 Comparison of stent occlusion risk between 125I groups and control groups. (A) Meta-analysis. (B) Subgroup analysis by population. RR, risk ratio; CI, confidence interval; W, weight; MBO, malignant biliary obstruction; MMBO, mixed MBO patients caused by various tumors; MHBO, patients with malignant hilar biliary obstruction.

survival [hazard ratio (HR) =0.46, IV, random, 95% CI: 0.34 to 0.63, P<0.001; I^2=0%) and stent patency rates (HR =0.45, IV, random, 95% CI: 0.25 to 0.80; P=0.007, I^2=59%) than those treated with conventional SEMS (16). Similarly, Xiang *et al.* discovered that stent combined with ^{125}I seeds showed longer mean survival (MD =125 days; 95% CI: 91 to 159 days; P<0.001) compared with stent placement alone (17). The X-rays emitted by ^{125}I (effective radiation radius of 17–20 mm, half-life of 60 days) can be kept within the tumor area to inhibit tumor growth into the mesh of the stent by directly killing the tumor cells, while ensuring that the surrounding normal tissues and adjacent organs are not

Table 4 The pooled stent occlusion risk of malignant biliary obstruction patients

Study	Control group		^{125}I group		RR (95% CI)	Sensitivity analysis
	SP	ST	SP	ST		
Asihaer Hasimu [2017] (20)	8	19	24	4	0.346 (0.190–0.630)	0.726 (0.568–0.927)
Hai-Dong Zhu [2012] (14)	0	11	1	11	0.361 (0.016–8.040)	0.647 (0.481–0.871)
Hui-Wen Wang [2021] (21)	16	19	14	18	1.045 (0.613–1.782)	0.594 (0.424–0.832)
Hao Jiang [2015] (23)	8	16	22	8	0.455 (0.248–0.833)	0.679 (0.505–0.913)
Chenglong Han [2015] (25)	5	13	15	7	0.407 (0.183–0.905)	0.677 (0.506–0.905)
Xuejun Wang [2019] (26)	24	6	30	5	0.933 (0.746–1.168)	0.598 (0.449–0.797)
Chao Zhu [2020] (27)	14	6	21	1	0.733 (0.543–0.991)	0.613 (0.421–0.894)
Shengxian Fei [2015] (28)	9	17	13	13	0.692 (0.360–1.331)	0.634 (0.457–0.879)
Xiaoxi Fan [2017] (29)	4	7	9	5	0.566 (0.236–1.355)	0.650 (0.476–0.887)
Pooled RR	88	114	149	72	0.645 (0.483–0.863)	0.645 (0.483–0.863)

^{125}I, ^{125}iodine; RR, risk ratio; CI, Confidence interval; ST, stent occlusion; SP, stent patency.

damaged, thereby improving the patient's liver function and working status (35-37). Cancer cells undergo a cumulative superposition of damage effects under continuous irradiation, which prolongs the cell cycle and increases the total radiation dose in the G2-M phase, thereby helping to improve the radiation sensitivity (38,39). Therefore, X-ray irradiated tumor cells can remain in the radiation-sensitive period, G2 and M phases, to ensure that the tumor cells can be killed to the greatest extent, thereby improving the survival time and stent patency of MBO patients.

In order to fill in the gaps identified in previous studies, subgroup analysis and meta-regression were further conducted in our study to explore the difference in the efficacy and safety of seed implantation for MBO patients caused by cholangiocarcinoma, hilar tumors, and various other tumors. The results indicated that the efficacy of seed implantation in patients with MBO caused by hilar tumors was not different from that in patients with MBO caused by various tumors, suggesting that ^{125}I seed implantation was suitable for all patients with tumor-induced MBO, and no difference was observed in its efficacy. The meta-regression found that the results observed in RCTs were no different to those observed in prospective studies. The study design of RCT controls the influence of confounding bias on the observation results through random grouping. The current study strictly included prospective studies that reported balanced and comparable baseline information to avoid the interference of confounding factors, which may be one of the reasons why it was not a source of heterogeneity in this study.

As we all know, particle radiation can interact with body cells, tissues, and body fluids, ionize atoms or molecules of the tissue, and directly destroy certain macromolecular structures of the body, such as protein molecules, ribonucleic acid molecular chains, and enzymes (40). Therefore, seed implantation therapy is often thought to be associated with a high complication rate. However, the current meta-analysis showed that ^{125}I seed implantation cannot increase the patients' complications risk, which was consistent with the previous 2 studies, illustrating the safety of seed implantation. The complications involved in the candidate articles included severe pain, pancreatitis, biliary tract perforation, stent migration, hemobilia, and asymptomatic amylase increase, among others. A meta-analysis for each complication was not performed, because of the lower complication rate. Regarding laboratory indicators, our meta-analysis found that serum ALT, AST, DBIL, and TBIL levels were decreased 1 week after surgery, and ^{125}I stent implantation was more conducive to the improvement of AST and TBIL levels in 1 week after surgery, but the effect on ALT and DBIL levels was not significant. The observation was slightly different from the results of Abuduwaili *et al.*, whose findings suggested that the seed implantation was not responsible for the decreased AST levels, compared to the control group (16). The difference may have been caused by the sample size. Abuduwaili *et al.* included only 2 studies with 54 cases, whereas our study included 3 studies with 108 cases.

In addition to further confirming the conclusions of previous studies, the current study found for the first time through subgroup analysis that the efficacy of seed implantation in patients with MBO caused by cholangiocarcinoma was no different from that of those with MBO caused by hilar tumors or various types of tumors. The included studies were all high-quality articles with a quality score of 7–9, which further guarantees the reliability of the research. In addition to advantages, this study has several limitations. First, according to the inclusion criteria, only 12 studies were included in the analysis, and the sample size (including 676 MBO patients) may be insufficient, which may hinder the applicability of this analysis. However, no significant publication bias was detected among the 12 studies. Second, the participants may not be sufficiently representative of the broader population. Since seed implantation therapy was only recently introduced in China, all the included articles were single-center studies conducted within China. Therefore, the efficacy and safety of seed implantation need to be further verified in other populations and other regions. Conversely, only a single-center study conducted within China would ensure that our research results were not affected by race and region. Third, high heterogeneity was observed in the survival and patency times reported by 12 studies, which may have been caused by the difference in follow-up time. Fortunately, the sensitivity analysis supported the robustness of the final results, indicating that our results were not affected by the heterogeneity. Fourth, since few patients with MBO caused by a single tumor were recruited in primary studies, the current study cannot further conduct a meta-analysis to explore the efficacy of ^{125}I therapy on patients with MBO caused by various tumors.

Conclusions

In conclusion, ^{125}I seed implantation treatment is a significantly superior MBO treatment method than stent placement alone, which can effectively prolong the survival of patients and reduce the death risk and stent occlusion risk. Further, it is a safe and tolerable method with comparable complication risk to stent placement alone. It may be a useful and promising therapy for MBO patients, and its efficacy and safety for MBO caused by hilar tumors are no different from those caused by various tumors. In future studies, ^{125}I seed implantation therapy should be verified in different populations and regions.

Acknowledgments

Funding: This work was supported by the National Natural Science Foundation of China (No. 81971716).

Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-22-824/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-824/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Gao F, Huang X, Wang Y. The efficacy and safety of ^{125}I seeds combined with biliary stent placement versus stent placement alone for malignant biliary obstruction: a systematic review and meta-analysis. Quant Imaging Med Surg 2023;13(7):4589-4602. doi: 10.21037/qims-22-824

Supplementary

Table S1 Details of article research

	Number of articles
PubMed	1485
Wiley Online Library	0
Cochrane library	0
Google Scholar	257
Web of Science	815
CNKI	0
VIP	53
Wanfang	1449

Table S2 The information of included studies

Study	Hospital	Baseline information	Producers of ^{125}I	half-life (days)	Mean ^{125}I seeds
Asihaer Hasimu (2017)	The First Affiliated Hospital o fXinJiang Medical University	Balanced	Beijing Atom Hi-Tech Co., Ltd. (Beijing, China)	59.43	energy of 27.4keV for x-rays,31.4keV for χ-rays, and 35.5keV for γ-rays, with a 20-mm effectiverange;15.46 ± 2.30 (range,9–18)
Hai-Dong Zhu (2012)	Zhong-Da Hospital, Medical School, Southeast University	Balanced	Nanjing MicroInvasive Medical Inc. (Nanjing, China)	59.6	energy of 27.4 keV for X rays and 35.5 keV for R rays;7.13 mCi (263.93 MBq), ranging from 6 to 8 mCi (222–296 MBq)
Hui-Wen Wang (2021)	Harbin Medical University Cancer Hospital	Balanced	Nanjing Minitron Co. Ltd. (Nanjing, China)	59.43	energy of 27.4 keV for X rays and 35.5 keV for R rays;33.3MBq
Chuanguo Zhou (2019)	Affiliated Hospital of Capital Medical University	Balanced	Zhibo Gaoke Biotechnology (Beijing, China).	60.1	energy of 27.4-31.4 keV for X rays and 35.5 keV for R rays; 11.1–37 MBq (0.3mCi-1.0mCi); 20mm;15.2 ± 4.1 [range, 8–25] seeds per patient
Hao Jiang (2015)	Affiliated Hospital of Nantong University	Balanced	Shanghai Kexin Co. Ltd. (Shanghai, China).	59.6	The reflection activity of a single particle, 0.60–0.80 mCi
Chuanguo Zhou (2018)	Beijing Chaoyang Hospital, Capital Medical University	Balanced	Zhibo Gaoke Biotechnology (Beijing, China).	60.1	The reflection activity of a single particle, 0.5–0.6 mCi; 16.0±4.5(10~24); energy of 27.4-31.4 keV for X rays and 35.5 keV for R rays; 11.1–37 MBq (0.3mCi-1.0mCi); 20mm
Chenglong Han (2015)	Affiliated Tumor Hospital of Guangxi Medical University	Balanced	Shanghai Kexin Co. Ltd. (Shanghai, China).	59.6	11 (8–15)
Xuejun Wang (2019)	Yancheng Third People's Hospital	Balanced	Ningbo Junan Technology Co., Ltd. (Ningbo, China)	59.6	energy of 27.4-31.4 keV for X rays and 35.5 keV for R rays ;10.4MBq~37 MBq (0.28~1.0) mCi
Chao Zhu (2020)	The First Affiliated Hospital of Bengbu Medical College	Balanced	Beijing Atom Hi-Tech Co.,Ltd. (Beijing, China)	59.43	energy of 27.4-31.4 keV for X rays and 35.5 keV for R rays ;11.1–37 MBq (0.3mCi-1.0mCi)
Shengxian Fei (2015)	The First Affiliated Hospital of Bengbu Medical College	Balanced	NA	59.6	energy of 27.4-31.4 keV for X rays and 35.5 keV for R rays ;11.1–37 MBq (0.3mCi-1.0mCi)
Xiaoxi Fan (2017)	The First Affiliated Hospital of Wenzhou Medical University	Balanced	Tianjin Saide Biotechnology Co., Ltd. (Tianjin, China)	60.1	The reflection activity of a single particle, 0.7–0.9 mCi; energy of 27.4-31.4 keV for X rays and 35.5 keV for R rays
Hongdou Xu (2020)	The First Affiliated Hospital of Nanjing Medical University	Balanced	Beijing Atom Hi-Tech Co.,Ltd. (Beijing, China)	59.43	energy of 27.4 keV for X rays and 35.5 keV forR rays; The reflection activity of a single particle, 0.8mCi

Balanced, the baseline data of the 2 groups are balanced and comparable.

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Table S3 Article quality assessment by NOS scale

Study	Representativeness of the exposed cohort (1)	Selection of the non-exposed cohort (1)	Ascertainment of exposure (1)	Demonstration that outcome of interest was not present at start of study (1)	Compare ability of cohorts on the basis of the design or analysis (2)	Assessment of outcome (1)	Was follow up long enough for outcomes to occur (1)	Adequacy of follow up of cohorts (1)	Total
Asihaer Hasimu (2017)	1	1	1	1	2	1	1	1	9
Hai-Dong Zhu (2012)	1	1	1	1	2	1	1	1	9
Hui-Wen Wang (2021)	1	1	1	1	2	1	1	1	9
Chuanguo Zhou (2019)	1	1	1	1	1	1	1	1	8
Hao Jiang (2015)	1	1	1	0	1	1	1	1	7
Chuanguo Zhou (2018)	1	1	1	1	1	1	1	1	8
Chenglong Han (2015)	1	1	1	1	1	1	1	1	8
Xuejun Wang (2019)	1	1	1	1	1	1	1	1	8
Chao Zhu (2020)	1	1	1	1	1	1	1	1	8
Shengxian Fei (2015)	1	1	1	0	1	1	1	1	7
Xiaoxi Fan (2017)	1	1	1	1	1	1	1	1	8
Hongdou Xu (2020)	1	1	1	1	1	1	1	0	7

NOS, Newcastle-Ottawa Scale.

Table S4 Article quality assessment by Cochrane risk of bias tool

Risk evaluation standard	
Domain1	Risk of bias arising from the randomization process
Domain2	Risk of bias due to deviations from the intended interventions
Domain3	Risk of bias due to missing outcome data
Domain4	Risk of bias in measurement of the outcome
Domain5	Risk of bias in selection of the reported result
Risk classification	
Low risk of bias	The study is judged to be at low risk of bias for all domains for this result.
Some concerns	The study is judged to raise some concerns in at least one domain for this result, but not to be at high risk of bias for any domain.
High risk of bias	The study is judged to be at high risk of bias in at least one domain for this result. Or the study is judged to have some concerns for multiple domains in a way that substantially lowers confidence in the result.

	Overall risk of bias				
Study	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5
Asihaer Hasimu (2017)	Low	Low	Low	Low	Some concerns
Hai-Dong Zhu (2012)	Low	Low	Low	Low	Some concerns
Hui-Wen Wang (2021)	Some concerns	Low	Some concerns	Low	Some concerns

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Table S5 Population composition of included studies

Study	Population[a]	Definition in the text	Cholangio-carcinoma	Gallbladder cancer	Liver cancer	Pancreatic cancer	Duodenal cancer	Metastatic cancer	Gastrointestinal cancer	Other cancer
20Asihaer Hasimu (2017)	1	Malignant biliary obstruction	49	6	--	--	--	--	--	--
21Hai-Dong Zhu (2012)	2	Malignant biliary obstruction	--	--	--	13	--	10	--	--
22 Hui-Wen Wang (2021)	2	Malignant biliary obstruction	--	19	--	35	--	13	--	--
23 Chuanguo Zhou (2019)	2	Malignant biliary obstruction	41	5	--	18	3	9	--	--
24Hao Jiang (2015)	0	Malignant biliary obstruction caused by Cholangiocarcinoma	54	--	--	--	--	--	--	--
25 Chuanguo Zhou (2018)	1	Malignant hilar biliary obstruction	11	3	--	14	4	6	--	--
26 Chenglong Han (2015)	1	Malignant biliary obstruction	15	--	11	--	--	14	--	--
27 Xuejun Wang (2019)	2	Malignant biliary obstruction	24	9	19	13	--	--	--	--
28 Chao Zhu (2020)	1	Malignant hilar biliary obstruction	34	5	--	--	--	--	--	3
29 Shengxian Fei (2015)	0	Malignant obstructive jaundice caused by cholangiocarcinoma	52	--	--	--	--	--	--	--
30 Xiaoxi Fan (2017)	1	Malignant hilar biliary obstruction	7	1	1	--	--	2	--	--
31 Hongdou Xu (2020)	2	Malignant biliary obstruction	52	16	17	22	1	--	19	15

[a] "0" represents malignant biliary obstruction patients caused by Cholangiocarcinoma, “1” represents malignant biliary obstruction patients caused by hilar malignant tumor; “2” represents malignant biliary obstruction patients caused by mixed tumors.

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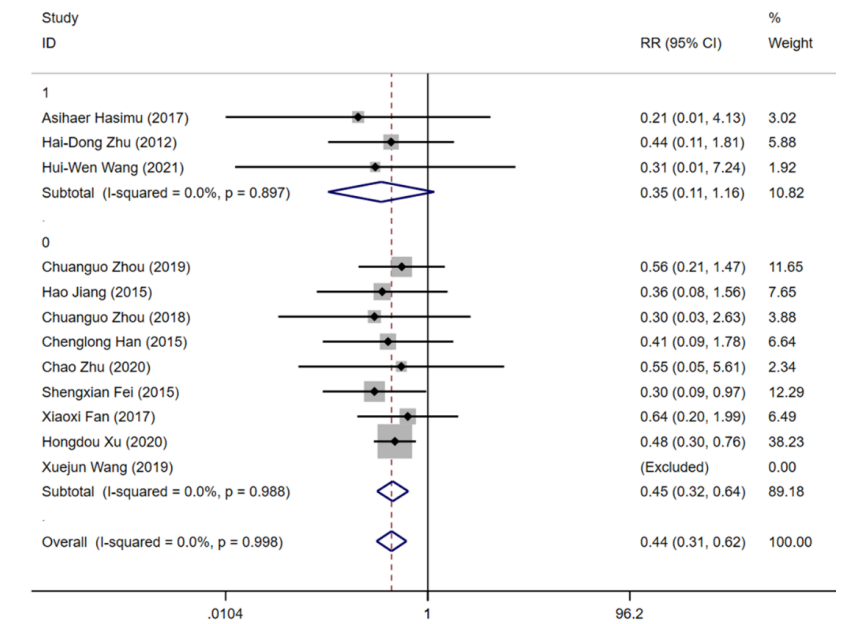

Figure S1 Subgroup analysis of death risk by study design. RCT, randomized controlled trial; RR, risk ratio; CI, confidence interval.

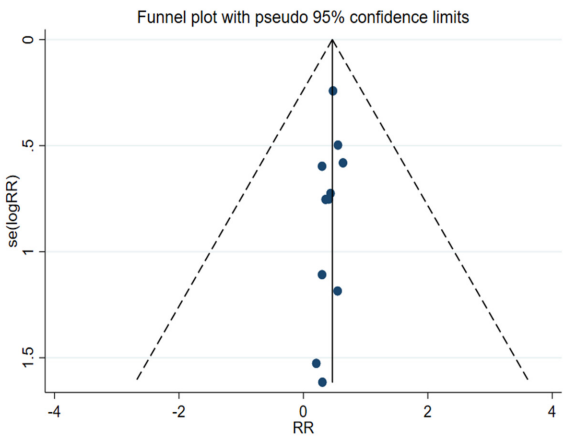

Figure S2 Funnel plot of death risk. RR, relative risk.

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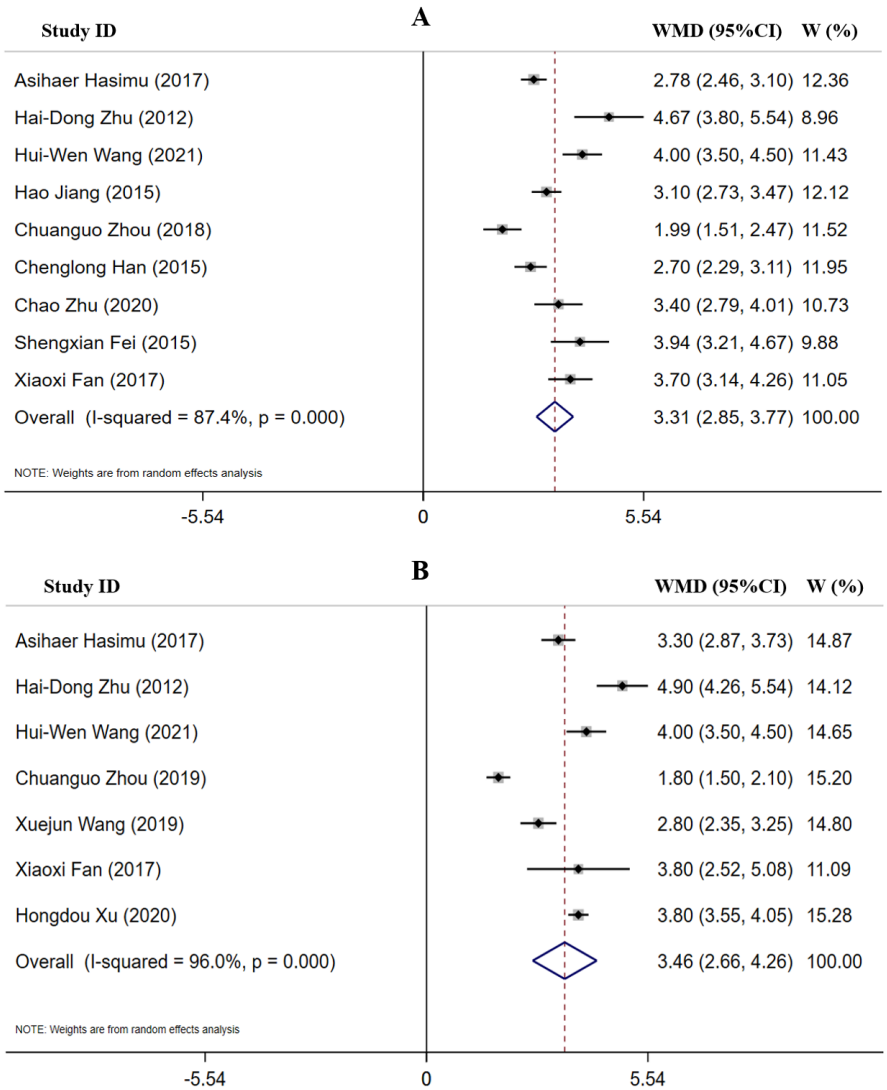

Figure S3 Comparison of survival between 125I groups and control groups. (A) Comparison of mean survival; (B) Comparison of median survival. WMD, weighted mean difference; CI, confidence interval; W, weight.

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Table S6 The pooled results of MBO patients' survival

Study	Control group		I^{125} group		WMD (95%CI)	Sensitivity analysis	Control group		I^{125} group		WMD (95%CI)	Sensitivity analysis
	Mean	SD	Mean	SD			M	SD	M	SD		
Asihaer Hasimu (2017)	4.64	0.49	7.42	0.72	2.780 (2.456, 3.104)	3.392 (2.854, 3.931)	4.73	0.82	8.03	0.79	3.300 (2.874, 3.726)	3.491 (2.538, 4.444)
Hai-Dong Zhu (2012)	3.36	1.13	8.03	0.99	4.670 (3.798, 5.542)	3.172 (2.728, 3.616)	2.50	0.90	7.40	0.63	4.900 (4.260, 5.540)	3.218 (2.405, 4.032)
Hui-Wen Wang (2021)	7.00	0.30	11.00	1.40	4.000 (3.505, 4.495)	3.214 (2.751, 3.676)	7.00	0.30	11.00	1.40	4.000 (3.505, 4.495)	3.368 (2.471, 4.264)
Chuanguo Zhou (2019)	--	--	--	--	--	--	4.10	0.70	5.90	0.61	1.800 (1.503, 2.097)	3.736 (3.222, 4.25)
Hao Jiang (2015)	8.60	0.60	11.70	0.80	3.100 (2.726, 3.474)	3.349 (2.803, 3.895)	--	--	--	--	--	--
Chuanguo Zhou (2018)	4.74	0.51	6.73	0.92	1.990 (1.510, 2.470)	3.465 (3.042, 3.888)	--	--	--	--	--	--
Chenglong Han (2015)	8.70	0.50	11.40	0.80	2.700 (2.294, 3.106)	3.398 (2.878, 3.918)	--	--	--	--	--	--
Xuejun Wang (2019)	--	--	--	--	--	--	5.53	0.49	8.33	1.25	2.800 (2.350, 3.250)	3.576 (2.642, 4.511)
Chao Zhu (2020)	7.80	1.00	11.20	1.00	3.400 (2.794, 4.006)	3.303 (2.796, 3.810)	--	--	--	--	--	--
Shengxian Fei (2015)	8.89	1.08	12.83	1.57	3.940 (3.208, 4.672)	3.240 (2.758, 3.722)	--	--	--	--	--	--
Xiaoxi Fan (2017)	12.70	0.50	16.40	0.90	3.700 (3.144, 4.256)	3.263 (2.767, 3.759)	7.40	1.96	11.20	10.60	3.800 (-1.872, 9.472)	3.416 (2.558, 4.275)
Hongdou Xu (2020)	--	--	--	--	--	--	6.90	0.37	10.70	0.87	3.800 (3.547, 4.053)	3.403 (2.45, 4.355)
Pooled-SMD	--	--	--	--	3.310 (2.848, 3.771)	3.310 (2.848, 3.771)	--	--	--	--	3.458 (2.658, 4.259)	3.458 (2.658, 4.259)

WMD, weighted mean difference; CI, confidence interval; SD, standard deviation; M, median.

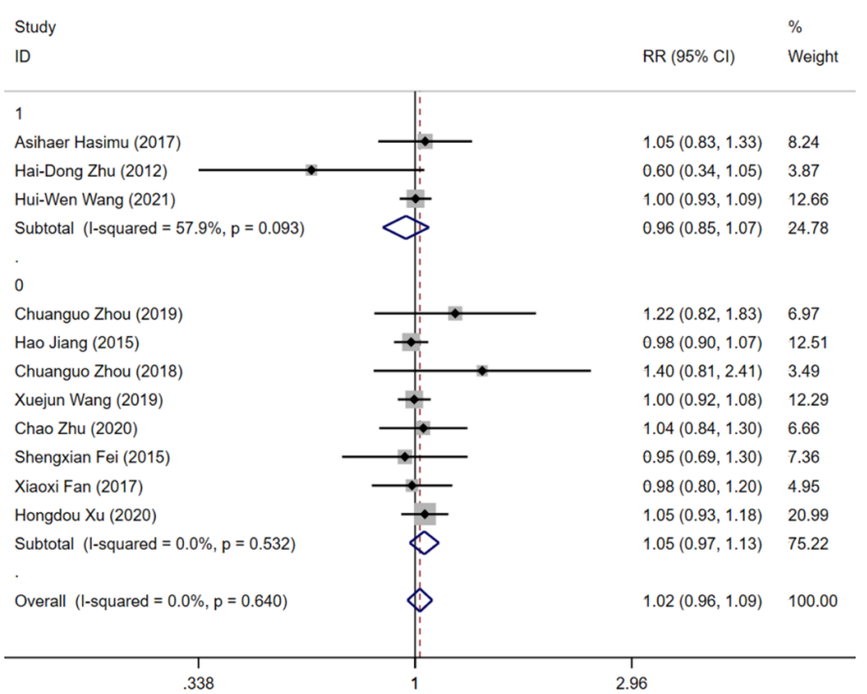

Figure S4 Subgroup analysis of complication risk by study design. RCT, randomized controlled trial; RR, risk ratio; CI, confidence interval.

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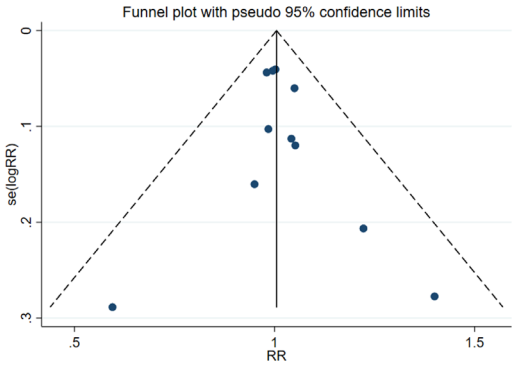

Figure S5 Funnel plot of complication risk. RR, relative risk.

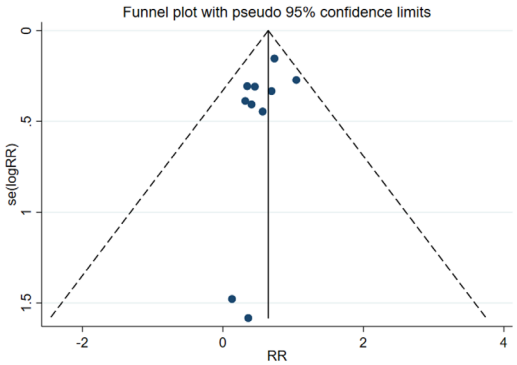

Figure S7 Funnel plot of stent occlusion risk. RR, risk ratio.

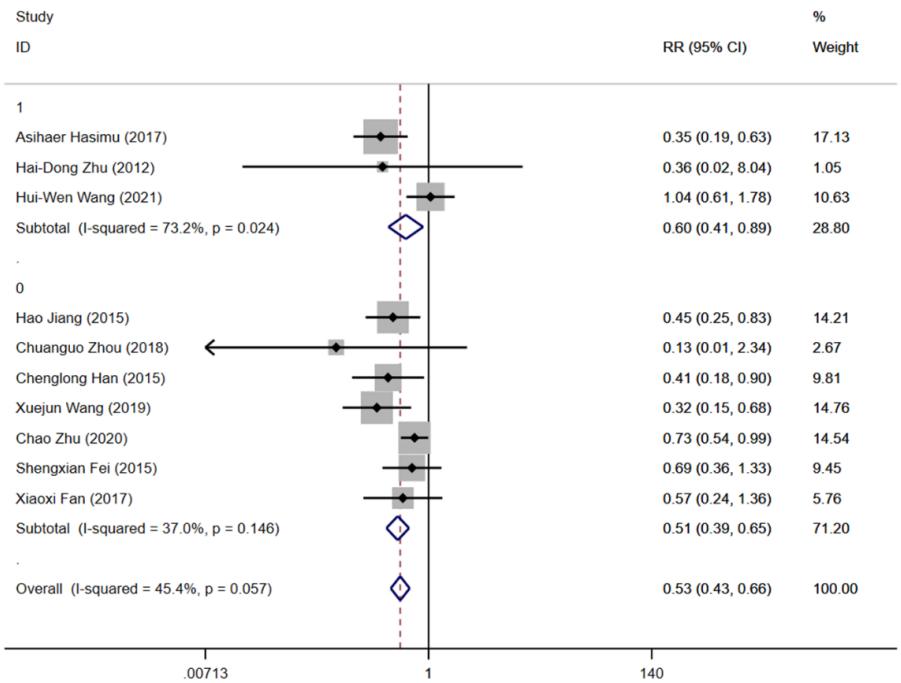

Figure S6 Subgroup analysis of stent occlusion risk by study design. RCT, randomized controlled trial; RR, risk ratio; CI, confidence interval.

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Table S7 The pooled results of MBO patients' stent patency time

Study	Control group		I^{125} group		WMD (95%CI)	Sensitivity analysis	Control group		I^{125} group		WMD (95%CI)
	Mean	SD	Mean	SD			Median	SD	Median	SD	
Asihaer Hasimu (2017)	2.94	0.45	6.36	0.66	3.420 (3.122, 3.718)	3.395 (2.440, 4.350)	2.57	0.18	5.97	1.53	3.400 (2.829, 3.971)
Hui-Wen Wang (2021)	5.80	0.20	9.50	0.60	3.700 (3.482, 3.918)	3.337 (2.383, 4.291)	6.00	0.30	9.00	1.40	3.000 (2.505, 3.495)
Hao Jiang (2015)	6.20	0.40	8.70	0.70	2.500 (2.203, 2.797)	3.578 (2.721, 4.436)	--	--	--	--	--
Chuanguo Zhou (2018)	4.05	0.51	6.43	0.95	2.380 (1.887, 2.873)	3.591 (2.756, 4.426)	--	--	--	--	--
Chenglong Han (2015)	6.20	0.40	8.70	0.70	2.500 (2.154, 2.846)	3.576 (2.719, 4.434)	--	--	--	--	--
Xiaoxi Fan (2017)	6.70	0.80	12.70	0.70	6.000 (5.402, 6.598)	2.915 (2.340, 3.490)	--	--	--	--	--
Pooled RR					3.394 (2.639, 4.148)	3.394 (2.639, 4.148)					3.174 (2.785, 3.562)

WMD, weighted mean difference; CI, confidence interval; SD, standard deviation; M, median.

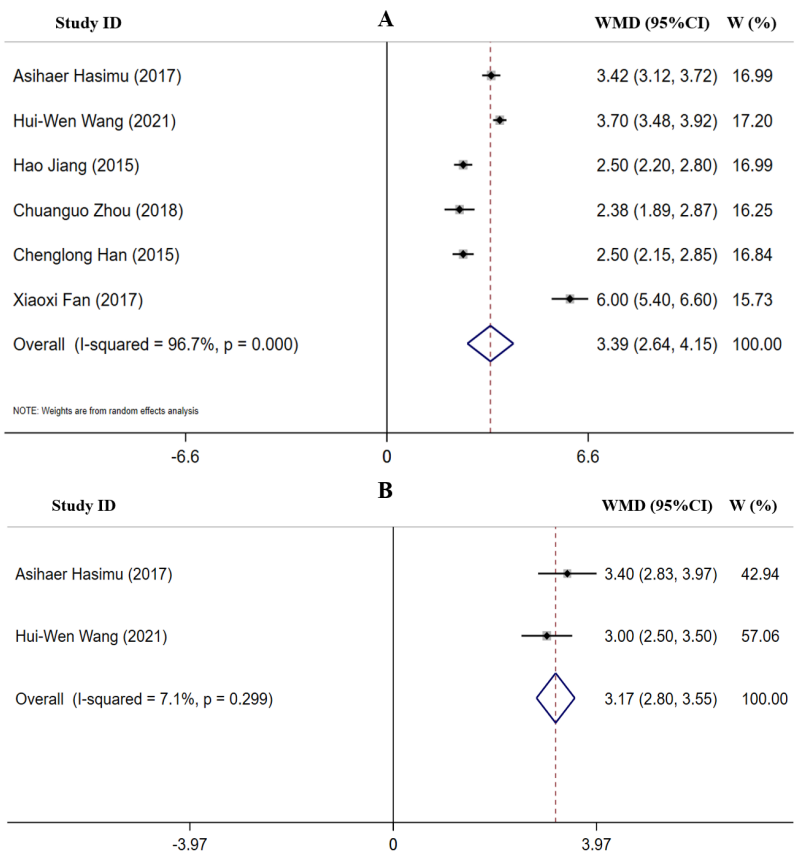

Figure S8 Comparison of stent patency time between 125I groups and control groups. (A) Comparison of mean stent patency time; (B) Comparison of median stent patency time. WMD, weighted mean difference; CI, confidence interval; W, weight.

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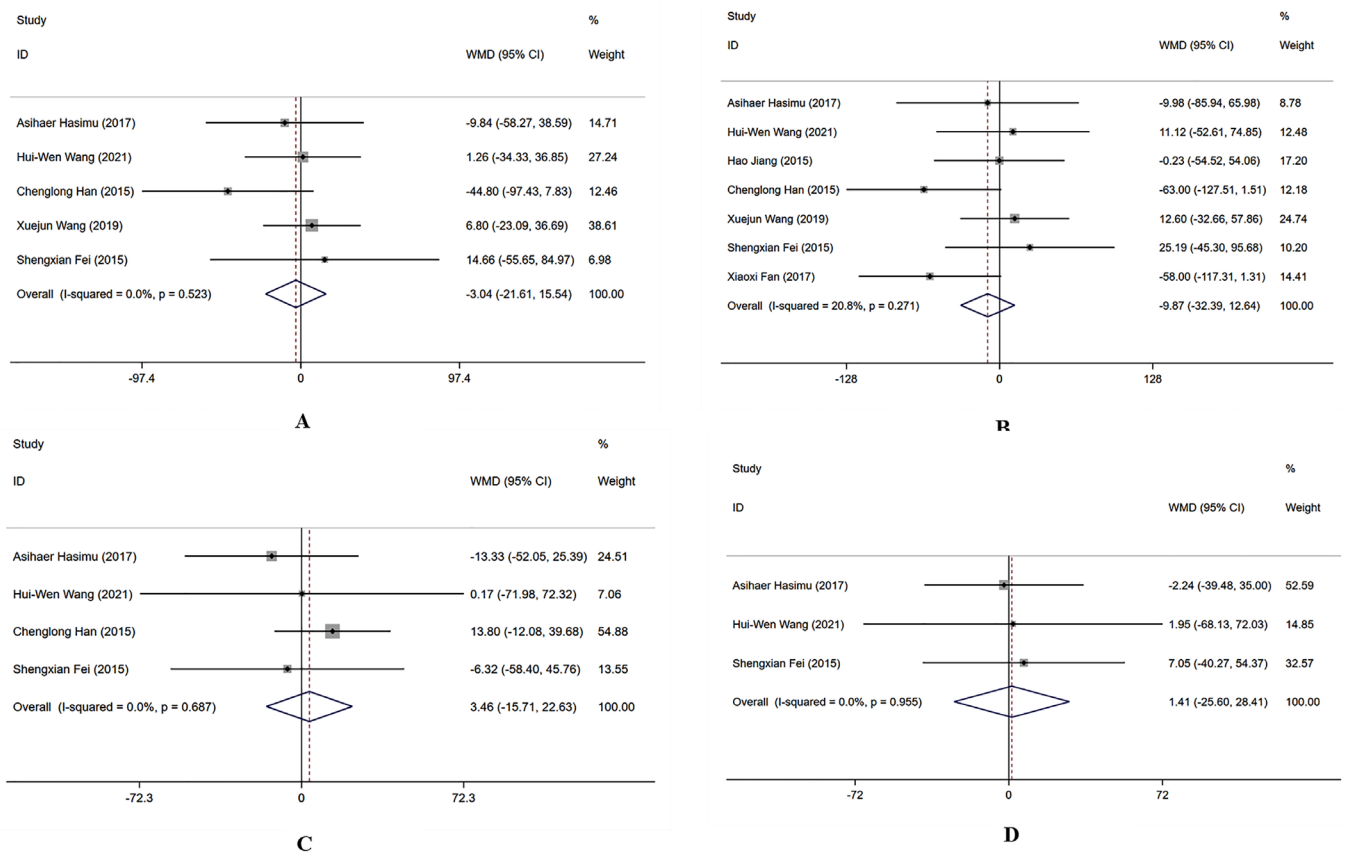

Figure S9 Baseline liver function index levels of 125I groups and control groups. (A) Serum TBIL levels; (B) Serum DBIL levels; (C) Serum ALT levels; (D) Serum AST levels. TBIL, total bilirubin; ALT, alanine transaminase; AST, aspartate transaminase; WMD, weighted mean difference; CI, confidence interval.

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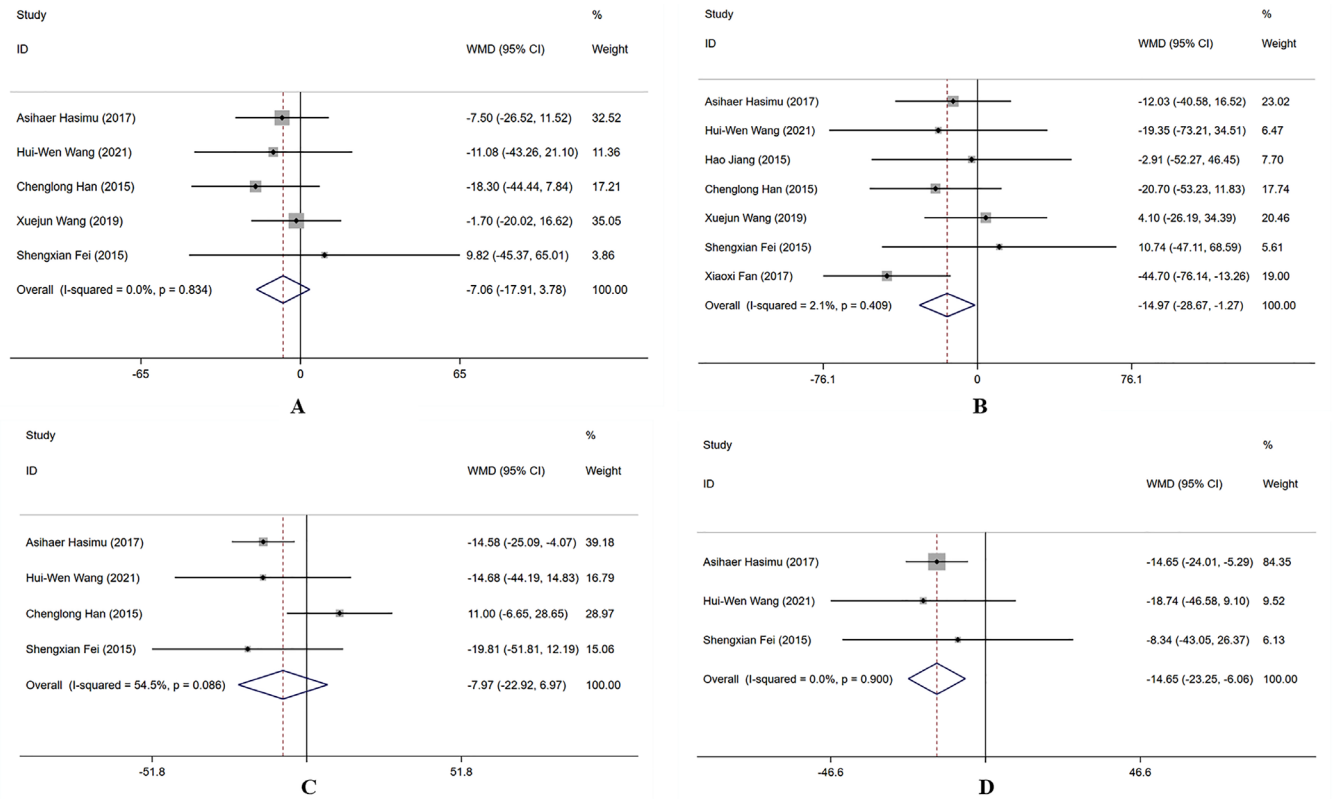

Figure S10 Liver function index levels of 125I group and control group one week after surgery. (A) Serum TBIL levels; (B) Serum DBIL levels; (C) Serum ALT levels; (D) Serum AST levels. TBIL, total bilirubin; DBIL, direct bilirubin; ALT, alanine transaminase; AST, aspartate transaminase; WMD, weighted mean difference; CI, confidence interval.

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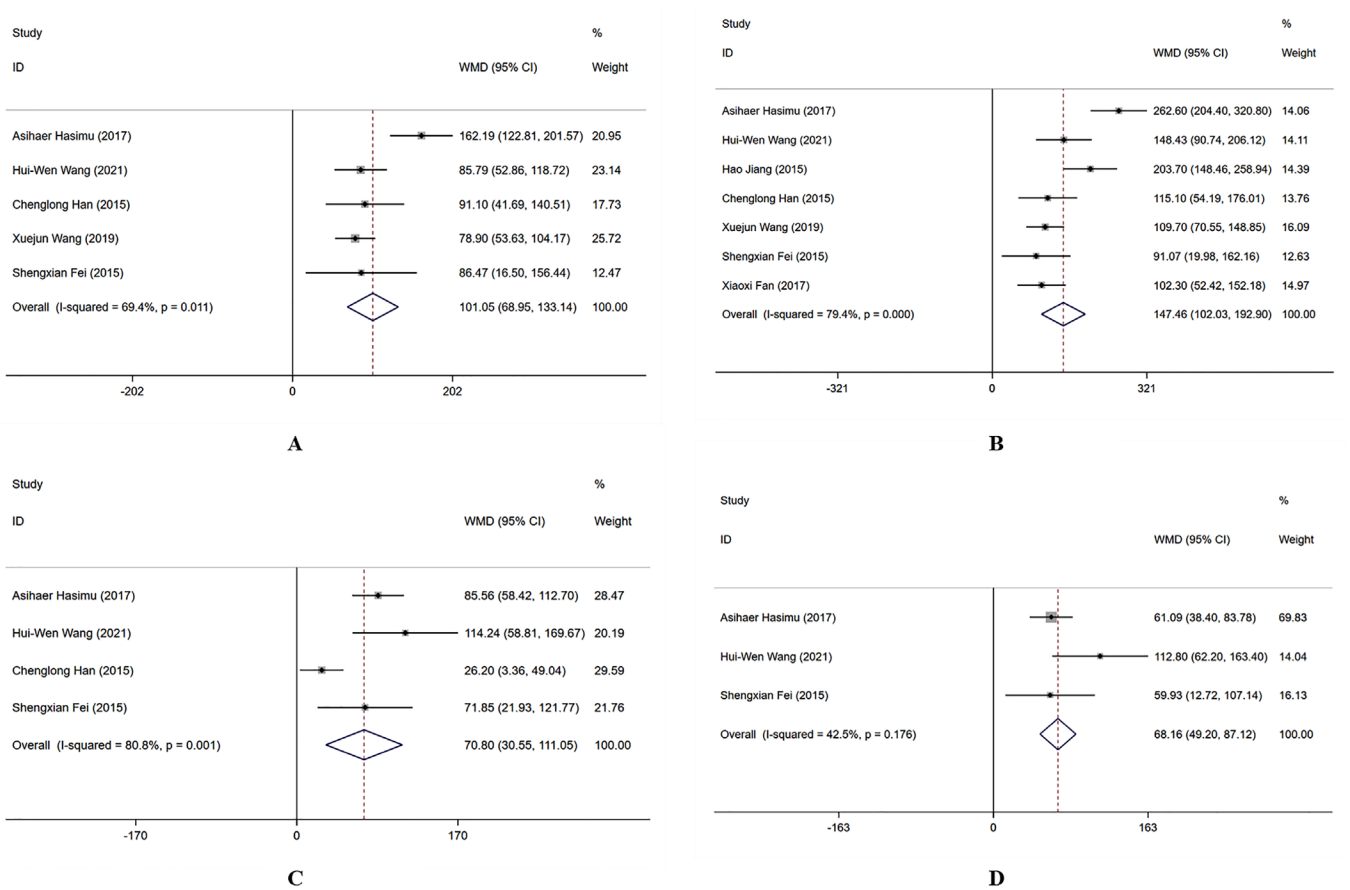

Figure S11 The changes of liver function index in control group before and after treatment. (A) Serum TBIL levels; (B) Serum DBIL levels; (C) Serum ALT levels; (D) Serum AST levels. TBIL, total bilirubin; DBIL, direct bilirubin; WMD, weighted mean difference; CI, confidence interval.

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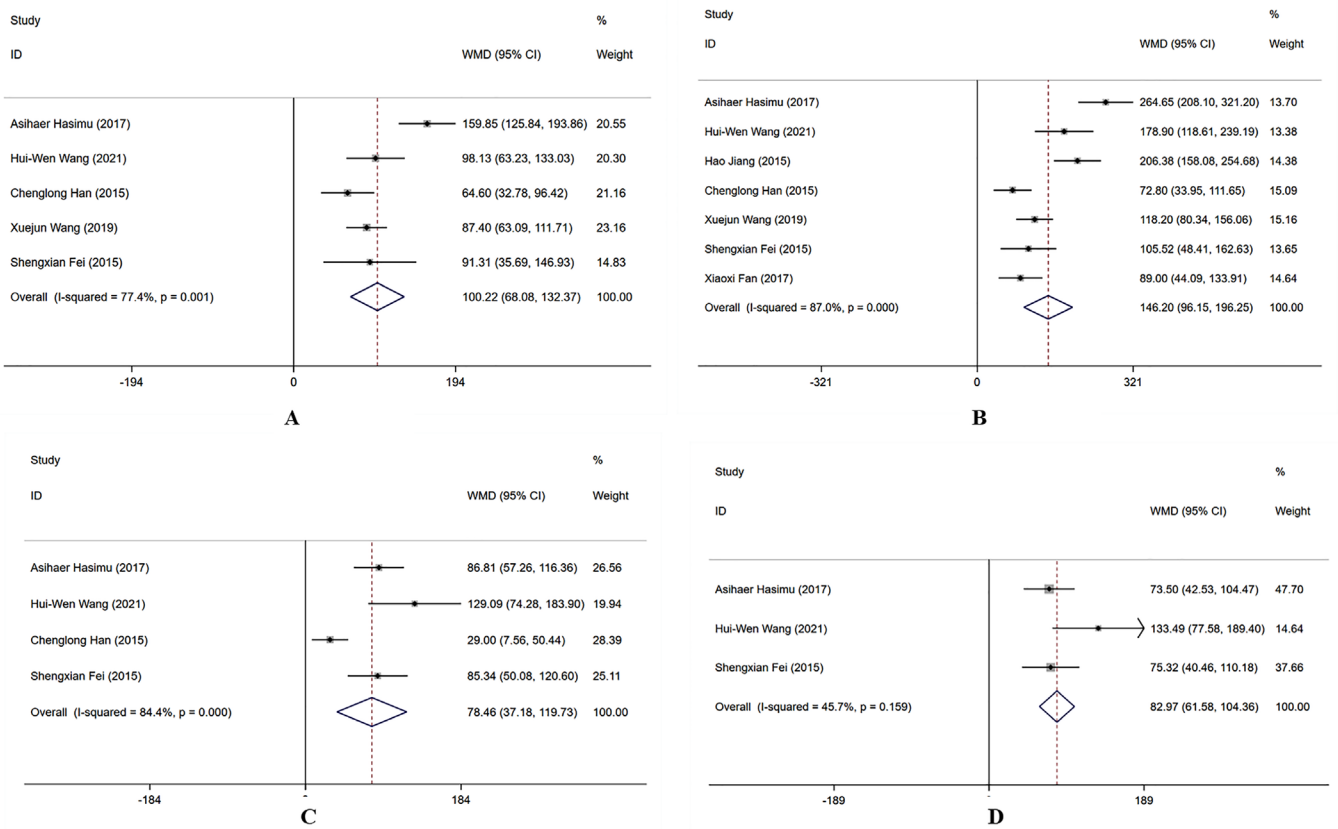

Figure S12 The changes of liver function index in 125I group before and after treatment. (A) Serum TBIL levels; (B) Serum DBIL levels; (C) Serum ALT levels; (D) Serum AST levels. TBIL, total bilirubin; DBIL, direct bilirubin; WMD, weighted mean difference; CI, confidence interval.

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Table S8 Heterogeneity test and Meta-regression of Biochemical Indicators

Biochemical Indicators		Heterogeneity test			Egger test	
		Heterogeneity χ^2	P-value	I^2	β	P-value
DBIL	Baseline	3.21	0.523	0.0%	-1.130	0.504
	1W	1.46	0.834	0.0%	0.076	0.941
	CG	13.09	0.011	69.4%	1.456	0.643
	IG	17.72	0.001	77.4%	1.355	0.780
TBIL	Baseline	7.57	0.271	20.8%	-1.406	0.632
	1W	6.13	0.409	2.1%	0.934	0.581
	CG	29.08	<0.001	79.4%	2.966	0.571
	IG	46.27	<0.001	87.0%	9.124	0.140
ALT	Baseline	1.48	0.687	0.0%	-1.040	0.393
	1W	6.59	0.086	54.5%	0.331	0.890
	CG	19.25	<0.001	84.4%	6.506	0.089
	IG	15.66	0.001	80.8%	3.710	0.351
AST	Baseline	0.09	0.955	0.0%	0.328	0.702
	1W	0.21	0.900	0.0%	0.084	0.893
	CG	3.48	0.176	42.5%	1.933	0.544
	IG	3.68	0.159	45.7%	4.812	0.111

Baseline, before surgery; 1W, 1 week after surgery; CG, control group; IG, ^{125}I group; TBIL, total bilirubin; DBIL, direct bilirubin; AST, aspartate transaminase; ALT, alanine transaminase.

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